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Review article: the pathogenesis and management of eosinophilic oesophagitis

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SUMMARY

Background
Eosinophilic oesophagitis is a clinicopathological disease affecting both children and adults that is characterized by symptoms of gastro-oesophageal reflux disease (feeding refusal, vomiting, heartburn, dysphagia and food impaction) and dense oesophageal eosinophilia both of which are unresponsive to proton pump inhibition.

Aim
To present a review of the recent literature examining the pathogenesis and treatments of eosinophilic oesophagitis.

Methods
We performed a PubMed search for eosinophilic oesophagitis, pathogenesis and treatments.

Results
Translational and basic studies suggest that this disease is sparked by food or by aeroallergens. To date, effective treatments include systemic/topical corticosteroids, specific food elimination or an elemental diet. While several studies identified oesophageal strictures as potential complications of unbridled eosinophilia, the natural history of the disease is still not certain. Recent studies suggest a role for interleukin-5 and eotaxin-3 in the pathogenesis of eosinophilic oesophagitis and suggest an impact of future targeted therapeutic agents.

Conclusions
Eosinophilic oesophagitis represents a immune-mediated disease of undetermined pathogenesis. While many patients develop clinicopathological findings following ingestion of foods, others do not. Natural history studies will be critical to defining future treatment paradigms.

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CLINICAL FEATURES OF EOSINOPHILIC OESOPHAGITIS

Introduction

When Paul Ehrlich first identified the eosinophil – named for Eos, the Greek goddess of dawn – in 1879, little could he know that the questions posed by this cell would still intrigue scientists more than a century later. The function of the eosinophil in health remains ambiguous and with the increasing recognition of eosinophilic infiltrates in many gastrointestinal diseases, its mystery in pathology is slowly being addressed. Indeed, we stand at the dawn of understanding one of these diseases, eosinophilic oesophagitis (EoE). Within the last 5 years, the literature focusing on EoE increased dramatically thus expanding knowledge of this enigmatic disease. This review focuses on clinical features, pathogenesis and treatments of EoE in adults and children.

Definition

Eosinophilic oesophagitis is defined as a clinicopathological disease characterized by oesophageal symptoms and dense oesophageal eosinophilia both of which persist despite prolonged treatment with proton pump inhibitors (PPI). Eosinophilic inflammation is absent in the stomach, small intestine and colon. Importantly, eosinophilic inflammation of the oesophagus has been identified in patients with gastro-oesophageal reflux disease (GERD) but the range of epithelial eosinophilia is not certain.[1]

Epidemiology

Previously considered obscure, the startling prevalence of EoE has reached epidemic proportions. But is this a true rise in incidence or simply increased disease awareness? Noel *et al*. provided the first paediatric demographic data for EoE when they reported a fourfold increase in prevalence among children from the Midwest (US) from 2000 to 2003.[2] With the purpose of gathering adult demographic data, Straumann and Simon prospectively followed adult patients with EoE in central Switzerland; during a 16-year period, the prevalence increased from two per 100 000 inhabitants to 27 patients per 100 000 inhabitants, with an average annual incidence of 1.4.[3] Both North American and European studies were conducted in demographically stable areas and recording practices were consistent indicating a measurable increase in EoE cases, not just an enhanced disease awareness.

Many non-infectious, inflammatory gastrointestinal diseases are considered diseases of 'western' civilization, and EoE likewise falls into this category. More than 100 adults from all continents except Africa have been recently reported.[4–6] EoE occurs in all age groups but symptoms typically appear either in the early childhood, adolescence or before fourth decade of life. Males are more frequently affected with >70% of reported cases occurring in men.[7]

Presenting symptoms

Presenting symptoms in EoE vary, depending on patient's age. Adults typically present with dysphagia and food impaction.[8, 9] In a private practice setting, Desai *et al*. found that 17 of 31 adults presenting with food impaction showed clinicopathological findings consistent with a diagnosis of EoE.[10] Additionally, they determined that all 17 patients with EoE complained of dysphagia lasting from a few seconds to several hours. Similar findings were recognized in other large adult series.[4–6]

Children with EoE show a wider variety of symptoms, such as abdominal pain, chest pain, food impaction, failure to thrive, vomiting and GERD-like symptoms which are recalcitrant to acid blockade.[11–16] Such a broad spectrum of symptoms can be explained by oesophageal dysmotility that is difficult for children to clearly translate.

Natural history

Little is known about long-term outcomes of patients with EoE but evidence to date suggests that EoE is a chronic disease (personal communications and observations). Most affected adults recall a history of upper intestinal discomfort during childhood that was thought to be due to GERD or a functional cause. In retrospect, this was likely due to eosinophilic oesophageal inflammation.

Isolated oesophageal strictures or pan oesophageal narrowing are the only complications reported to date.[17] When this narrowing encompasses the length of the oesophagus, it is termed the 'small caliber esophagus', a finding probably resulting from long-standing eosinophilic inflammation with collagen deposition, fibrous remodelling. In the longest follow-up to date (11.5 years), Straumann *et al*. found strictures in 13 of

