What's new for eosinophilic oesophagitis? A case-based discussion of patient care

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Exploring the pathophysiology and clinical manifestations of EoE

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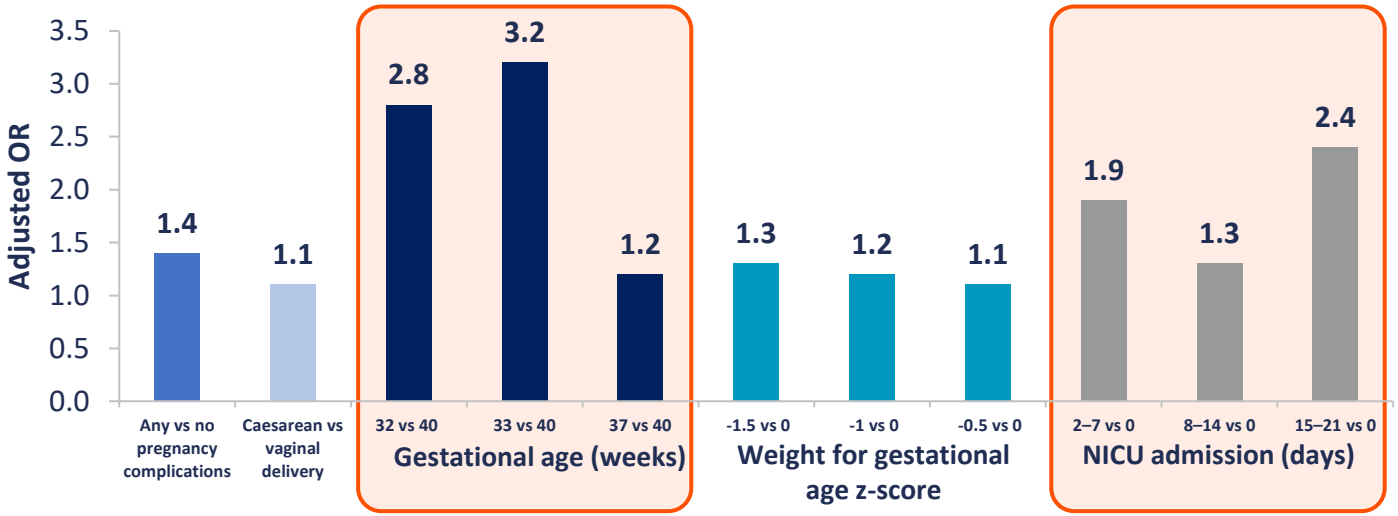
Perinatal factors and risk of EoE

Population and registry case-control study in Denmark, including all paediatric patients with EoE with birth years 1997–2018

n=393 EoE cases, n=3,659 controls (after exclusions for missing data)

Association of perinatal factors with the development of EoE



Perinatal factors, particularly preterm delivery and NICU admission, are associated with the development of EoE

EoE, eosinophilic oesophagitis; NICU, neonatal intensive care unit; OR, odds ratio.

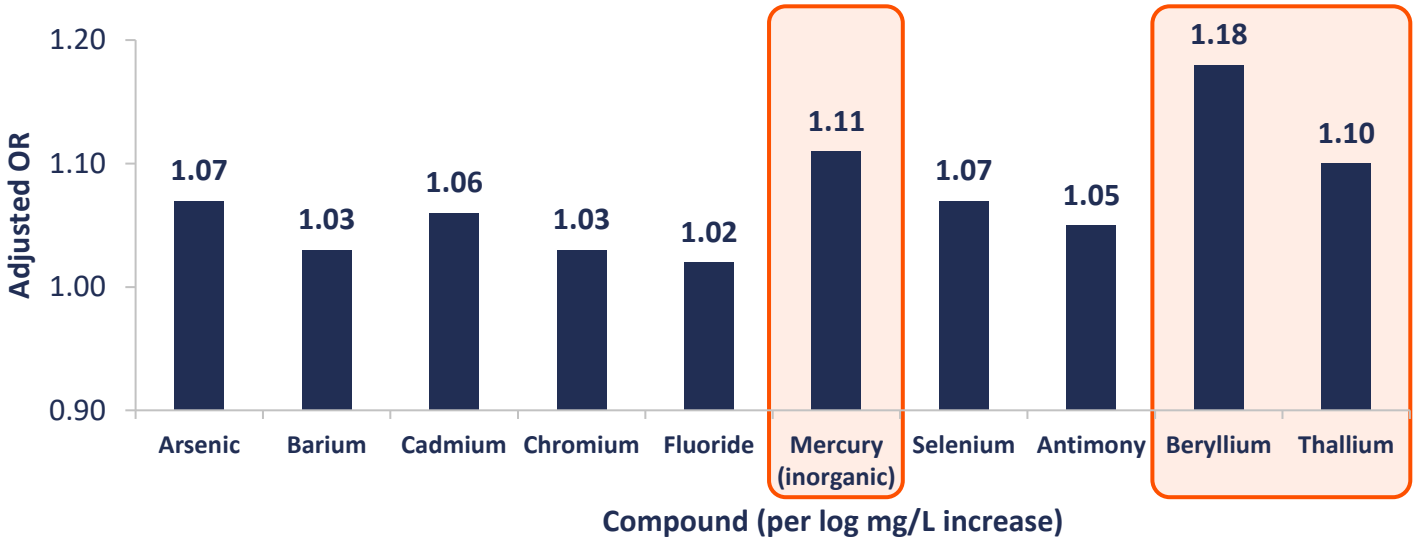
Kurt G, et al. Presented at: DDW 2022, Virtual/San Diego, CA. 21–24 May 2022. Poster Su1181.

