Exploring eosinophilic oesophagitis: How can multidisciplinary management improve outcomes?

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Expert panel

Prof. Jonathan Spergel
Children's Hospital of Philadelphia, Philadelphia, USA

Prof. Arjan Bredenoord
Amsterdam University Medical Center, Amsterdam, Netherlands

Dr Isabel Skypala
Royal Brompton and Harefield NHS Foundation Trust, London, UK

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Agenda

Pathophysiology of EoE: What do we see in patients?

Symptoms of EoE: What is the burden for patients?

Managing EoE: What options are emerging for patients?

EoE, eosinophilic oesophagitis.

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Conversation 1

Pathophysiology of EoE: What do we see in patients?

Prof. Jonathan Spergel
Allergist/immunologist

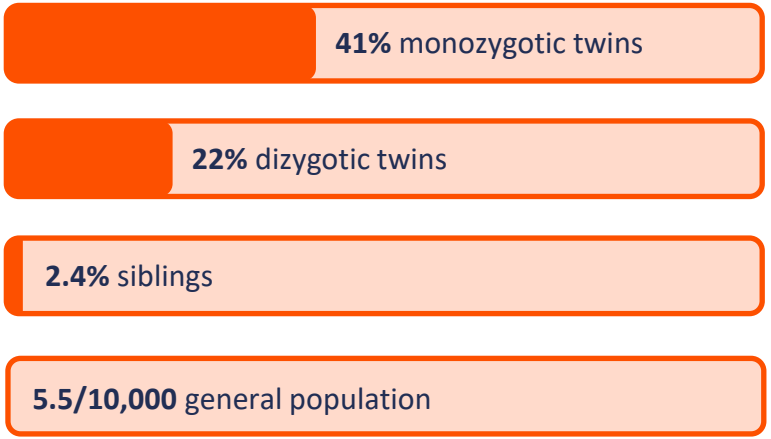
Prof. Arjan Bredenoord
Gastroenterologist

Environmental and genetic factors that contribute to EoE development

~3:1 male to female ratio[1]

Over 30 candidate genes identified, primarily affecting epithelial barrier function or Th2-mediated immune response[2,3]

EoE frequency in twins and siblings compared with general population prevelance[4]



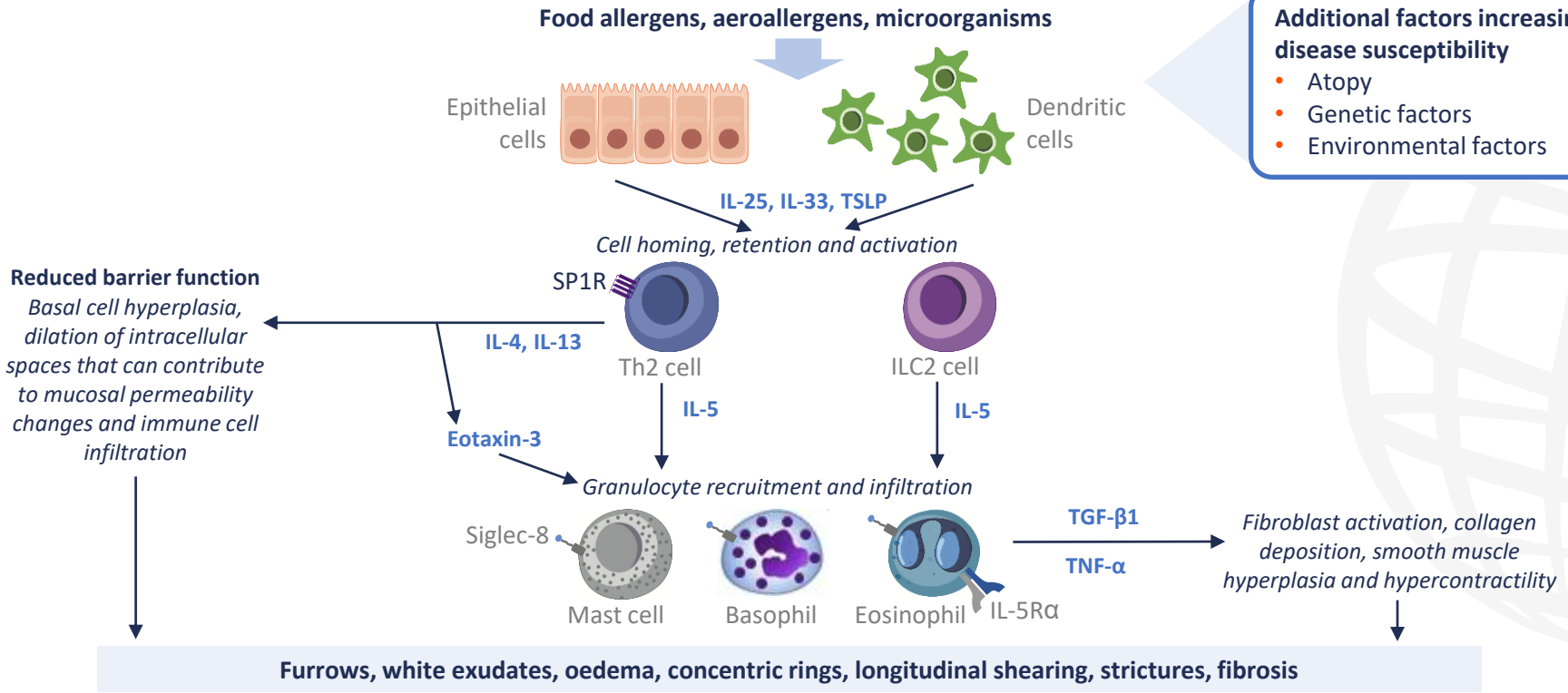
Environmental risk factors associated with EoE

