MEDICINE - GASTRO

NEET SS

GASTROESOPHAGEAL REFLUX DISEASE

Introduction 00:00:25

Seen in 10 % of general population.
GERD → Barrett's esophagus → Adenocarcinoma.

Types :

1. Erosive ERD : 30 %, refractory to PPI (20 to 30 %).
2. Non erosive ERD (NERD) : 70 %, refractory to PPI (40 %).

Based on the nature of reflux :

- Acidic, weakly acidic, weakly alkaline, gaseous, bile reflux and rereflux.

Pathophysiology :

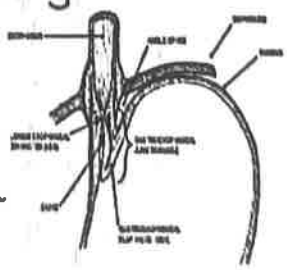
A. Protective factors.
B. Aggressive factors.

Protective factors :

A. Antireflux barrier :

Components :

- Intrinsic LES : 3 to 4 cm (2 cm above and 2 cm below) and resting pressure is 10 to 30 mmHg.
- Diaphragmatic crura.
- Intra abdominal location of LES.
- Phrenico esophageal ligament.
- A/c angle of His : Between cardia and lower end of esophagus.



mechanism of GERD :

1. ↑ LESR : Diaphragm inhibition (distention of proximal stomach) mediated by stretch receptor of vagal pathway (responsible for 50 to 80 % reflux in GERD).
2. Swallowing ↑- LESR : 5 to 10 % of reflux.

Active space

3. Hypotensive LES : < 10 mmHg (strain causes reflux) and < 5 mmHg (free reflux) ↑ associated with esophagitis.
4. HH : Esophageal shortening d/t esophagitis ↑ decrease in intra abdominal esophagus and in this case there will be increased t-LESR ↑ hypotensive LES : 6 to 8 weeks of PPI will improve symptoms.
5. Acid pocket : Large cardiac acid pocket.

B. Oesophageal acid clearance :
   1. Primary > secondary peristalsis (esophagitis can occur as dysmotility).
   2. Gravity will assist (first and second constitute volume clearance).
   3. Salivary secretion and oesophageal secretion protect and increase GERD in xerostomia and smoking (secretion clearance).

C. Tissue resistance :
   1. Pre epithelial : mucin production.
   2. Epithelial : EGF, TGF increase cell turnover.
   3. Post epithelial blood supply.
   4. Dilated intercellular spaces is seen in early GERD.

Aggressive factors :
1. Gastric acid secretion.
2. Duodenogastric reflux.
3. Delayed gastric emptying.

Clinical features :

Oesophageal :
- Heart burn (90 % specific and 40 % sensitive) : Pyrosis and m/c symptom and TRPV1 mediated.
- Regurgitation : Stooping forward.
- Dysphagia : Stricture (GERD improves) and Schatzki ring.
- Water brash.
- Odynophagia.
- Hiccups.

A ring	B ring (Schatzki's ring)
Upper end of LES covered by squamous epithelium	Squamocolumnar junction and upper part by squamous and lower by columnar
Muscular ring	No muscle layer
Less common	More common
No GERD association	GERD association
Treatment : • Dilation • POEM • Botulinum	Treatment : • Dilatation • Endoscopic resection

Extra oesophageal :

- Chest pain.
- Pulmonary : Asthma, c/c bronchitis, IPF and bronchiectasis.
- ENT : Globus, hoarseness, leucoplakia, post laryngitis.
- Sleep : OSAS.

Decrease LES pressure	Increase LES pressure
• VIP • CCK • Secretin • Somatostatin • Alpha antagonist • Beta agonist • Ach antagonist • Serotonin, Dopamine • Morphine, CCB • Barbiturate, BCZ • Fat, peppermint	• Gastrin • Motilin • Substance P

Diagnosis 00:27:49

Endoscopy : Look for esophagitis, Barrett's esophagus, HH.
Landmarks :

- Location of hiatus.
- Anatomical GE junction.
- Squamocolumnar junction.

Distance between hiatus and anatomical GE > 2 cm : Hiatus hernia.
ESBM (Endoscopically significant Barrett's mucosa) : Distance between SCJ and anatomical GE > 1 cm.
Biopsy should be taken (Prague guidelines).
Histology : Gastric or intestinal metaplasia.
According to UK guidelines : ESBM with either one.

According to USA guidelines : Only intestinal metaplasia is associated.