Metal contaminants in drinking water and EoE

US-based case-control study in a pathology database of oesophageal biopsies

n=29,560 EoE cases, n=587,826 controls

Association between metal contaminants* in drinking water and having EoE



Data show a positive association between certain metal contaminants* in drinking water and having EoE, in particular thallium, inorganic mercury and beryllium

*Generated through manufacturing, mining, and refining processes.
EoE, eosinophilic oesophagitis; OR, odds ratio.
Siebrasse A, et al. Presented at: DDW 2022, Virtual/San Diego, CA. 21–24 May 2022. Poster Su1191.

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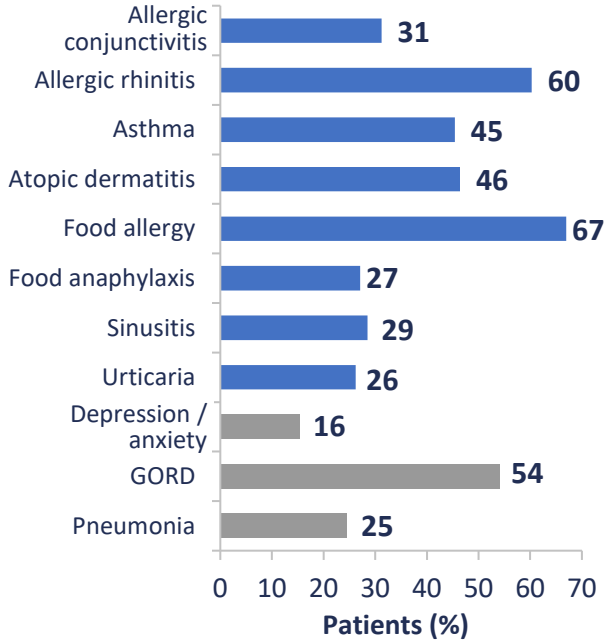
EoE and other type 2 inflammatory diseases

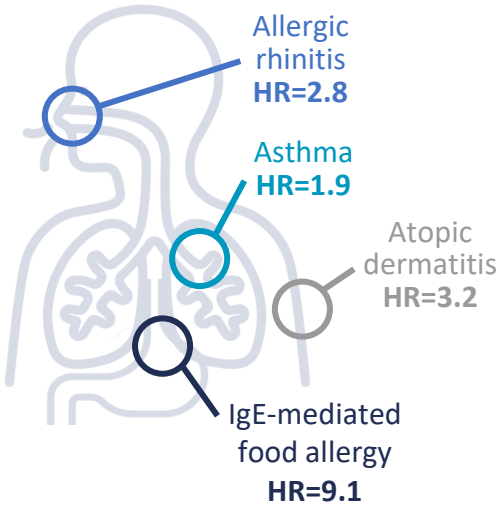
Comorbidities are prevalent in paediatric and adult patients with EoE[1]

Comorbidities in patients with EoE



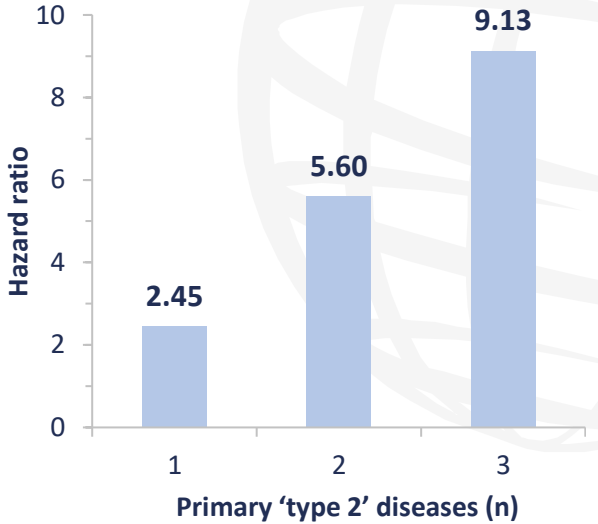
Primary type 2 diseases increase likelihood of a secondary EoE diagnosis[2]

Likelihood of secondary EoE diagnosis in patients with primary type 2 disease



Rate of EoE diagnosis is higher in those with ≥1 comorbid allergic disease[2]

Rate of EoE diagnosis by number of primary allergic diseases



EoE, eosinophilic oesophagitis; GORD, gastro-oesophageal reflux disease; HR, hazard ratio; IgE, immunoglobulin E.