- Pre-term labour[1]
- Caesarean delivery[1,5]
- Supplemented breastfeeding[1,5]
- Neonatal ICU admission[1,5]
- Antibiotic or anti-secretive drug use in infancy[1,5]
- Furred pet ownership in infancy[5]
- *Helicobacter pylori*

EoE, eosinophilic oesophagitis; ICU, intensive care unit; Th2, T-helper cell type 2.

1. Lucendo AJ, et al. *Ther Adv Gastroenterol*. 2022;15:1–16; 2. Lyles J, Rothenberg M. *Curr Opin Immunol*. 2019;60:46–53; 3. Muir A, Falk GW. *JAMA*. 2021;326:1310–18; 4. Alexander ES, et al. *J Allergy Clin Immunol*. 2014;134: 1084–92; 5. Jensen ET, Dellon ES. *J Allergy Clin Immunol*. 2018;142:32–40.

EoE pathophysiology[1–5]



IL-5Rα, IL-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;326:1310–18; 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.

Conversation 2

Symptoms of EoE: What is the burden for patients?

Prof. Jonathan Spergel
Allergist/immunologist

Prof. Arjan Bredenoord
Gastroenterologist

Dr Isabel Skypala
Dietitian

Clinical case – Martin

PATIENT HISTORY

- Male, 33 years old
- Personal history of rhinitis and asthma, diagnosed in late teens
- Family history of allergy and asthma
- Non-smoker, social drinker

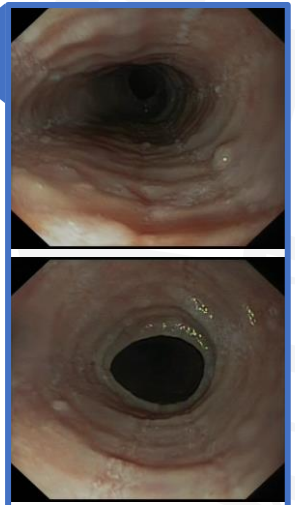
- Presents in A&E with food impaction
- Over the last 5 years, dysphagia has become more severe and he frequently experiences heartburn when eating
- Reports adapting his eating habits to try to reduce future impactions, and having a fear of eating solids
- Symptoms are impacting his mood and social life

CLINICAL EXAMINATION

Endoscopy:
- White exudates
- Mucosal oedema with multiple rings
- Linear vertical furrows in oesophageal mucosa

Biopsy:
- Eosinophils: up to 48/hpf

Blood tests:
- Complete blood count and basic biochemical tests were normal
- No eosinophilia



Endoscopy findings

A&E, accident and emergency department; hpf, high power field.
Images provided courtesy of Prof. Arjan Bredenoord.

Conversation 3

Managing EoE: What options are emerging for patients?

Prof. Jonathan Spergel
Allergist/immunologist

Prof. Arjan Bredenoord
Gastroenterologist

Dr Isabel Skypala
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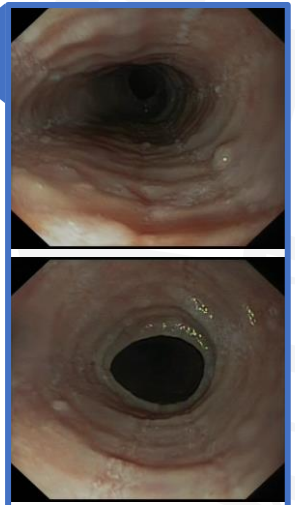