If biopsy is inconclusive : Repeat biopsy after 8 to 12 months.
If no esophagitis then NERD (Bx : Barrett's + r/o EOE).

Table 2: Classification of Visual or Macroscopic Esophagitis in Children and Adults – Hetzel-Dent and LA Classification

Hetzel Dent Classification

Grade 0	Normal mucosa
Grade 1	Mucosal edema, hyperemia, and friability
Grade 2	Superficial erosions involving less than 10% of the distal 5 cm of the esophageal mucosal surface
Grade 3	Superficial erosions and ulcerations involving 10-50% of the distal esophagus
Grade 4	Deep peptic ulceration anywhere in the esophagus or confluent erosion of more than 50% of the distal esophagus

Los Angeles Classification

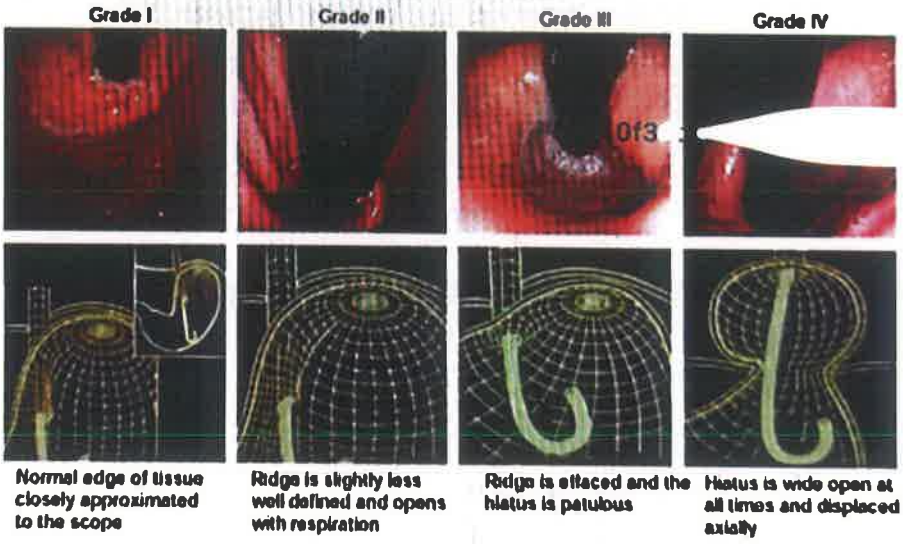
Grade A: One (or more) mucosal break no longer than 5 mm that does not extend between the tops of two mucosal folds

Grade B: One (or more) mucosal break more than 5 mm that does not extend between the tops of two mucosal folds

Grade C: One (or more) mucosal break that is continuous between the tops of two mucosal folds but which involves less than 75% of the circumference

Grade D: One (or more) mucosal break which involves at least 75% of the esophageal circumference

Hill grading :



Active space

Pathological GERD :

Grade C/D esophagitis	Barrett's oesophagus
Peptic stricture	AET > 6%

Indication for GERD testing :

Incomplete or lack of response to PPI
Prior and following anti-reflux Sx
Atypical symptoms like cough, belching, suspected rumination

Types of testing include :

- PH metry (gold standard for diagnosis of GERD).
- PH metry + impedance testing : Can detect weakly acidic + weakly alkaline + gaseous and rereflux.

Demister score (pH metry + impedance) :

Total AET	Recumbent AET	Upright AET
Number of reflex	Longest reflex	Reflux with PH < 4 Or > 5 min

AET < 4 % is normal and > 6 % is abnormal and 4 to 6 % is grey area.

> 80 reflux/24 hr is abnormal and < 40 reflux/24 hr is normal.

Probe is placed 5 to 6 cm from squamocolumnar junction.

Testing with or without PPI.

Demister score (pH metry + impedence) :

With PPI	Without PPI
Prior PH testing +ve	Confirm reflux is the cause of symptom
Barrett's oesophagus	Testing prior to anti reflux sx
Grade C/D esophagitis	Non erosive disease
Peptic stricture	Grade A/B esophagitis
	No Barrett's
	Atypical presentation
	Absent or incomplete response to PPI
	Recurrent or persistent symptoms following anti-reflux sx
	Better symptom reflux association

Lifestyle modification :

Weight loss	Head elevation	Avoid Smoking and R-OH
Avoid late snack	Lying down following meal	Tight clothes

OTC : Gaviscon is better than antacid.

Prokinetics :

- Increase LES pressure and gastric emptying.
- Not effective alone (80 % due to ↑ LESR and prokinetic do not alter it.