1. Chehade M, et al. *J Allergy Clin Immunol Pract*. 2018;6:1534–44; 2. Hill DA, et al. *J Allergy Clin Immunol Pract*. 2018;6:1528–33.

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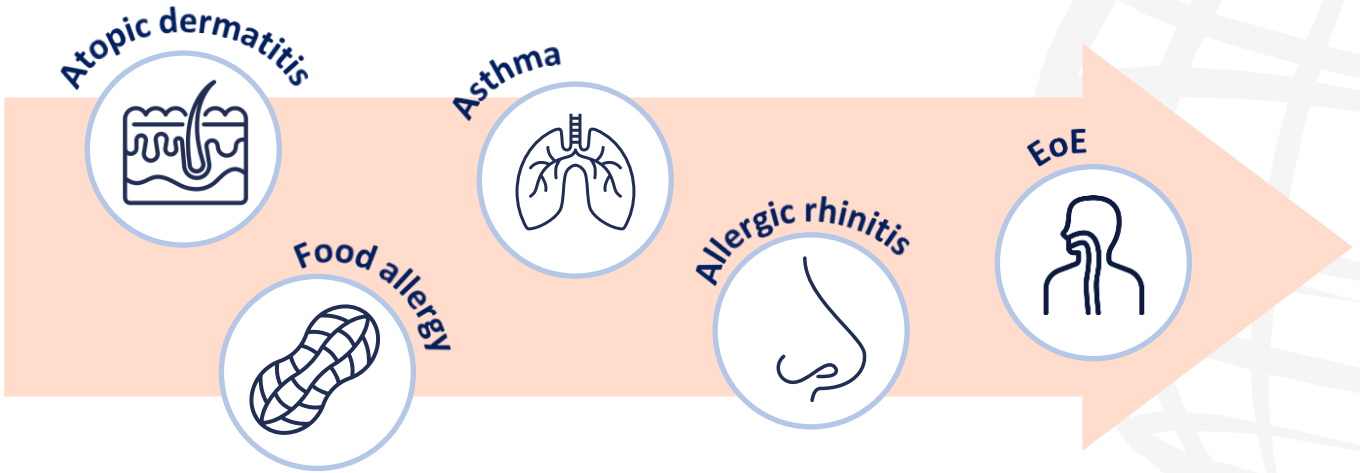
Allergic/atopic march

Influencing factors[1,2]

- Genetic
- Family history
- Environmental
- Immunological
- Psychosocial
- Microbiome

Allergic/atopic march[1,2]



Number and sequence of atopic conditions is variable[2]

EoE, eosinophilic oesophagitis; eos/hpf, eosinophils per high power field.

1. Capucilli P, Hill DA. *Clin Rev Allergy Immunol*. 2019;57:111–27; 2. Maiello N, et al. *Children (Basel).* 2022;9:450.

The role of IgG4 in EoE: Data from AAAAI 2022

	Masuda M, et al.[1]	Erwin E, et al.[2]	Li R-C, et al.[3]
Study details	Prospective assessment of food-specific IgG4 levels in plasma and upper GI tract in adults undergoing upper endoscopy	Investigation of the role of milk-specific IgG4 in EoE, in paediatric patients undergoing OGD	Pilot study investigating co-localization of IgG4 and milk proteins in patients from the UVA EoE cohort undergoing oesophageal biopsy
Study groups	Controls (n=15) Active EoE (n=24) Inactive EoE (n=8)	EoE (n=66) Non-EoE controls (n=113)	Active EoE (n=5) Remission (oral steroids; n=5) Remission (diet; n=5) Non-EoE controls (n=5)
Key findings	Median IgG4 for milk and wheat were elevated in plasma and throughout the upper GI tract in patients with active EoE vs controls	Associations between IgG4, symptoms and disease provide evidence that milk may be causal for EoE	IgG4-milk deposits were present in active EoE but significantly decreased in remission and controls; direct interactions may occur between IgG4 and milk proteins

AAAAI, American Academy of Allergy, Asthma & Immunology; EoE, eosinophilic oesophagitis; GI, gastrointestinal; IgG4, immunoglobulin G4; OGD, oesophago-gastro-duodenoscopy; UVA, University of Virginia.

1. Masuda M, et al. *J Allergy Clin Immunol.* 2022;149:AB210; 2. Erwin E, et al. *J Allergy Clin Immunol.*2022;149:AB209. 3. Li R-C, et al. *J Allergy Clin Immunol.* 2022;149:AB201.

