



# Eosinophilic Esophagitis

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# Introduction

- **Esophagitis** is general term refers to inflammation that occurs due to injury or irritation to the esophageal mucosa
- There are many causes of esophagitis and essentially the presentation is similar which include **retrosternal chest, heartburn, dysphagia or odynophagia**

# Eosinophilic Esophagitis (EoE)

- **Definition:** Chronic immune mediated or antigen mediated esophageal disease characterised by symptoms related to esophageal dysfunction and eosinophil predominant mucosal inflammation

# Epidemiology

- **Prevalence** in developed countries is between 45 and 55 cases per 100,000 population
- **EoE** is a disease of cold climate with wide range of age distribution at presentation. More common among the white ethnicity and in male

# Pathophysiology

- **EoE** is a disease with a complex genetic cause and inheritance is due to the effects of multiple genetic loci that increase disease risk in the context of environmental and host immune factors.

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# Journal of Allergy and Clinical Immunology

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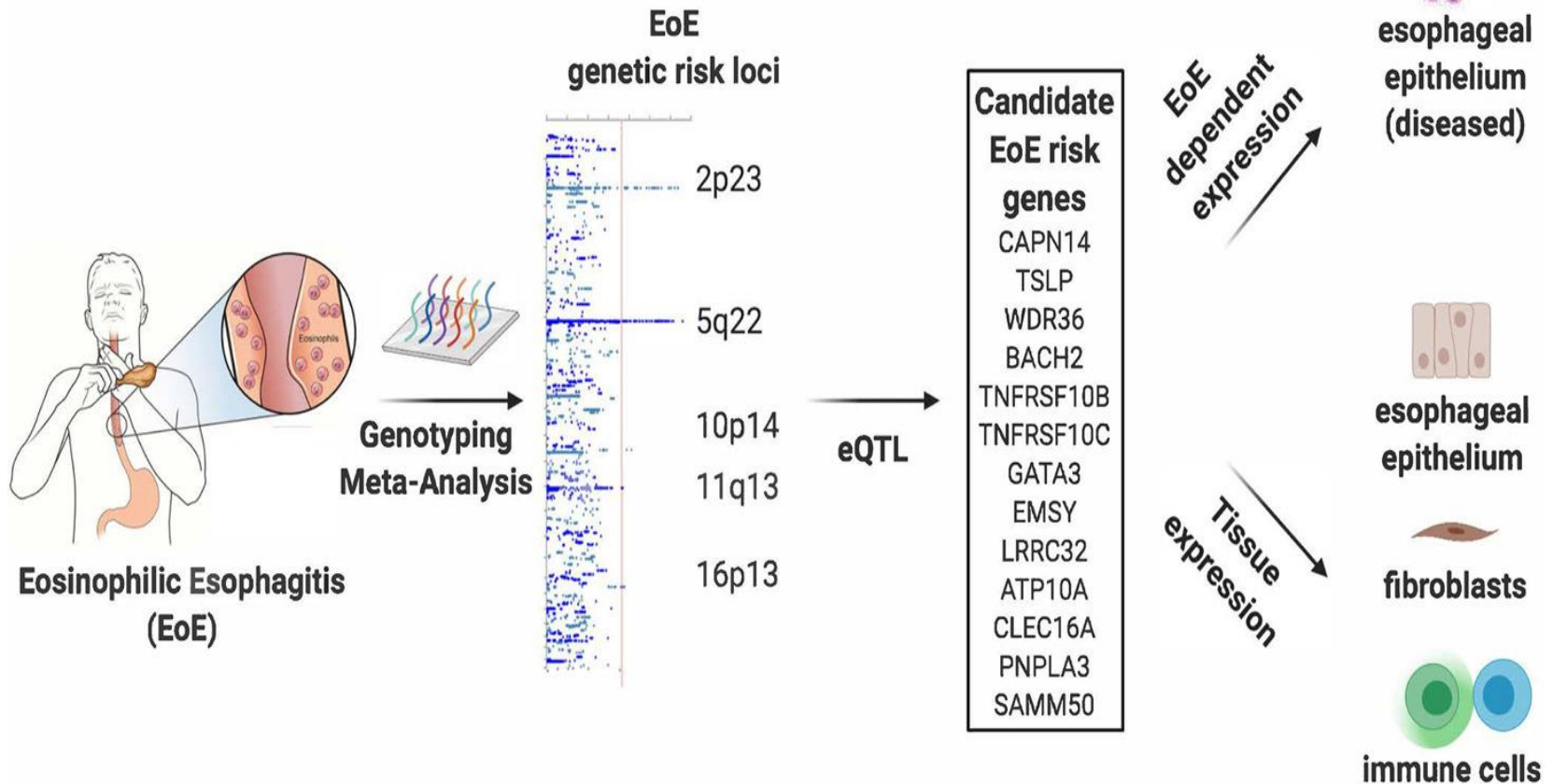
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Food allergy and gastrointestinal disease