Cisapride → arrythmia	Metoclopramide → EPS
Domperidone → QT prolongation	Bethanechol→ flushing +blurring+ increase HZ

↑ LESR inhibitors :

- Baclofen (GABA agonist).
- Placarbil, lesogaberan, arbaclofen : Better tolerability.
- No significant benefit.

H2R antagonist :

- Less effective than PPI.

PPI :

- Response is better for erosive ERD than NERD.
- Double dose more effective when given in divided doses.
- Ex : 80 mg OD pantoprazole < 40 mg BD pantoprazole, 80 mg > 40 mg.
- Decrease heartburn and esophagitis but reflux will continue.
- Give for 8 week and if no response for 12 week.
- Esomeprazole : superior than others in Los angels C & D.

Maintenance of PPI if :

Low LES pressure	Esophagitis
Young patient require maximum therapy	

Fundic polyp	Gastric carcinoid	Ca colon
Increase pneumonia	Enteric infection and SBP	Osteoporosis
SIBO	Hypomagnesemia	Decrease iron absorption
Interstitial nephritis	Inhibit clopidogrel absorption	

Endoscopic procedures :

Anti-Reflux surgery by endoscopy		
RFA	TOF (Transoral fundoplication)	MUCOSAL RESECTION
• Stretta	• GERD • MUSE (Medigus ultrasound surgical endostapler) • ESOPHY	• Anti-Reflux mucosectomy • Anti-Reflux mucosal ablation

RFA :

- Upto 14 application of radiofrequency energy via needle balloon catheter system to LES muscle & gastric cardia.
- MOA : Hypertrophy of muscularis propria and reduced LES relaxation + fibrosis of GE jn.
- Confounding result b/w stretta vs PPI.
- No RCT comparing Stretta vs Anti Reflux Sx.
- A/e : Chest pain, fever, oesophageal ulcer, rarely gastroparesis (vagal nerve injury).

TOF :

- 270° fundoplication under GA.
- Better response in :

Hills grade I-II	Small hiatus hernia
Typical GERD symptoms	Normal HRM oesophagus

ARM (Anti Reflux mucosectomy) :

- mucosa resected and heal with scar formation.
- Resect 2 cm gastric and 1 cm oesophageal mucosa in crescentic fashion.

Surgery :

- Preprocedure : Do pH metry + HRM (r/o CREST and

Achalasia).

- For refractory GERD (20 to 30 % of erosive ERD and 40 % NERD have poor response to PPI.
- If achalasia, partial fundoplication + myotomy is required other wise cause dysphagia, in others : 360 Nissen fundoplication.
- A/e : Dysphagia, bloating and flatulence.

Indication :

- PPI controlled → desiring alternative treatment
- Vol regurgitation and aspiration
- Recurrent peptic stricture in young
- ❖ Barrett's rarely regress

Failed surgeries :

- Too tight fundoplication
- Breakdown fundoplication
- Malposition fundoplication
- Herniation of fundoplication
- Paraesophageal hernia

HH surgery + Nichol Collin lengthening procedure.
Fundoplication : No difference in recurrence between laparotomy and laparoscopy.

Types :

1. Complete :
   - Nissen 360°.
2. Partial :
   - Posterior :
     - Toupet 270°.
     - Lind 300°.
   - Anterior :
     - Belsey mark IV.
     - Dor hemifundoplication.

25 % require PPI on follow up and 15 to 30 % require reintervention.

MSA (Magnetic Sphincter Augmentation)/LINX system) :

- Newer surgical technique where titanium beads with magnetic core placed around lower oesophagus and it separated during swallowing and belching.
- A/e : Dysphagia, perforation.

EOSINOPHILIC ESOPHAGITIS

Food hypersensitivities 00:00:28

BOX 10.2 Gastrointestinal Food Hypersensitivities

IMMUNOGLOBULIN E-MEDIATED FOOD HYPERSENSITIVITIES
GI allergy
Infantile colic (minor subset)
Pollen-food allergy (oral allergy syndrome)

MIXED IMMUNOGLOBULIN E- AND NON–IMMUNOGLOBULIN E-MEDIATED HYPERSENSITIVITIES
Eosinophilic esophagitis
Eosinophilic gastritis
Eosinophilic gastroenteritis
Allergic eosinophilic proctocolitis

NON–IMMUNOGLOBULIN E-MEDIATED FOOD HYPERSENSITIVITIES
Dietary protein-induced enteropathy
  Celiac disease
  Dermatitis herpetiformis
Food protein-induced enterocolitis syndrome

MECHANISM UNKNOWN
Cow's milk-induced occult GI blood loss and iron deficiency anemia of infancy
GERD
Infantile colic (subset)
IBD

Infantile colic :

- 5 to 10 % : IgE mediated.
- 90 to 95 % : mechanism is unknown.