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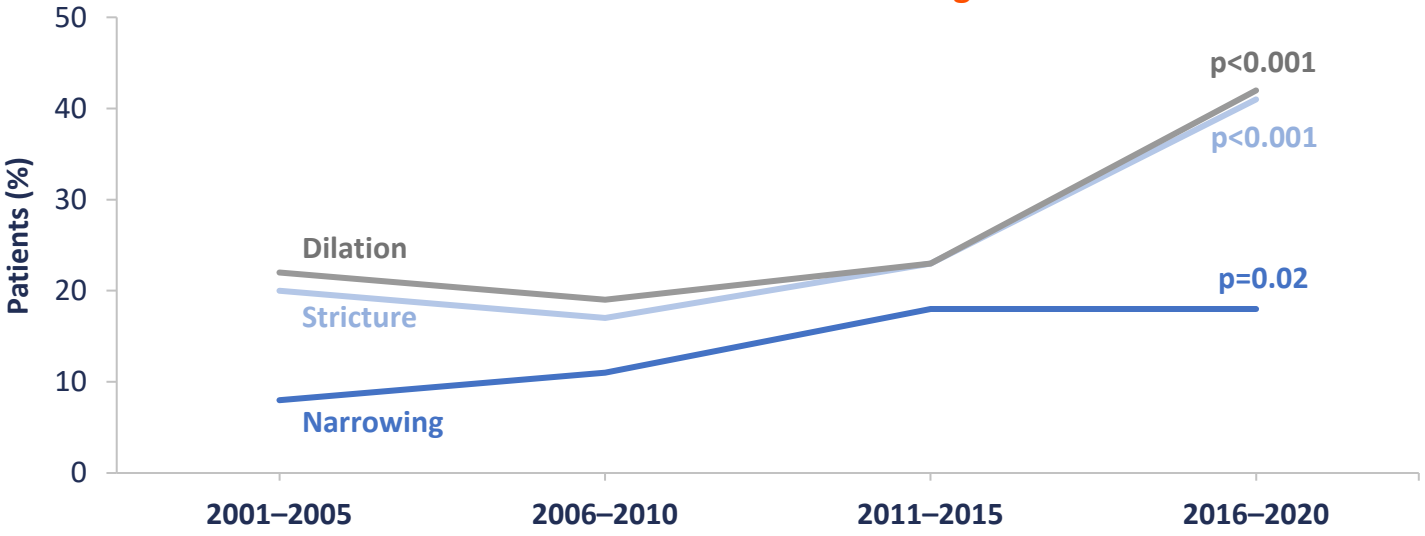
Clinical manifestations of EoE

Retrospective cohort study of patients in the University of North Carolina EoE Clinicopathologic Database

- N=1,064 adults and children with EoE

EoE clinical characteristics at diagnosis



18% increase in odds of stricture annually after accounting for age and symptom length pre-diagnosis (aOR 1.18, 95% CI 1.12–1.23)

aOR, adjusted odds ratio; CI, confidence interval; EoE, eosinophilic oesophagitis.
Greenberg SB, et al. Presented at: DDW 2022, Virtual/San Diego, CA. 21–24 May 2022. Poster Su1193.

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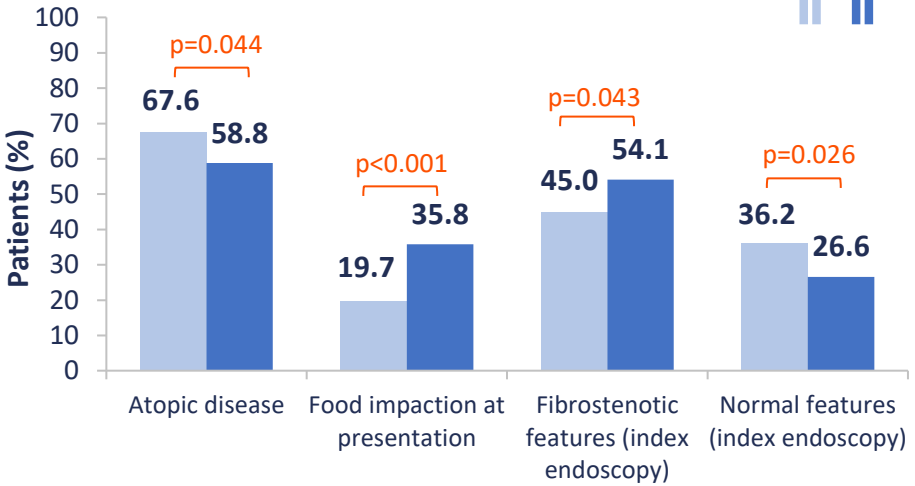
Clinical manifestations of EoE

US-based retrospective single-centre observational study of medical records of patients with EoE (n=489)[1]

Sex differences in EoE clinical features



Odds of dilation, males vs females: OR 1.985, p<0.01

US-based retrospective, case-control study on patients with food bolus who had OGDs (N=146, n=51 with EoE)[2]

Seasonal variation in food bolus cases

Spring/summer vs autumn/winter

Patients with EoE

65% vs 35%

p=0.0027

Patients without EoE

55% vs 45%

p=0.3173

aOR, adjusted odds ratio; CI, confidence interval; OGD, oesophago-gastro-duodenoscopy; EoE, eosinophilic oesophagitis; OR, odds ratio.

1. Folga R, et al. Presented at: DDW 2022, Virtual/San Diego, CA. 21–24 May 2022. Poster EP1110; 2. Alali F, Piper MS. Presented at: DDW 2022, Virtual/San Diego, CA. 21–24 May 2022. Poster Su1198.