**Replication and meta-analyses nominate numerous eosinophilic esophagitis risk genes**



# Replication and Meta-Analyses Nominate Numerous Eosinophilic Esophagitis Risk Genes



## Abbreviations

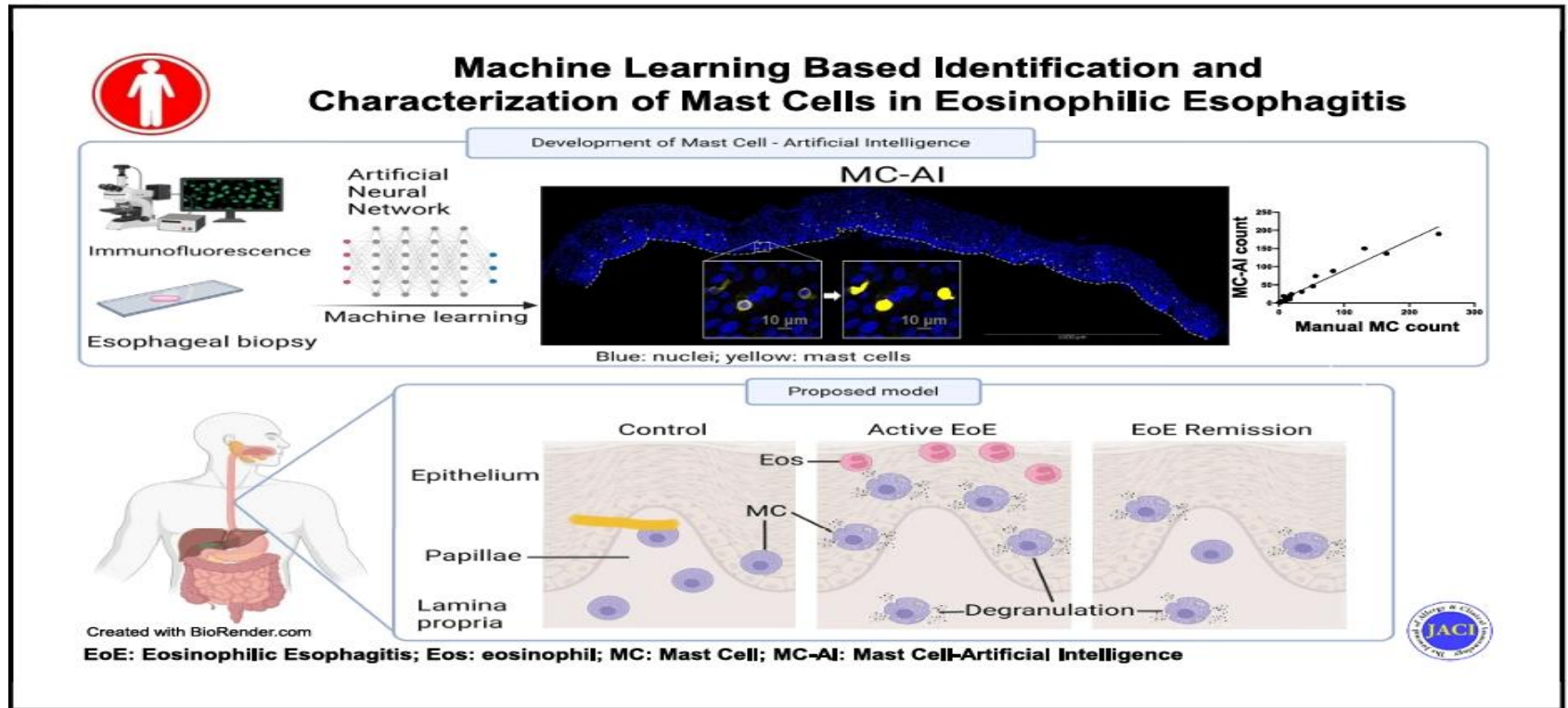
eQTL: Expression quantitative trait loci





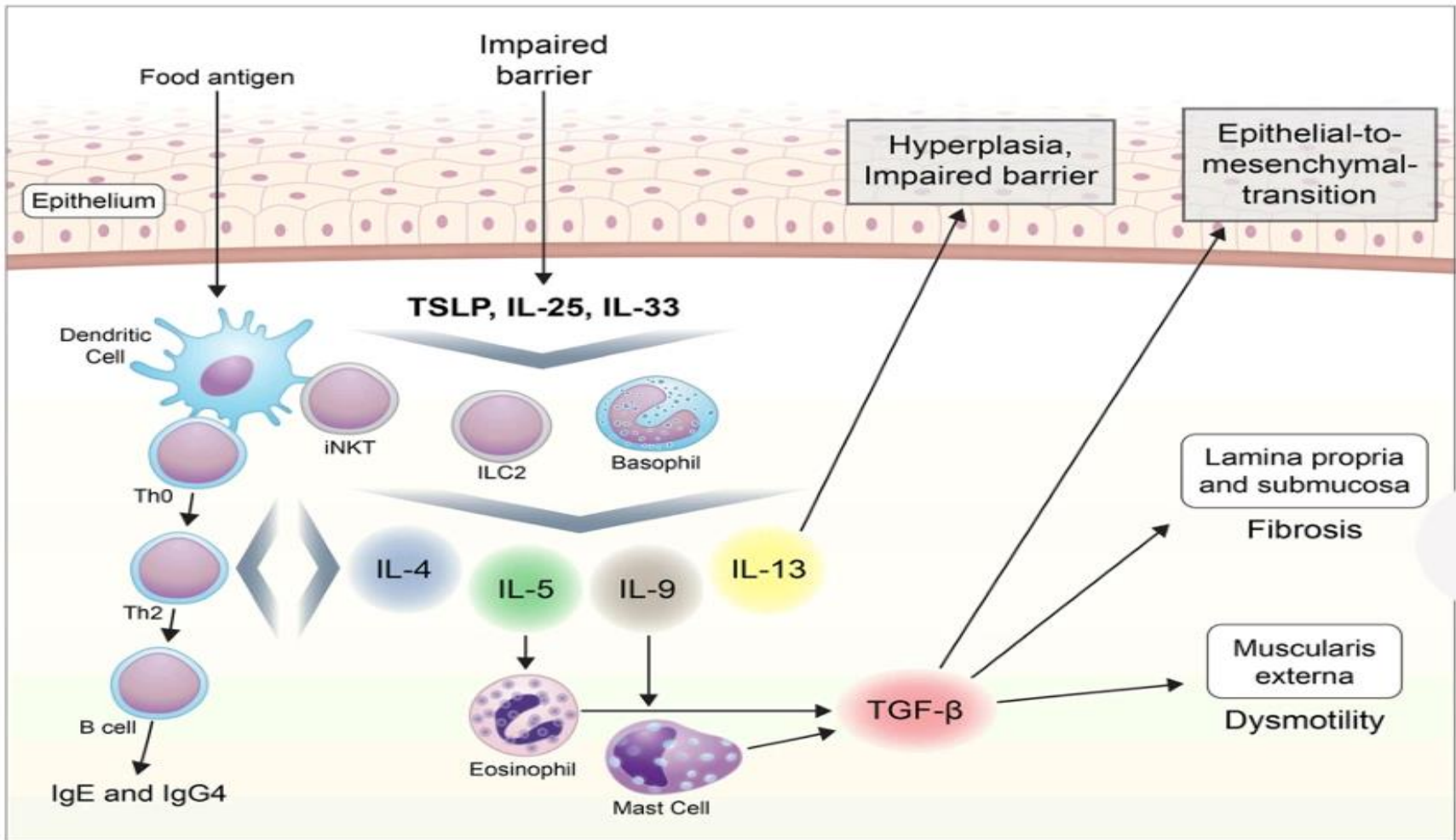
# Role of Mast Cells in EoE

## GRAPHICAL ABSTRACT



**Capsule summary:** A machine learning protocol for identifying mast cells, designated Mast Cell-Artificial Intelligence, readily identified spatially distinct and dynamic populations of mast cells in eosinophilic esophagitis, providing a platform to better understand this cell type in eosinophilic esophagitis and other diseases.