Background :

AGREE : Awaking Group On PPI Responsive Esophageal Eosinophilia.

Eosinophilic esophagitis (EOE) :

2007 definition :

Dysphagia, food impaction, chest pain, abdominal pain, vomiting, failure to thrive.

Other causes :

Achalasia, collagen vascular disease, coeliac disease, crohn's disease, drugs, other EGIT disease, GERD, GVHD, vasculitis, hypereosinophilic syndrome, pemphigus vegetans.

Modification in 2011 :

Subset of patients who responded to PPI were excluded from the definition.

New phenotype – PPI REE (PPI responsive Eosinophilia) needed to be addressed

The updated guidelines still required three criteria to be met, but with some modifications:

1) clinical symptoms of esophageal dysfunction

2) a maximum esophageal eosinophil count of at least 15 eos/hpf, *with few exceptions*

3) exclusion of *other possible causes of esophageal eosinophilia, including PPI-REE.*

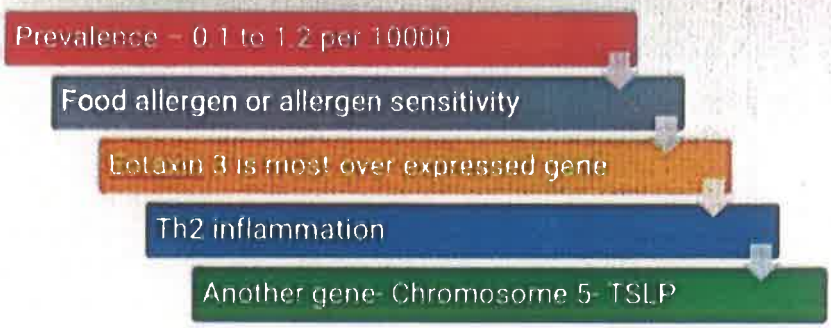
In 2017, AGREE consensus :

PPI responsive patients were again included in the definition.

PPI is used as treatment option.

Active specs

Epidemiology and etiology :



Eotaxin a : Associated with eosinophilic gastroenteritis.

Clinical features :

- Typical Presentation
- Atopic male (Male : Female, 3:1)
- Presents in childhood or the 3rd or 4th decade
- Dysphagia (solid food), chest pain, food impaction (requiring endoscopic removal in 33 to 54 %)and upper abdominal pain.

a/3rd of patients will have allergic manifestations/atopy.

SYMPTOMS ACCORDING TO AGE

Infants and toddlers- Failure to thrive and feeding difficulties

School aged children- Vomiting or pain

Adults- Dysphagia, food impaction, chest pain and upper abdominal pain.

Active space

Table 2. Clinical presentation of adult EoE patients enrolled in a European multicenter trial [14]

Patients	76
Males, %	83
Mean age (range), years	39.7 (18–70)
Mean BMI (range)	24.8 (19.0–36.7)
Symptoms, %	
Dysphagia	100.0
Food impaction	65.8
Odynophagia	35.5
Retrosternal pain	38.3
Heartburn	32.9
Regurgitation	35.5
Abdominal pain	18.4
Diarrhea	7.8
Weight loss	2.6
Allergic comorbidities, %	64.5
Allergic rhinitis	50.0
Allergic conjunctivitis	19.7
Allergic asthma	19.8
Atopic eczema	9.2
Food allergies	21.1
Duration of dysphagia >1 year, %	50

Table 1. Similarities and differences in the clinical appearance of pediatric and adult EoE (adapted from [5])

	Adults	Children
Symptoms	dysphagia (solid food), food impaction, retrosternal pain	abdominal pain, chest pain, heartburn, coughing, decreased appetite, food refusal, anorexia, dysphagia, nausea, regurgitation, sleeping difficulties
Demographics	male Caucasians predominant	
Physical exam	normal	sometimes failure to thrive
Allergic predisposition	airborne allergens predominant	food allergens predominant
Concomitant allergic diseases	asthma, eczema, allergic rhinitis	
Lab values	peripheral eosinophilia 5–50%, total serum IgE ≈70%	

Endoscopic features :

None of them are pathognomonic.