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Managing EoE: Diagnosis and treatment of paediatric patients

Dr Mário Vieira

Centre for Paediatric Gastroenterology
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Curitiba, PR, Brazil

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Case presentation

Presentation and history

Age: 6 years

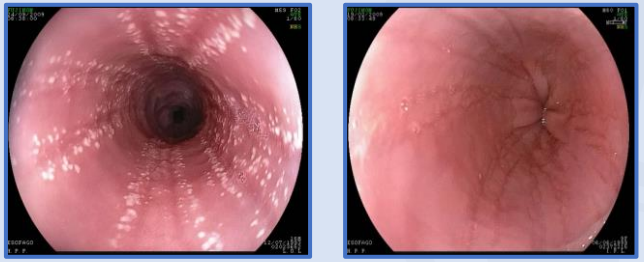
Presentation: Feeding difficulties, mild abdominal pain, occasional vomiting, gagging when eating since 4 years of age. Avoids meat and fruit unless pureed, prefers liquids and eats slowly. His mother reports that he drinks after every bite. His weight gain began to slow a year ago, then stopped completely 6 months ago

Personal medical history: Asthma and allergic rhinitis

Family history: Father has asthma and reflux symptoms with frequent heartburn

Clinical examination

Endoscopy: White exudates, mucosal oedema and linear furrows



Biopsy: up to 63 eos/hpf

Blood tests: Complete blood count and basic biochemical tests were normal, no eosinophilia

EoE, eosinophilic oesophagitis; eos/hpf, eosinophils per high power field.
Images provided courtesy of Dr Mário Vieira.

Clinical manifestations of EoE during childhood

Infants and toddlers[1]

- Feeding aversion/ intolerance
- Vomiting
- Food refusal
- Choking during meals
- Failure to thrive
- Sleep disturbance

Children[1]

- Dysphagia
- Food impactions
- Vomiting/regurgitation
- Choking/gagging with coarse textures
- Abdominal/chest pain
- Throat pain
- Nausea
- Sleep disturbance
- Decreased appetite

Adolescents[2]

- Dysphagia
- Food impactions
- Heartburn
- Gastro-oesophageal reflux

EoE, eosinophilic oesophagitis.

1. Carr S, et al. *Allergy Asthma Clin Immunol.* 2018;14(Suppl. 2):58; 2. Barni S, et al. *Ital J Pediatr*. 2021;47:230.

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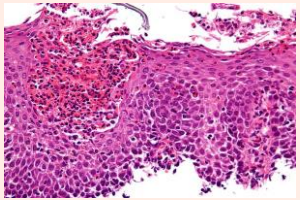
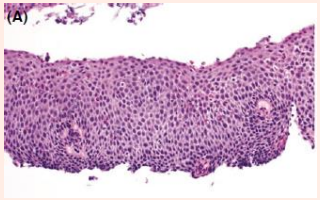
Endoscopic and histopathological manifestations of EoE

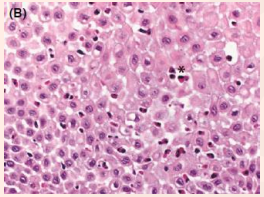
Histopathological findings



≥15 eos/hpf[1]
(required for diagnosis)



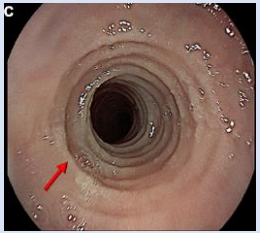
Basal cell hyperplasia[2]



Dilated intercellular spaces[2]

Endoscopy findings (EREFS)

Oedema[3]



Concentric rings[3]

Vertical furrows[4]

White exudates[4]

EoE, eosinophilic oesophagitis; eos/hpf, eosinophils/high-power field; EREFS, endoscopic reference score.

1. Image from Wikimedia Commons. Eosinophilic esophagitis – very high mag. Available at: https://commons.wikimedia.org/wiki/File:Eosinophilic_esophagitis_-_very_high_mag.jpg (accessed 18 July 2022). License for use under the Creative Commons Attribution-Share Alike 3.0 Unported (https://creativecommons.org/licenses/by-sa/3.0/deed.en); 2. Warners MJ, et al. *Aliment Pharmacol Ther*. 2018;47:940–50; 3. Racca F, et al. *Front Physiol*. 2022;12:815842; 4. Images provided courtesy of Dr Mário Vieira.

Treatment approach for children with EoE

Step 1

Discuss available treatment options with patient and carer[1–3]

Considerations:[2]

- Age
- Treatment burden
- Anticipated efficacy
- Disease severity
- Availability of treatments and staff, e.g. dietitians

Step 2

Initiate treatment

Diet therapy[1,3]

- Empiric elimination
- Elemental

Medical therapy[1,3,4]

- PPIs
- TCS
- *Dupilumab**

Step 3

Review clinical and histological response regularly[1,2]

Response:[1,3,5]

- Maintain current regimen

No response:

- Rule out non-adherence
- Escalate current regimen
- Switch/add treatment
- Mechanical dilation

*Dupilumab is approved by the FDA for patients ≥12 years of age with EoE weighing ≥40 kgs.