# Pathophysiology



# Clinical Presentation

- Food bolus **impaction** (may be masked by compensating behaviours) 46%
- **Dysphagia** 7.3% and in 22% of patients with non obstructive dysphagia
- **Reflux** symptoms 7.7%
- Non cardiac **chest pain** 6%

# Diagnosis

- Good clinical **history**
- Good esophageal **endoscopic** examination
- Proper esophageal **biopsies**
- **Histological** examination

# Clinical history

- **I**mbibing fluids with meals to lubricate foods
- **M**odifying food (cutting into small pieces)
- **P**rolonged meal times
- **A**voidance of hard textured foods
- **C**hewing excessively
- **T**urning away pills

## **The IMPACT acronym**

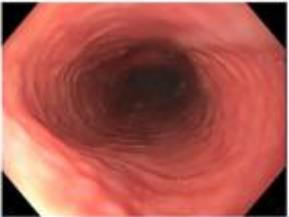




*Young age, male, dysphagia and food allergies*

# Esophageal Endoscopic Examination

- Esophageal rings
- Edema
- Furrows
- Strictures
- Exudates

**Normal findings do not exclude diagnosis**

# EREFS Score

|   |  |                  |  |
|---|--|------------------|--|
| <p>Rings = 1</p>     | <p>Edema = 1</p>        | <p>Edema</p>     | <ul style="list-style-type: none"><li>• Grade 0: Distinct vascularity</li><li>• Grade 1: Absent or decreased</li></ul>   |
| <p>Furrows = 1</p>  | <p>Exudate = 2</p>      | <p>Exudate</p>   | <ul style="list-style-type: none"><li>• Grade 0: None</li><li>• Grade 1: Mild (<math>\leq 10\%</math> surface area)</li><li>• Grade 2: Severe (<math>&gt;10\%</math> surface area)</li></ul> |
| <p>Total EREFS = 6</p>  | <p>Stricture = 1</p>  | <p>Furrows</p>   | <ul style="list-style-type: none"><li>• Grade 0: None</li><li>• Grade 1: Mild</li><li>• Grade 2: Severe</li></ul>  |
|   |  | <p>Stricture</p> | <ul style="list-style-type: none"><li>• Grade 0: Absent</li><li>• Grade 1: Present</li></ul>   |

# Esophageal Biopsies

## Who

- **Endoscopic Signs Associated with EoE**
- **Patient with Dysphagia or Food Bolus Obstruction, with a normal looking Esophagus**

## When

- **Eosophageal biopsies should be taken at index endoscopy in patients with food bolus obstruction**
- **Out Patient Endoscopy if Food Obstruction Resolved**

## How

- **At Least 6 Biopsies From Different Parts Of The Esophagus For Diagnosis and Follow Up**
- **Biopsy Stomach and Duodenum to assess for EGID**

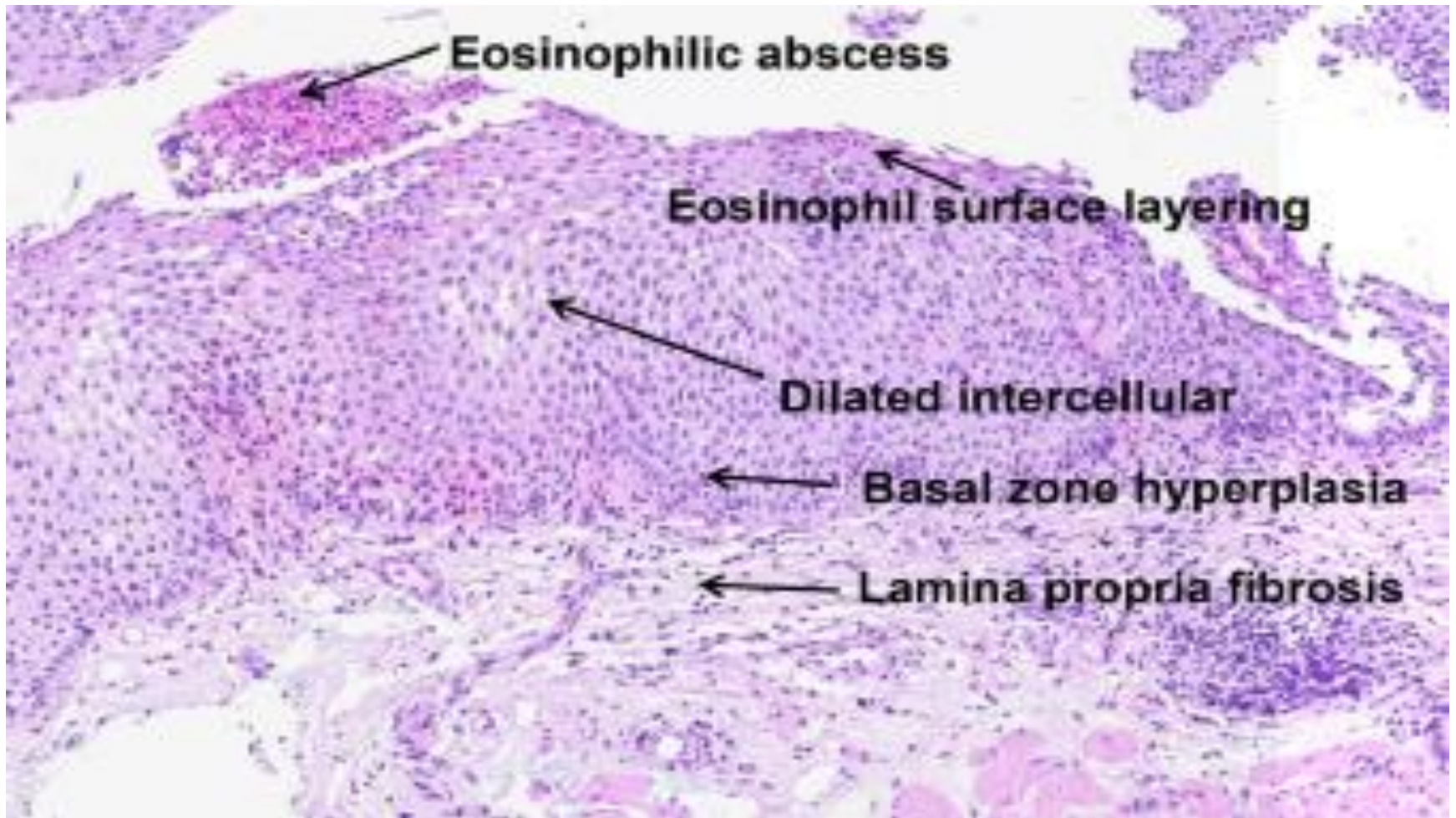
**Endoscopy and Biopsies to Exclude EoE in Patients with GERD Symptoms Refractory to PPI Usually Not Indicated**



# Histology

- **Stop** PPI prior to endoscopy and biopsy for at least 3 weeks
- Mucosal Eosinophils ( $\geq 15$  per  $0.3 \text{ mm}^2$ ) is **diagnostic**
- Other histological features of EoE (eg: basal cell hyperplasia, oedema, microabscesses, eosinophil layering, eosinophil degranulation and subepithelial sclerosis)
- **Re-scope** patients with high index of suspicion if the initial histology was not diagnostic

# Histological Appearance



# Other Causes of Esophageal Eosinophilia

|           | Condition  |
|-----------|--|
| Primary   | Gastro-oesophageal reflux disease                                      |
|           | Achalasia  |
|           | Eosinophilic gastroenteritis or colitis with eosinophilic oesophagitis |
|           | Infection (fungal or viral)  |
|           | Pill oesophagitis  |
| Secondary | Hyper-eosinophilic syndrome  |
|           | Drug hypersensitivity reactions  |
|           | Connective Tissue diseases   |

Eosinophilia in the oesophagus is rare and data for an eosinophil density of  $\geq 15/0.3$  mm<sup>2</sup> for causes other than eosinophilic oesophagitis is limited.