- Fixed esophageal rings or trachealization/corrugated rings
- Transient esophageal rings (felinization or feline folds)
- Whitish exudates
- Longitudinal furrows
- Edema
- Diffuse esophageal narrowing
- Narrow calibre esophagus
- Esophageal lacerations induced by the endoscope

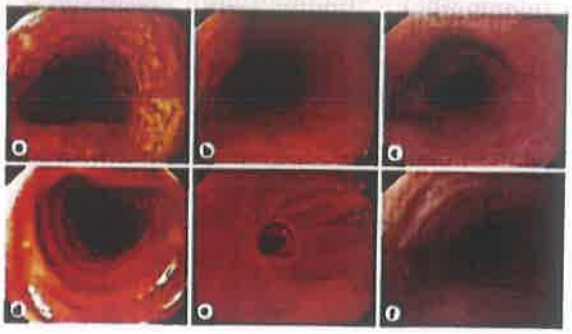


Fig. 1. Endoscopic manifestations in adult EoE patients enrolled in a European multi-center trial: white exudate (a), longitudinal furrows (b), diffuse edema (c), fixed rings (d), severe stricture (e), and rings, furrows and edema (f) [14].

Endoscopic biopsy :

2 to 4 biopsies from the proximal and distal esophagus should be obtained.

In children – Gastric and duodenal biopsies also

Histopathology :

Eosinophils > 15/hpf

- **Eosinophil micro abscess formation**
- **Superficial layering of eosinophils**

Extracellular eosinophil granules

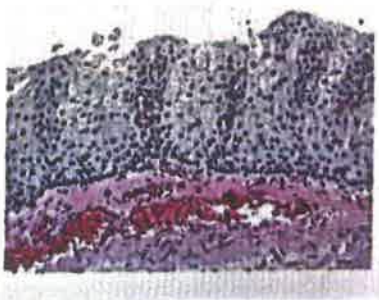
Dilated intercellular spaces

Elongated papillae with inflammation and fibrosis and lamina propria

Basal cell hyperplasia

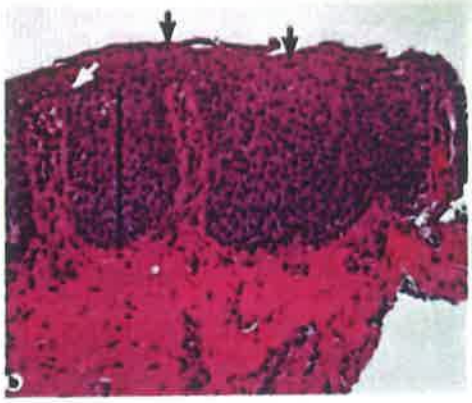
Eosinophilic gastroenteritis : > 30 eosinophils/hpf. Rule EOE.

Normal esophagus :



Active space

Eosinophilic esophagitis :



Esophageal epithelium from a patient with EoE shows a markedly thickened basal layer (bar) numerous intraepithelial eosinophils (arrows) dilated intercellular spaces (white arrow) and thickened fibers in the lamina propria (asterisk). Eosinophilic microabscesses at the surface (arrows). Dilated intercellular spaces are also seen (white arrow).

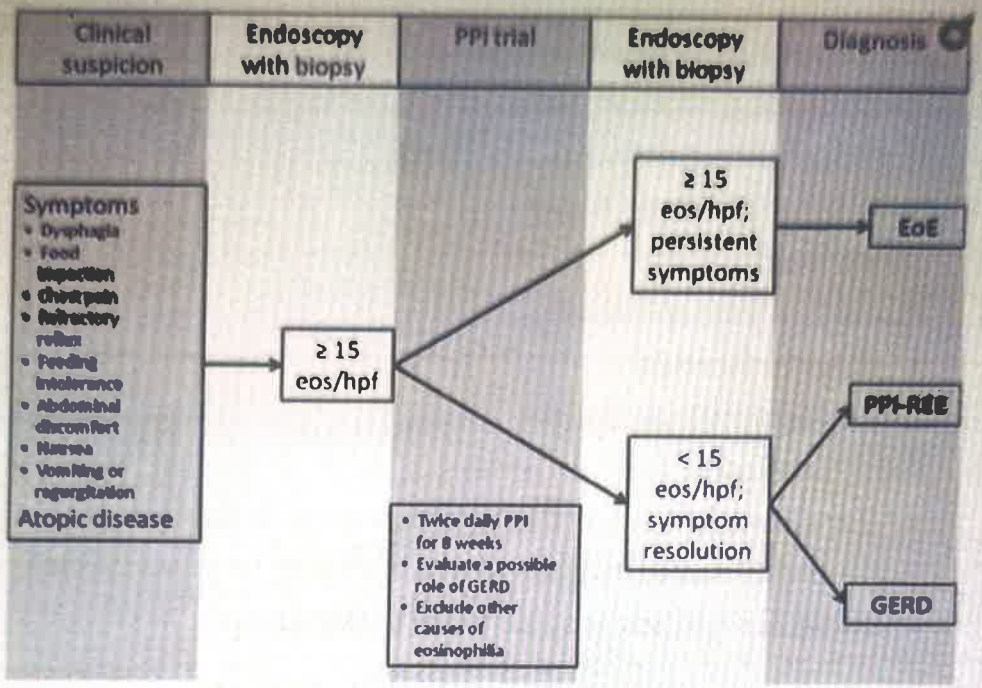
Other diagnostic modalities :