EoE, eosinophilic oesophagitis; FDA, US Food and Drug Administration; PPI, proton pump inhibitor; TCS, topical corticosteroids.

1. Barni S, et al. *Ital J Pediatr*. 2021;47:230; 2. Hirano I, Furuta GT. *Gastroenterology.* 2020;158:840–51; 3. Gutiérrez Junquera C, et al. *An Pediatr (Engl Ed).* 2020;92:376.e1–376.e10;
4. FDA. Dupilumab PI. 2022. Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2022/761055s040lbl.pdf (accessed 7 June 2022);
5. Gonsalves NP, Aceves SS. *J Allergy Clin Immunol.* 2020;145:1–7.

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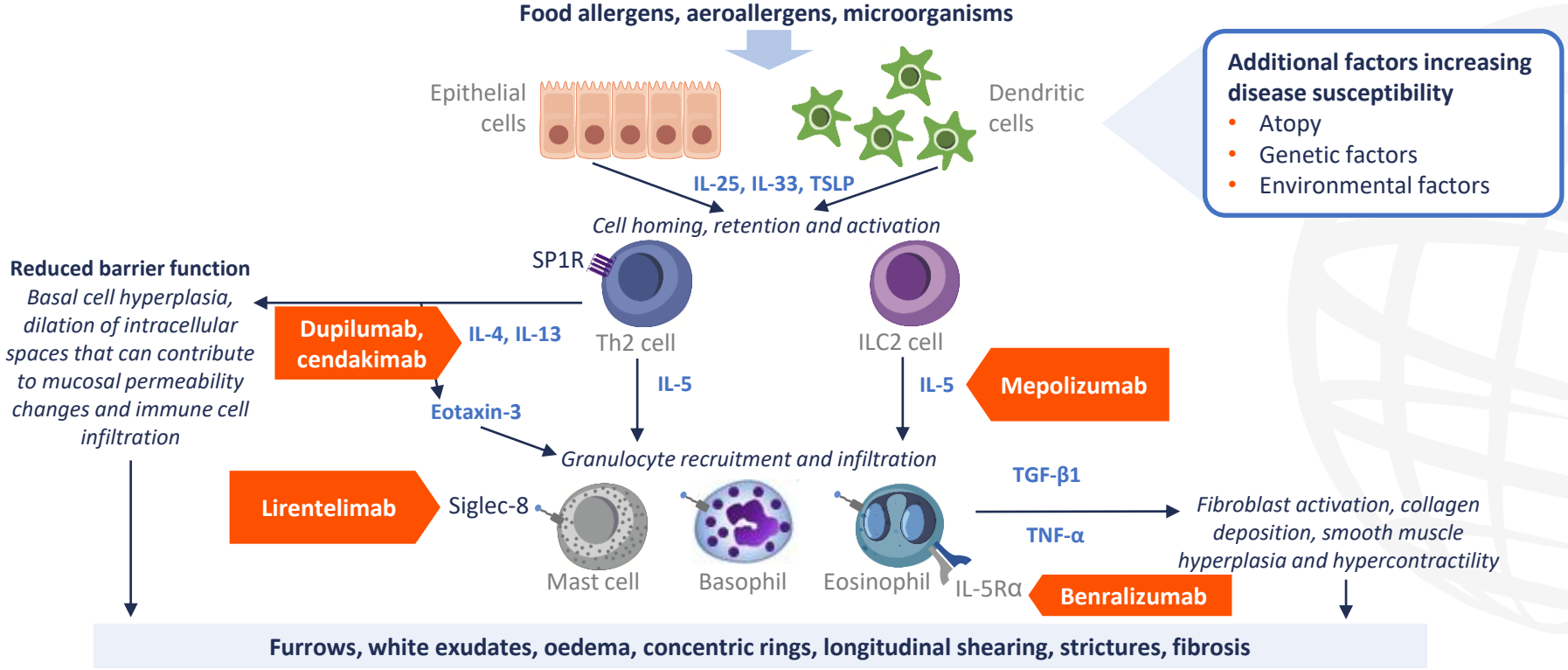
Agents in development targeting EoE pathophysiology[1–5]



EoE, eosinophilic oesophagitis; IL-5Rα, interleukin-5 receptor α; ILC2, type 2 innate lymphoid cells; Siglec-8, sialic acid-binding Ig-like lectin 8; SP1R, sphingosine-1-phosphate receptor; TGF-β, transforming growth factor-β; Th2, T-helper cell type 2; TNF-α, tumour necrosis factor-α; TSLP, thymic stromal lymphopoietin.

1. Muir A, Falk GW. *JAMA*. 2021;326:1310–8; 2. Racca F, et al. *Front Physiol*. 2022;12:815842; 3. Furuta GT, Katzka DA. *N Engl J Med.* 2015;373:1640–8; 4. Hill DA, Spergel JM. *J Allergy Clin Immunol*. 2018;142:1757–8; 5. Lam AY, et al. *Curr Opin Pharmacol.* 2022;63:102183.