# Eosinophilic Esophagitis and GERD

- Can **coexist** in the same patient
- EoE that responds clinically to a PPI is **the same** disease as EoE that fails to respond to a PPI

# Treatment of Eosinophilic Esophagitis

- **Goal:** Induce long-term clinical and histological remission
- **Symptoms degree do not** reflect histological status
- **Treatment Options:**  
Medical - Dietary - Endoscopic

# Medical Treatment

- **Proton Pump Inhibitor** monotherapy is widely practiced as **first line treatment**
- Dose: **40 mg** omeprazole daily or equivalent, should be given twice for **8-12** ws before assessing response
- Appears effective in maintaining **remission**
- high risk of **relapse** on stopping therapy

# Medical Treatment

- **Topical Steroids:** Effective for **inducing** histological and clinical remission
- Likely reduce the development of **strictures**
- **Relapse** is high after withdrawal, maintenance treatment is recommended
- Systemic steroids **are not** recommended

# Efficacy of Steroids

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Volume 18, Issue 13, December 2020, Pages 2903-  
2911.e4

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Original Article  
Alimentary Tract

## Efficacy of Therapy for Eosinophilic Esophagitis in Real- World Practice

### Conclusions

In an analysis of data from a large cohort of patients with EoE in Europe, we found topical steroids to be the most effective at inducing clinical and histologic remission, but PPIs to be the most frequently prescribed. Treatment approaches vary with institution and presence of fibrosis or strictures.



# Medical Treatment

| Drug class                               | Adults and adolescents (≥ 12 yr)   |
|--|--|
| Proton pump inhibitors                   | <ul style="list-style-type: none"><li>• Induction: twice daily (e.g., pantoprazole 40 mg twice daily)</li><li>• Maintenance: once or twice daily (e.g., pantoprazole 40 mg daily or twice daily)</li></ul> |
| Topical corticosteroids*                 |  |
| Orodispersable tablets                   | <ul style="list-style-type: none"><li>• Induction: 1 mg twice daily</li><li>• Maintenance: 0.5–1 mg twice daily (children &lt; 18 yr not approved)</li></ul>   |
| Inhalers (e.g., fluticasone propionate)† | <ul style="list-style-type: none"><li>• Induction: 1–2 mg twice daily</li><li>• Maintenance: 250 µg–1 mg twice daily or 1 mg at bedtime</li></ul>  |
| Slurry (e.g., budesonide slurry)‡        | <ul style="list-style-type: none"><li>• Induction: 1 mg twice daily</li><li>• Maintenance: 0.25–1 mg twice daily</li></ul>   |

# Medical Treatment

- **Novel Biologics** that used in other allergic conditions (such as Dupilumab, Cendakimab and Benralizumab) have shown promise

# Medical Treatment

- **BSG not recommend**
  - Monoclonal Antibody Therapies
  - Immunomodulators
  - Sodium Cromoglycate
  - Montelukast
  - Antihistamines

# Diet Treatment

- Elimination diets are **effective** in achieving clinicohistological **remission**
- **Dietitian** support is strongly **recommended**
- Exclusive elemental diets have a **limited** role
- Milk, Wheat, Soy, Eggs, Nuts and Fish

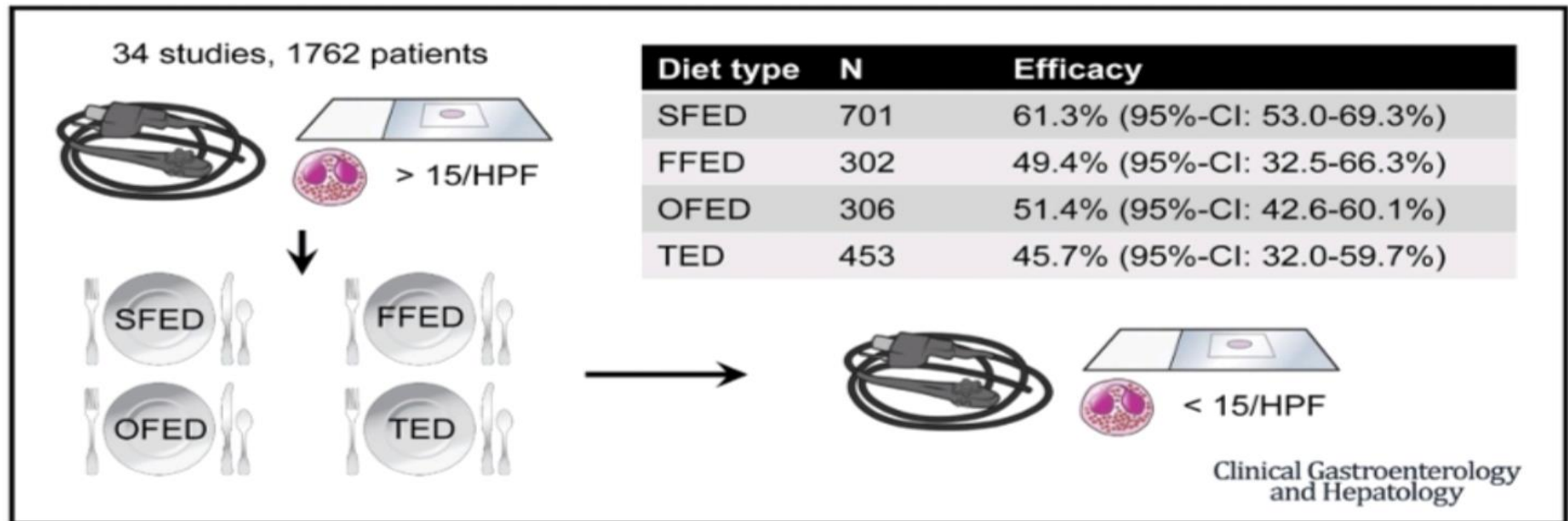
# Elimination Diets

## Efficacy of Elimination Diets in Eosinophilic Esophagitis: A Systematic Review and Meta-analysis



Christoph Mayerhofer,<sup>1</sup> Anna Maria Kavallar,<sup>1</sup> Denise Aldrian,<sup>1</sup>  
Andrea Katharina Lindner,<sup>2</sup> Thomas Müller,<sup>1</sup> and Georg Friedrich Vogel<sup>1,3</sup>