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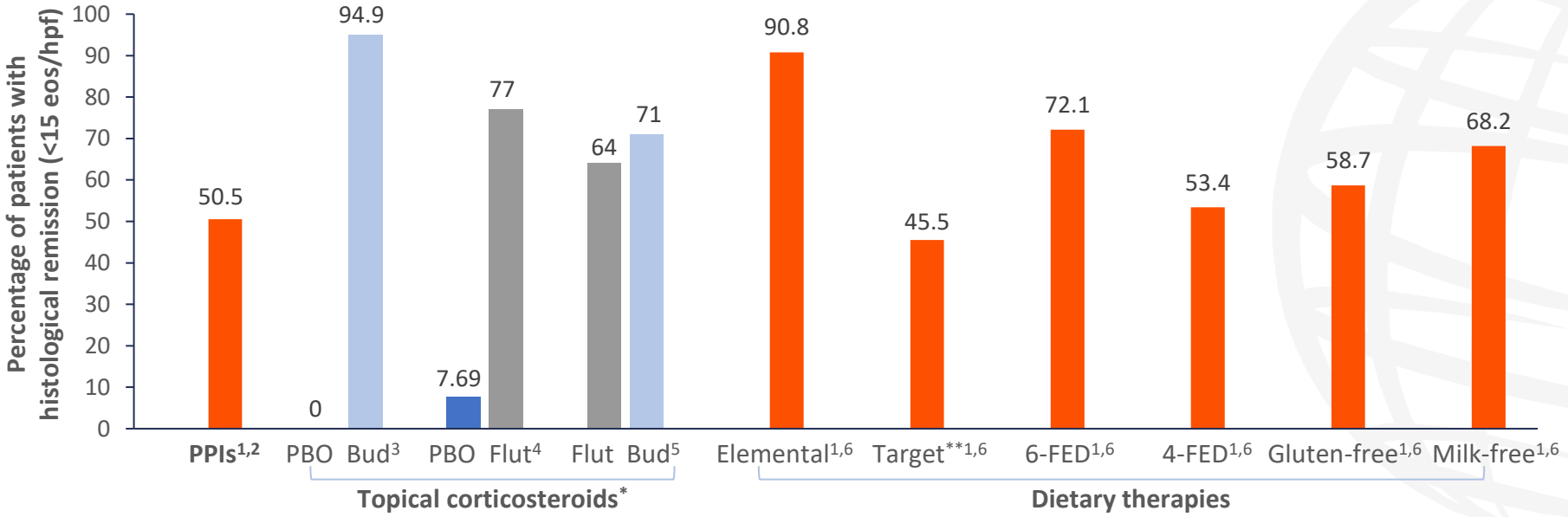
Histological remission with therapeutic interventions in EoE



*Data regarding the efficacy of topical corticosteroids are from randomized placebo-controlled trials that differed in medication, dosages, administration methods, but with homogeneous cut-offs of <15 eos/hpf indicating histologic remission; **Allergy test result–directed food elimination.

Bud, budesonide; EoE, eosinophilic oesophagitis; eos, eosinophils; 4-FED, four-food elimination diet; 6-FED, six-food elimination diet; flut, fluticasone; hpf, high power field; PBO, placebo; PPI, proton pump inhibitor.

1. Visaggi P, et al. *Ther Adv Gastroenterol*. 2020;14:1–17; 2. Lucendo AJ, et al. *Clin Gastroenterol Hepatol.* 2016;14:13–22; 3. Lucendo AJ, et al. *Gastroenterology*. 2019;157:74–86; 4. Butz BK, et al. *Gastroenterology*. 2014;147:324–33; 5. Dellon ES, et al. *Gastroenterology*. 2019;157:65–73; 6. Arias Á, et al. *Gastroenterology.* 2014;146:1639–48.