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Monitoring disease activity in children with EoE

Currently used monitoring tools and techniques

Histologic/ endoscopic	Endoscopy and biopsy (eos/hpf, EREFS, additional features, e.g. basal cell hyperplasia)[1,2]
Clinical/ symptoms	Dysphagia Symptom Questionnaire (DSQ), Pediatric EoE Symptom Score (PEESS) v2.0[2]

Emerging monitoring tools and techniques

Histologic/ endoscopic	Transnasal endoscopy, oesophageal string test, oesophageal sponge, biophotonic imaging, EoEHSS[1–3]
Functional	Functional lumen imaging probe, mucosal impedance, high-resolution manometry, endoscopic ultrasound[1–4]
Biomarkers	Serum/blood/urine, immunohistochemical, epigenetic[3,5]
Clinical/ histologic/ endoscopic	Index of Severity for EoE (I-SEE)[6]

EoE, eosinophilic oesophagitis; EoEHSS, the EoE Histologic Severity Score; eos/hpf, eosinophils per high power field; EREFS, endoscopic reference score.

1. Nguyen N, et al. *Front Pediatr*. 2021;9:713027; 2. Godwin B, et al. *Ann Allergy Asthma Immunol*. 2020;124:240–7; 3. Hiremath G, Gupta SK. *Clin Gastroenterol Hepatol*. 2017;15:1655–64; 4. Pytrus T, et al. *Pediatr Rep*. 2022;14:13–9; 5. Votto M, et al. Acta Biomed 2021;92(Suppl. 7):e2021530; 6. Dellon ES, et al. *Gastroenterology*. 2022; 163:59–76.

Index of Severity for EoE (I-SEE)

Scoring:

Total score:
<1: Inactive EoE
1–6: Mild active EoE
7–14: Moderate active EoE
≥15: Severe active EoE

Points are accrued for each EoE feature a patient has

Assessed at initial diagnosis and each subsequent visit

Features assessed:

Symptoms	Based on frequency of occurrence: weekly, daily, multiple times per day or when disrupting social functioning
Complications	Food impaction requiring ER visit or endoscopy; hospitalization due to EoE; perforation; malnutrition; need for elemental formula, systemic steroids or immunomodulatory treatment
Inflammatory features	**Endoscopic:** localized or diffuse oedema, furrows, and/or exudates **Histologic:** 15–60 eos/hpf or >60 eos/hpf
Fibrostenotic features	**Endoscopic:** rings/strictures present, but endoscope passes easily or requires dilation **Histologic:** basal zone hyperplasia, lamina propria fibrosis or surface epithelial alteration and dyskeratotic epithelial cells

Included steering committee, session chairs, presenters, working group.
EoE, eosinophilic oesophagitis; eos/hpf, eosinophils per high power field; ER, emergency room.
Dellon ES, et al. *Gastroenterology*. 2022;163:59–76.

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Managing EoE: Diagnosis and treatment of adult patients

Prof. Arjan Bredenoord

Amsterdam University Medical Center
Amsterdam
Netherlands

Patient case

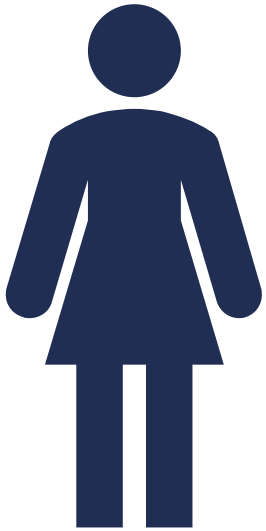
Presentation and history

Age: 29 years

Presentation: Symptoms of epigastric discomfort, heartburn and dysphagia over the past 5 years, which has led to adaptation of eating habits, e.g. drinking after every bite of food

Personal medical history: Allergies to nuts, soy and legumes. The patient attempts to maintain a targeted elimination diet for her allergies, but admits she is not consistently adherent

Family history: None reported



Clinical examination

Endoscopy: Furrows, rings, mucosal oedema

Biopsy: Up to 63 eos/hpf

Blood tests: Complete blood count and basic biochemical tests were normal, no eosinophilia

EoE, eosinophilic oesophagitis; eos/hpf, eosinophils per high power field.
Image provided courtesy of Prof. Arjan Bredenoord.

GORD: A key differential diagnosis for EoE[1,2]

Feature	EoE	GORD
Dominant symptom	Dysphagia	Heartburn, regurgitation
Food impaction	Common	Uncommon
Gender	Male predominance (3:1)	Male = female
Endoscopic findings	Oedema, rings, exudates, furrows, strictures, crêpe paper oesophagus, narrow calibre oesophagus. Minority have normal findings	Erosions, ulcers, Barrett's adenocarcinoma, strictures. Majority have normal findings
Histology, eos/hpf	≥15	<5
Aetiology	Immune-mediated or antigen-mediated response	Acid reflux
Associated atopic conditions	Allergic asthma, atopic dermatitis and allergic rhinitis	None
Ambulatory pH testing	Usually negative, sometimes positive	Positive

EoE, eosinophilic oesophagitis; eos/hpf, eosinophils per high power field; GORD, gastro-oesophageal reflux disease.