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# Endoscopic Treatment

- Endoscopic dilatation is **effective** in improving symptoms in patients with fibrostenotic disease
- Endoscopic dilatation is **safe** in patients with eosinophilic esophagitis and can be performed using either **balloon** or **bougie** dilators
- Better outcome if therapeutic dilatation is **combined** with effective antiinflammatory therapy such as topical **steroids**

# Treatment of Refractory and Recurrence

- **Refractory** EoE should be **jointly managed** by a gastroenterologist and allergy specialist to optimise treatment
- **Recurrence** while on treatment manage by **repeating** endoscopy for assessment and to obtain tissue for histology

# Complications

- **Strictures** and narrow lumen esophagus (commonly **underestimated**)
- Treatment: Endoscopic dilatation is **recommended** with better outcome when combined with topical steroid
- Targeted size is 16 to 18mm, recommended to be done gradually and in more than one session



# Complications

- **Perforation:** EoE is the **most** common cause of spontaneous perforation of the oesophagus
- CT chest with contrast to assess the **degree** of extravasations
- **Limited** extravasations (<3 cms) should be drained by an endoscopically placed drain and with esophageal stenting for slow healing tear

# Complications

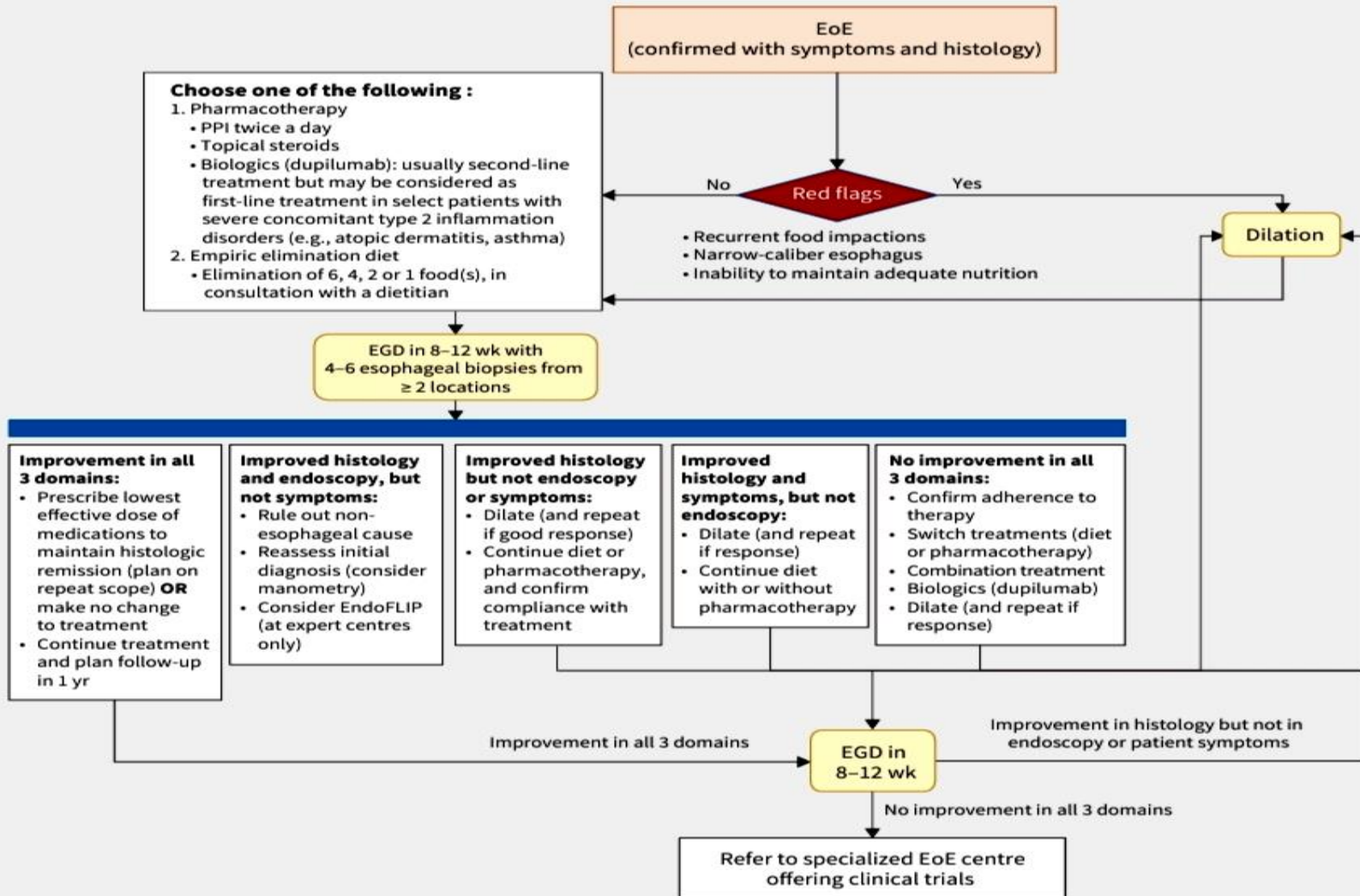
## Anxiety and depression

- Due to persistent symptoms and social restrictions and is alleviated by effective therapy