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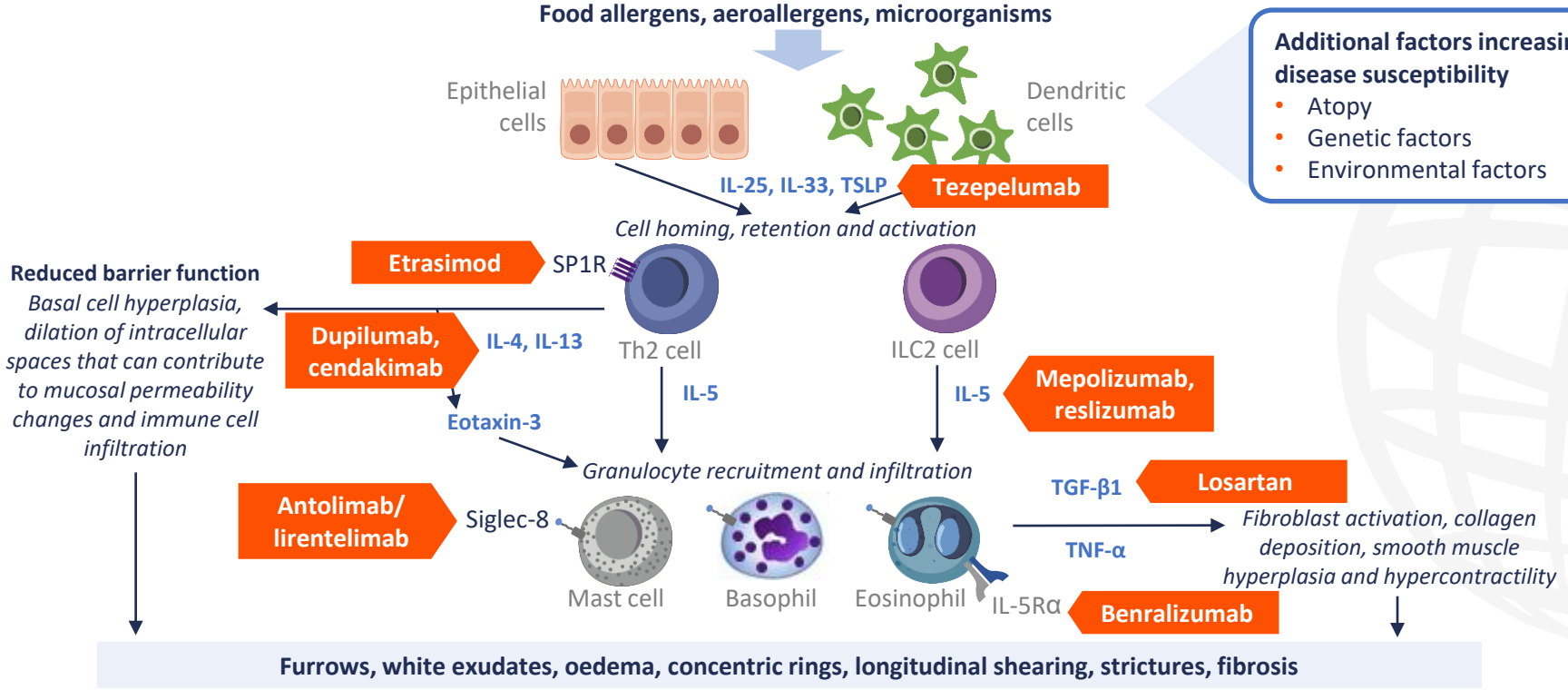
Agents in development targeting EoE pathophysiology[1–5]



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Dupilumab outcomes in EoE

Retrospective chart review of patients prescribed dupilumab for primary atopic disease* with a clinical diagnosis of EoE (N=45)[1]

Histology[1] (Follow-up, n=26)	Overall improvement (pre vus post dupilumab): 52.9 versus 4.5 eos/hpf, p<0.001 22 patients <6 eos/hpf
Improvement of EoE symptoms (Follow-up, n=34)[1]	28/28 patients 6 patients had no symptoms prior to starting dupilumab
Reduction in EoE medications/diet expansion[1]	29/29 patients

Dupilumab significantly improved histologic control of EoE, improved symptomatic control of EoE and reduced EoE medication/diet expansion, when initiated for primary atopic disease[1]

Three-part (A, B and C) placebo-controlled phase III trial of dupilumab in adolescents/adults with EoE (LIBERTY EoE TREET, NCT03633617)[2]

Part B: patients randomized to weekly dupilumab 300 mg (n=80) or placebo (n=79)[2]

Week 24 clinical and histologic outcomes with dupilumab vs placebo:[2]

Histological remission†	Dysphagia improvement	Safety
58.8% vs 6.3% (p<0.0001)	Least squares mean absolute changes in DSQ score: - 23.78 vs -13.86 (p<0.0001)	**Overall TEAEs:** 83.8% vs 70.5% **Most common TEAEs:** injection site reactions (37.5% vs 33.3%), fever (6.3% vs 1.3%)

Weekly dupilumab was associated with significant improvements in EoE symptoms over 24 weeks vs placebo, with a greater proportion of patients achieving histological remission; dupilumab had an acceptable safety profile[2]

*Reason for dupilumab prescription: AD (n=27), asthma (n=11), compassionate use (n=4), nasal polyps (n=3); †Peak oesophageal intraepithelial eosinophil count of ≤6 eos/hpf.
AD, atopic dermatitis; DSQ, Dysphagia Symptom Questionnaire; EoE, eosinophilic oesophagitis; eos, eosinophils; hpf, high power field; TEAE, treatment-emergent adverse event.
1. Spergel B, et al. *Ann Allergy Asthma Immunol*. 2022;00:1–5; 2. Rothenberg M, et al. *J Allergy Clin Immunol*.2022;149:AB312.

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