1. Attwood SE. *Br J Hosp Med (Lond).* 2019;80:132–8; 2. Capucilli P and Hill DA. *Clin Rev Allergy Immunol.* 2019;57:111–27.

Current treatment options for adults with EoE

Proportion of patients achieving histological remission (<15 eos/hpf)*

PPIs	TCS	Diet†	Dupilumab‡	Mechanical dilation
				
49.6%[1]	64–94.9%[2–4]	45.5–90.8%[5]	58.8%[6]	No effect[7]

*Data are from trials that differed in therapy, dosage and administration methods, but with homogeneous cut-offs of <15 eos/hpf indicating histologic remission; †Response varied by diet type: allergy test-directed food elimination was associated with lowest remission rates, elemental diet has highest remission rates; ‡In the US.
EoE, eosinophilic oesophagitis; eos/hpf, eosinophils/high power field; PPI, proton pump inhibitor; TCS, topical corticosteroids.

1. Lucendo AJ, et al. *Clin Gastroenterol Hepatol.* 2016;14:13–22; 2. Lucendo AJ, et al. *Gastroenterology*. 2019;157:74–86; 3. Butz BK, et al. *Gastroenterology*. 2014;147:324–33; 4. Dellon ES, et al. *Gastroenterology*. 2019;157:65–73; 5. Arias Á, et al. *Gastroenterology.* 2014;146:1639–48; 6. Rothenberg M, et al. *J Allergy Clin Immunol.* 2022;149:AB312; 7. Visaggi P, et al. *Ther Adv Gastroenterol*. 2021;14:doi: 10.1177/1756284820980860.

Emerging therapies for adults with EoE

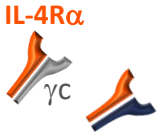
Etrasimod[1,2]
Phase II: NCT04682639 (VOYAGE)
Age 18–65 years
May 2023

Cendakimab[1,2]
Phase III: NCT04753697, NCT04991935
Age 12–75 years
July 2024; August 2026

Mepolizumab[1,2]
Phase II: NCT03656380
Age 16–75 years
July 2022

Benralizumab[1,2]
Phase III: NCT04543409 (MESSINA)
Age 12–65 years
May 2024

Lirentelimab[1,2]
Phase II/III: NCT04322708 (KRYPTOS)
Age 12–80 years
May 2022



Dupilumab[1,2]
Phase III: NCT03633617 (LIBERTY EoE TREET)
Age ≥12 years
July 2022

Phase IV: NCT05247866
Age 6–25 years
September 2025

EoE, eosinophilic oesophagitis; IL, interleukin; IL-4Rα, IL-4 receptor α subunit; IL-5R, IL-5 receptor; IL-5Rα, IL-5 receptor α subunit; IL-13Rα1, IL-13 receptor α subunit-1; siglec-8, sialic acid-binding Ig-like lectin 8; SP1R, sphingosine-1-phosphate receptor; Th2, T-helper cell type 2.

1. Racca F, et al. *Front Physiol*. 2022;12:815842; 2. ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/home (accessed 15 June 2022).

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Monitoring disease activity and treatment response in adults with EoE

Currently used monitoring tools and techniques

Clinical/ symptoms	Dysphagia Symptom Questionnaire (DSQ), EoE Activity Index (EEsAI)[1,2]
Histological	Biopsy (eos/hpf, additional features, e.g. basal cell hyperplasia)[1,2]
Endoscopy	EREFS[1,2]
Quality of life	Adult EoE Quality of Life Instrument (EoO-QOL-A)[1,2]

Emerging monitoring tools and techniques

Histological	String test, oesophageal sponge[1,2]
Functional	Functional lumen imaging probe, high-resolution manometry, endoscopic ultrasound[1,3-6]
Biomarkers	Serum/blood, immunohistochemical, epigenetic[7–10]

EoE, eosinophilic oesophagitis; eos/hpf, eosinophils per high power field; EREFS, endoscopic reference score.

1. Lucendo AJ, et al. *United European Gastroenterol J*. 2017;5:335–58; 2. Schoepfer A, et al. *Dis Esophagus*. 2016;29:959–66; 3, Pannala R, et al. *VideoGIE*. 2022;7:1–20; 4. Visaggi P, et al. Presented at: DDW 2022, Virtual/San Diego, CA. 21–24 May 2022. Poster Su1189; 5. Wong S, et al. *JGH Open*. 2020;4:851–5; 6. Pytrus T, et al. *Pediatr Rep*. 2022;14:13–9; 7. Votto M, et al. *Acta Biomed.* 2021;92(Suppl. 7):e2021530; 8. Venkateshaiah SU, et al. *Int J Basic Clin Immunol*. 2021;4:1–8; 9. Sarbinowska J, et al. *Biomolecules.* 2021;11:890; 10. Bhardwaj N, et al. *Allergy Rhinol (Providence)*. 2020;11:2152656720953378.