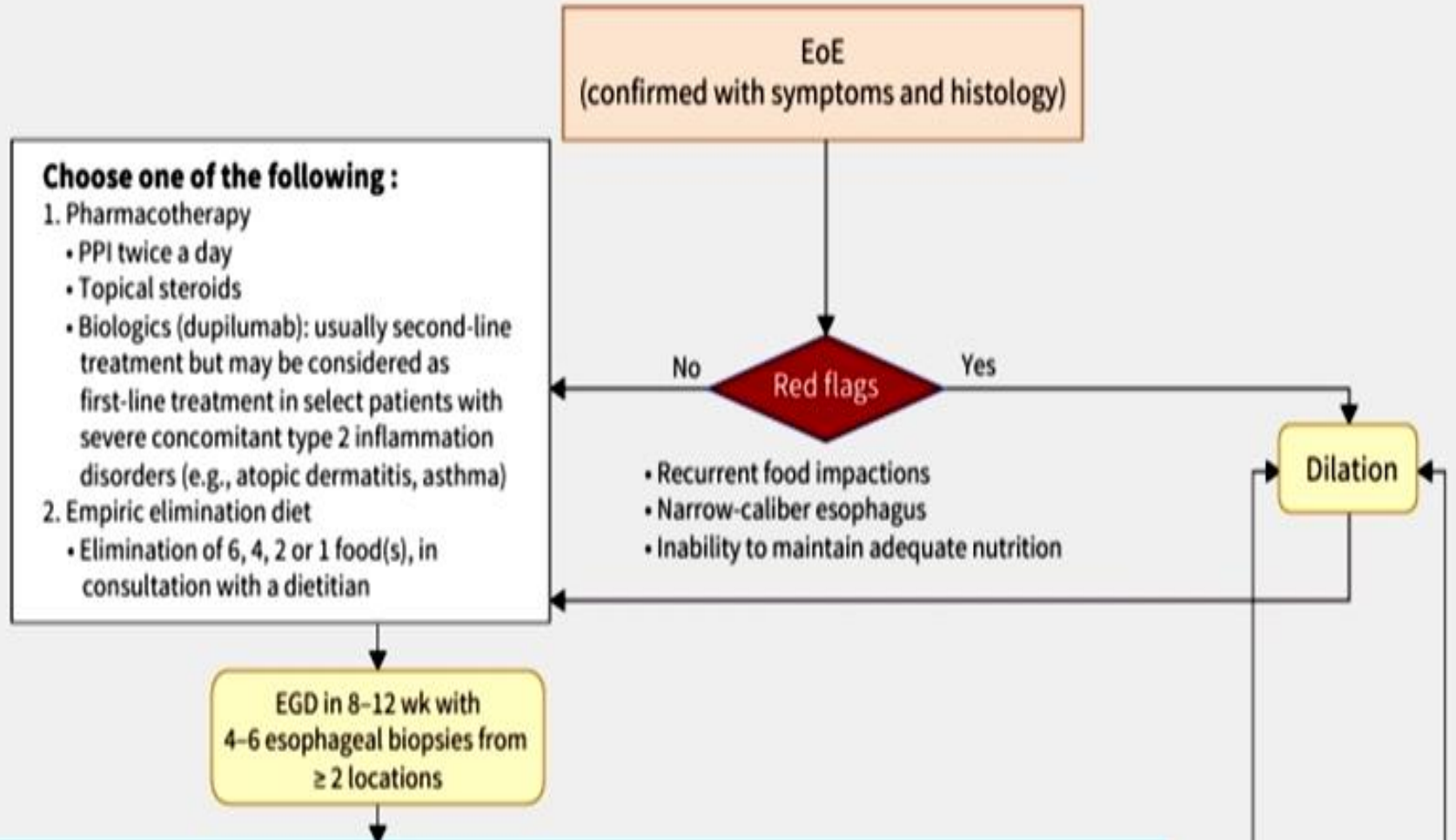
## Drugs side effects

- PPI side effects (diarrhoea, gastrointestinal infections or magnesium deficiency), then consider switching to alternative treatments such as diet or topical steroid
- Steroid side effects eg: candida infection ,Treated with topical antifungal while continuing steroid