- Esophageal pH monitoring and impedence to evaluate GERD
- EUS- may show greater mucosal and muscular thickness
- Radiography is no routinely indicated, Maybe used in the likelihood of strictures

Lab investigations :

- Peripheral eosinophilia and elevated serum IgE levels are usually found in 50 and 75% of patients, respectively.
- Food-specific IgE or skin prick test results may be positive in over 80% of adult EoE patients
- However, elimination of foods that gave positive results failed to achieve disease remission.
- None of the currently available techniques has proven useful or reliable for the management of EoE in clinical practice

Active space



Treatment

00:26:00

Dietary therapy improves symptoms and reduces the number of eosinophils.

Trial of specific food allergen and aero allergen elimination is tried.

Results are usually unsatisfactory.

Elemental diet- amino acid based formula food is tried.

Avoidance of the most common allergic foods are tried; Six Food Elimination Diet (SFED)

Elemental diet has shown the best results.

SFED : Six Food Elimination Diet.

- Cow's Milk
- Soy
- Wheat
- Egg
- Peanut/Tree nut
- Seafood/ Shellfish

Reintroduction should begin with least likely food trigger :

ADULTS
- Wheat -60 %
- Milk- 50 %
- Soy- 10%
- Nuts - 10%
- Eggs- 5%

PAEDIATRICS
- Milk- 35%
- Egg- 13%
- Wheat- 12%
- Soy- 9%

Drug therapy :

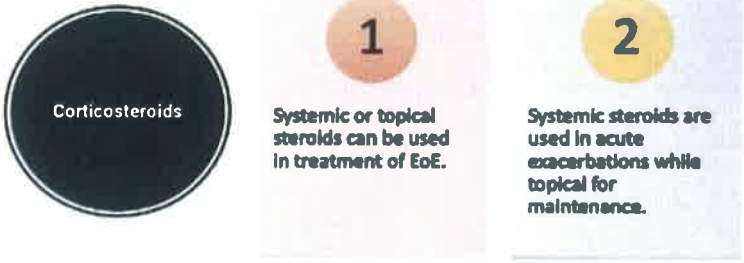


TABLE III. Recommended doses of corticosteroids for EoE

Topical swallowed corticosteroids
- Initial doses (see references for preparation and administration information)
  - Fluticasone (puffed and swallowed through a metered-dose inhaler)
    - Adults: 440-880 µg twice daily
    - Children: 88-440 µg twice to 4 times daily (to a maximal adult dose)
  - Budesonide (as a viscous suspension)
    - Children (<10 y): 1 mg daily
    - Older children and adults: 2 mg daily

Systemic corticosteroids
- For severe cases (eg, small-caliber esophagus, weight loss, and hospitalization)
  - Prednisone: 40 mg/d

In trial :

IL-5 humanized antibodies- Mepolizumab and Rezlizumab.

Chemoattractant receptor of Th2 cells (CRTH2) antagonists

Active space

Eosinophilic esophagitis

Dilatation :

Mild stricture : Diet + steroids.

Severe stricture : Dilatation.

If stenosis is not severe, first dietary and medical therapy is given, followed by dilatation.

Cases of severe stenosis, dilatation may be given as the first line of management.

Through the scope or bougie dilators maybe used.

Gradual esophageal dilatation with a target goal of 15- 18 mm.

Limiting the progression of dilatation to 3mm/ session

Prognosis :

Requires prolonged treatment like allergic asthma.

Recent 15 year old study has shown ongoing symptoms in patients from childhood to adulthood in majority of the patients.

Left untreated can lead to scarring .

Tears

Full thickness- requires surgical intervention.

Partial tears - conservatively