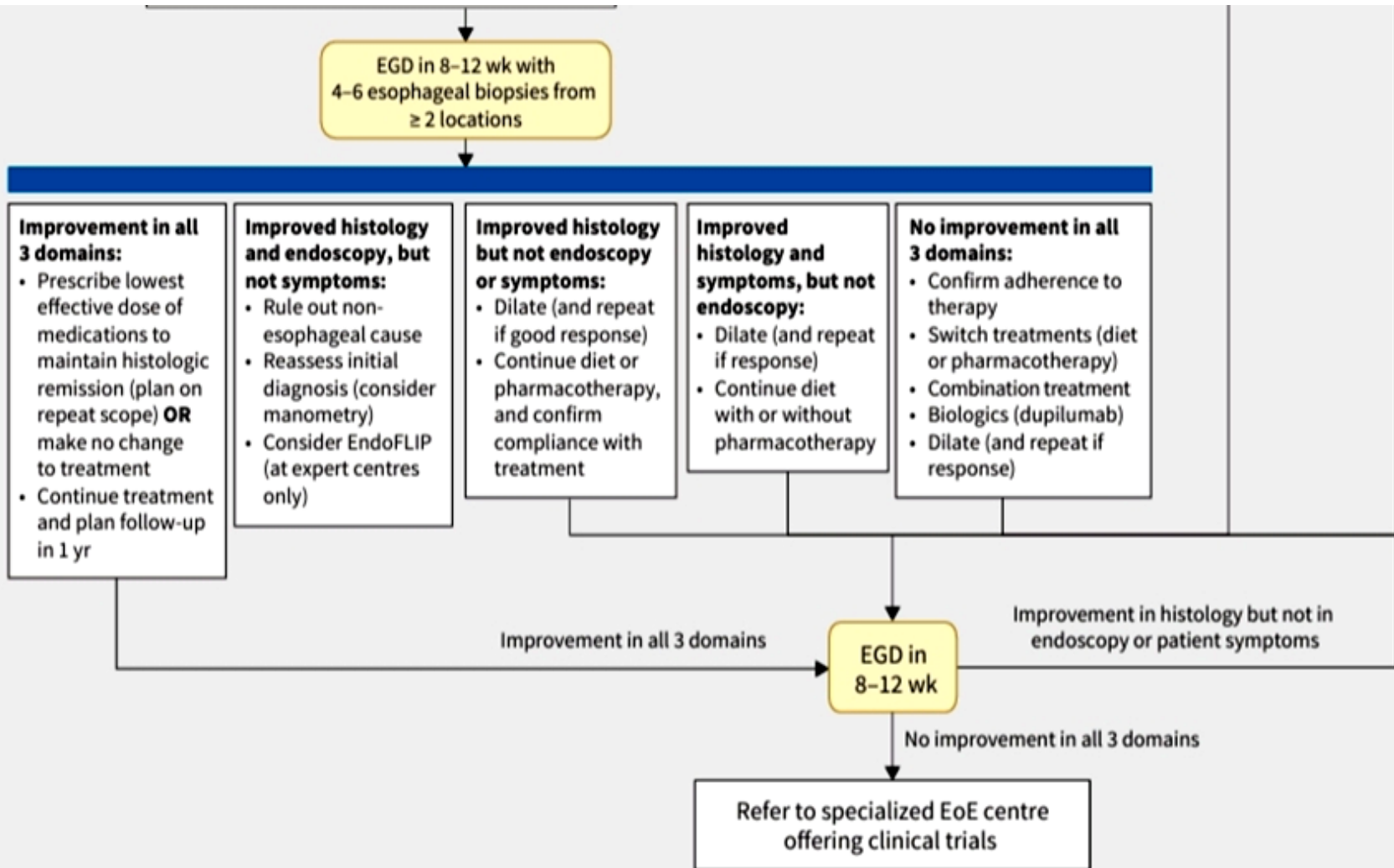
# Proposed Management Algorithm



# Proposed Management Algorithm



# Proposed Management Algorithm



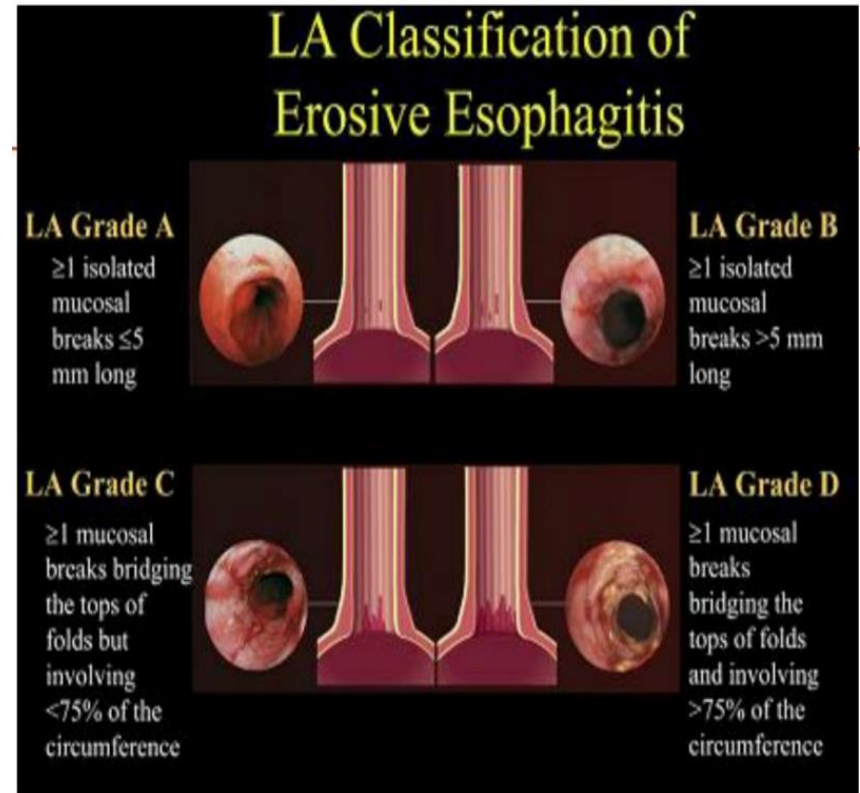
# **Other Causes of Esophagitis**

# Differential Diagnosis

- All other causes of esophagitis.
- Symptoms are very **similar** among this group
- Retrosternal chest pain, Odynophagia, Heart pain and Dysphagia are **the main** presenting symptoms
- Detailed workup is very **essential** for diagnosis

# Reflux Esophagitis

- **Erosive Esophagitis** due to the reflux of gastric contents
- **Symptoms:** Heart burn, Non cardiac chest pain and Regurgitation are the disease defining symptoms
- **Diagnosis:** History, OGD and PH study
- **Treatment:** PPI and life style modification





# Medication Induced Esophagitis

- Esophageal mucosa injury due to direct toxic effect of pills
- Prolong pills contact can cause direct irritant effect and disruption of mucosal cytoprotective barriers
- **Symptoms:** Dysphagia, Odynophagia and Retrosternal Chest Pain
- **Diagnosis:** History and OGD



# Medication Induced Esophagitis

- **Medications:** NSAIDs, Tetracycline, Clindamycin, Doxacycline, Bisphosphonates, Potassium chloride and Ferrous Sulphate
- **Treatment:** Supportive. Offending drug can be restarted after complete resolution of symptoms

## Patient-related

- Geriatric age group
- Bedridden
- Decreased salivation
- Ingestion of medications while supine
- Inadequate fluid intake when ingesting drugs
- Polypharmacy

## Pathological (delayed esophageal or gastric emptying)

- Esophageal motility disorders
- Extrinsic compression (eg, abnormal vasculature, mass)
- Gastroesophageal reflux disease
- Impaired acid clearance
- Left atrial enlargement
- Thoracic surgery

## Drug-related

- Chemical structure
- Formulation of pill
- Solubility characteristics
- Caustic characteristics of agents (acidic or alkaline)
- Osmolality
- Pill size
- Pill shape

# Infectious Esophagitis

- **Causes:** Bacteria, Viruses, Fungal and Parasitic microorganisms with the least common being bacteria and the most **common** being fungal
- **Pathophysiology:** Involves **colonization** with mucosal adherence and **proliferation**. The second step involves **impairing** the host defense mechanisms
- **Risk Factors:** **Immunocompromized** patients

# Fungal Esophagitis “Candidiasis”

- **Endoscopic signs:** Small, diffuse, linear, yellow-white, cheese-like plaques adherent to the mucosa
- **Diagnosis:** OGD/ Histology
- **Treatment:** Fluconazole 200mg stat, then 100mg daily for 2ws. Ketoconazole 200mg daily for 2ws



# Viral Esophagitis

- Herpes simplex virus (HSV) is the **most common** cause of viral esophagitis. It infects the squamous epithelium leading to vesicles and then ulcerations
- Cytomegalovirus (CMV), Epstein-Barr (EBV) and varicella-zoster (VZV) are other viral causes of viral esophagitis

# HSV vs CMV

**Endoscopic appearance:** HSV esophagitis results in multiple small, deep ulcerations.  
**Biopsy:** Edges of ulcer



**Histology:** Multinucleated giant cells with ballooning and degeneration squamous cells with inclusion is pathognomonic for diagnosis



**Treatment:** Oral or intravenous acyclovir. Foscarnet for those who are non-responders

**Endoscopic appearance:** CMV esophagitis is characterized by several large, shallow, superficial ulcerations.  
**Biopsy:** Center of ulcer

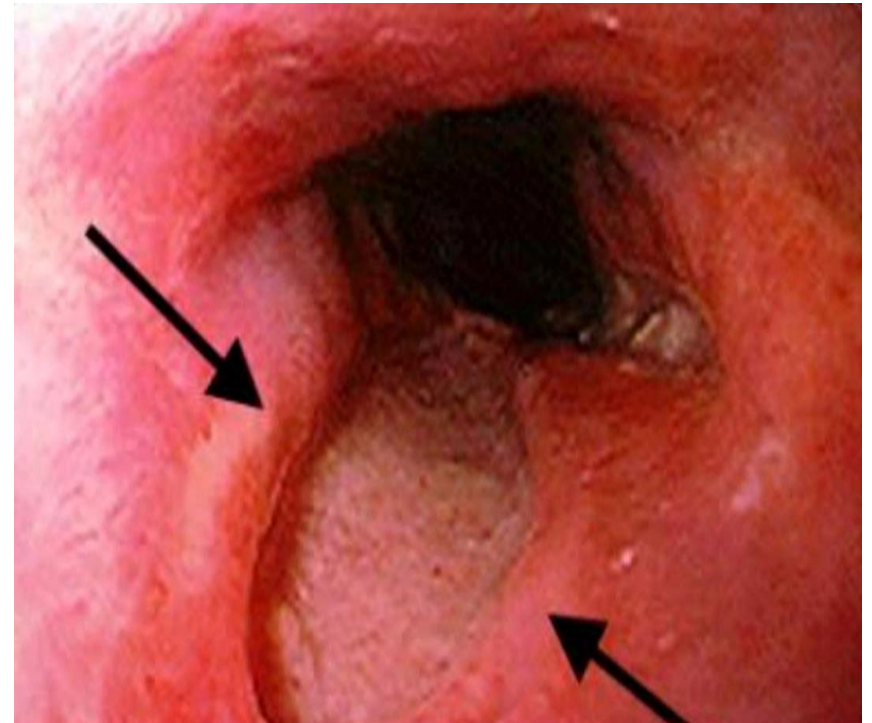


**Histology:** Large cells with both intracytoplasmic inclusions and amphophilic intranuclear inclusions are seen in CMV esophagitis.



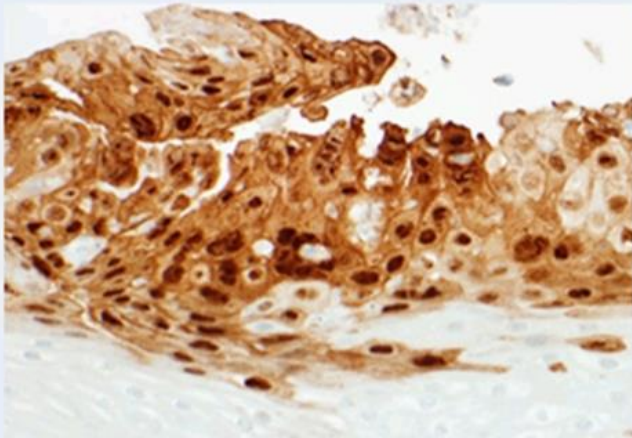
**Treatment:** CMV esophagitis is treated with Gancyclovir or Valganciclovir

# HSV vs CMV

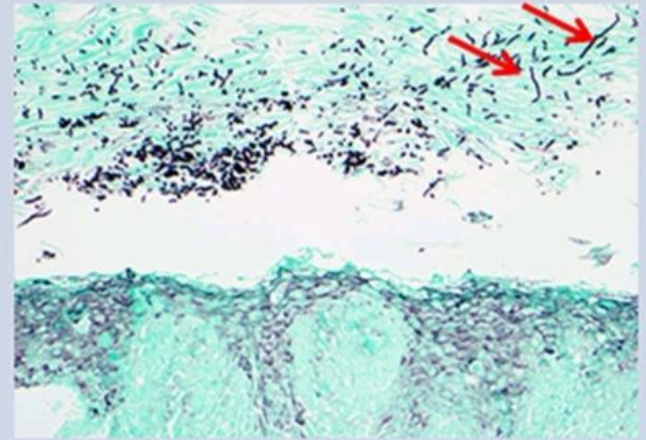


Endoscopy image demonstrating a single, large linear ulcer (black arrow).

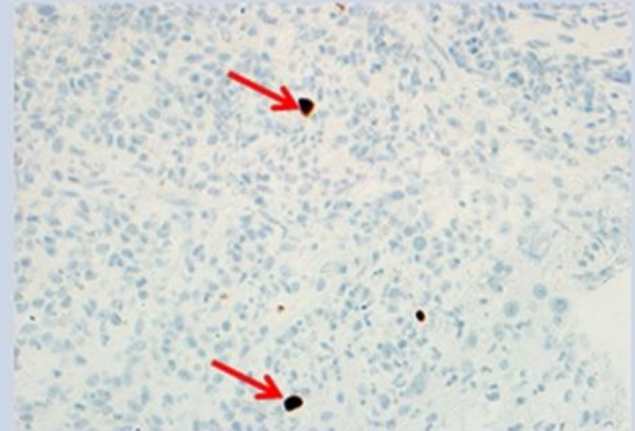
# Histological Appearance of Candida, HSV and CMV



B) HSV1/2 immunohistochemical stain demonstrating nuclear and granular cytoplasmic positivity in infected cells.



A) GMS stain demonstrating numerous yeast forms including pseudohyphae (arrows) consistent with *Candida* species.

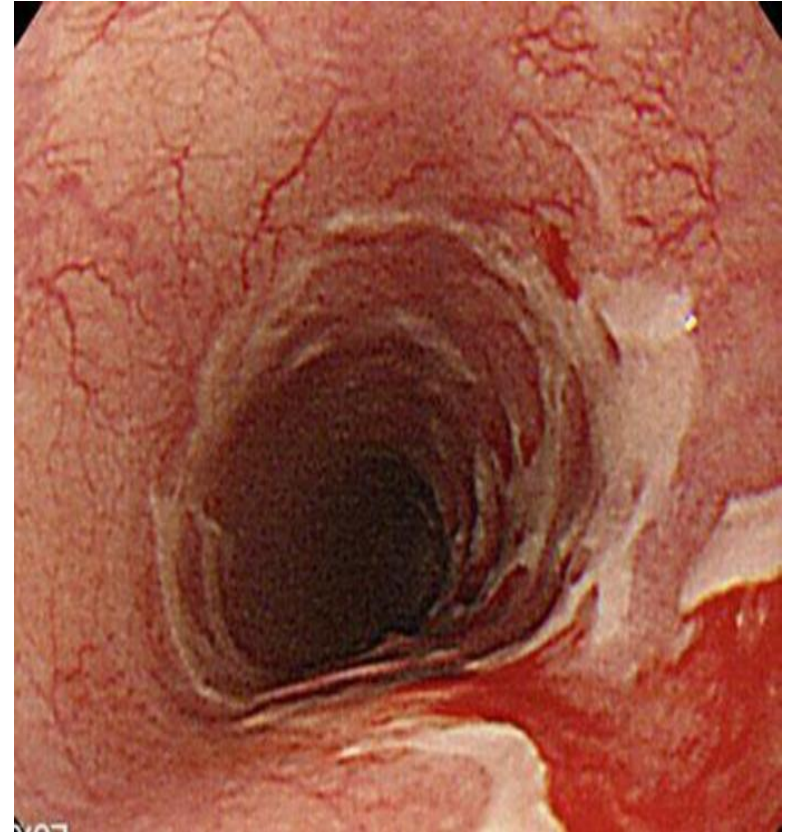


C) CMV immunohistochemical stain demonstrating intranuclear and cytoplasmic positivity in infected cells.



# Radiation Induced Esophagitis

- **Pathophysiology:**  
Involves DNA damage and cell death from high-energy electrons
- **Complications:**  
strictures, ulceration, fistula and perforation



**THANK YOU**