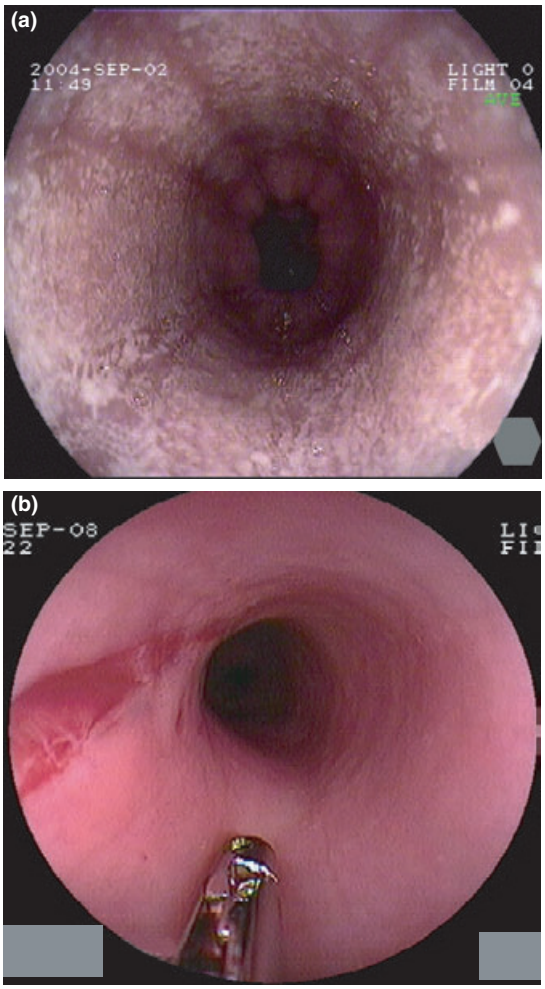

Figure 1. (a) Endoscopic picture of the oesophagus of a 26-year-old male patient with eosinophilic oesophagitis (EoE), suffering from dysphagia for 1 month. The image shows an oesophageal mucosa covered with white exudates, reflecting a highly active eosinophilic inflammation. (b) Endoscopic picture from the same patient, suffering still from dysphagia. This second endoscopy was performed exactly 1 year later and shows a rigid and crêpe-paper-like mucosa with a laceration after a contact with the biopsy forceps. This impressive metamorphosis illustrates the mucosal remodelling, which occurred during the first year in an untreated EoE.

30 patients.[6] Strictures are often resistant to medical intervention, thereby underscoring their fibrotic nature. Strictures are uncommon in children suggesting that this complication requires years of unbridled eosinophilic inflammation.

Even though strictures are the only known lasting complication, EoE can otherwise exert a marked impact on patient's daily life. In a prospective observational study of 30 adult EoE patients, Straumann *et al.* found that daily activities of over half of patients were negatively impacted by EoE. In all but one patient, dysphagia occurred on a regular basis.[6] No case of oesophageal carcinoma has been reported but long-term follow-up is required to confirm this.

An interesting subset of patients has intense oesophageal eosinophilia but no symptoms referable to the oesophagus. Upper endoscopic analysis was performed for bleeding or other non-oesophageal complaints and revealed endoscopic evidence of oesophageal inflammation and histological findings of significant oesophageal epithelial eosinophilia (personal observation and communications). The exact meaning of this finding is still uncertain; these patients could have early stages of EoE and will manifest symptoms eventually or could have experienced an incidental momentary exposure to an allergen leading to acute oesophageal inflammation. More longitudinal studies will be required to determine the correct treatment and follow-up of this group of patients.

Endoscopic findings

During oesophageal endoscopy, a heterogeneous mix of abnormalities are found including subtle reddish, longitudinal furrows, white nodule- or plaque-like exudates that mimic topical anaesthetic spray or fungal infections, transient or fixed corrugated rings, crêpe-paper mucosa due to a loss of the mucosal elasticity and strictures of variable length.[4, 10, 17, 18–31] Whitish exudates (see Figure 1a; representing eosinophilic abscesses) and longitudinal furrowing occur secondary to local oedema and acute inflammation. The crêpe-paper mucosa/fragile mucosa and strictures, are likely a consequence of the chronic eosinophilic inflammation (see Figure 1b).

Histological features and diagnostic criteria

Consensus opinion as to the histological diagnostic criteria for EoE is lacking. Most would agree that EoE is a clinicopathological disease whose diagnosis is made based on symptoms and characteristic histological findings (>20 eosinophils/high power field (HPF)) that do not respond to treatment with PPIs. Traditionally, the finding of intraepithelial eosinophils was associated with GERD but during the last decade, a significant body of evidence identified that large numbers (>20 eosinophils/HPF), eosinophilic

microabscesses, superficial layering of eosinophils along the luminal surface, basal zone hyperplasia and increased papillary size are all features highly suggestive of EoE in the proper clinical context.[13, 27, 32] EoE exclusively involves the oesophagus; gastric and duodenal biopsies are normal.

Clinical differences between EoE and GERD

Differentiating between EoE and GERD can be difficult.[32] Oesophageal eosinophilia can occur in patients with GERD but the degree of eosinophilia (numbers of eosinophils per HPF) and longitudinal extent of eosinophilia (proximal to distal oesophagus) is currently unknown. A recent case series suggests that patients with GERD can have similar endoscopic and histological findings similar to that seen in EoE. Ngo *et al.* reported three children with GERD-like symptoms, endoscopic findings of longitudinal furrowing, whitish exudates and >20 eosinophils/HPF. These patients responded both symptomatically and histologically to PPI providing strong evidence that these clinicopathological features occurred as a result of GERD. This case series emphasizes the importance of treating all children suspected of having EoE with high-dose PPI before assigning a final diagnosis of EoE.[1]

The recent translational study by Blanchard *et al.* brings molecular clarity to clinical suspicions that GERD and EoE are distinct.[33] In this study, microarray analysis was performed on oesophageal biopsy samples from three different patient populations: (i) patients with abdominal symptoms and normal oesophageal histology, (ii) patients with symptoms compatible with GERD and (iii) patients with clinicopathological features of EoE. Microarray analysis revealed a distinct EoE signature panel with eotaxin-3 being identified as the most upregulated gene. Additional basic studies utilizing a murine model of EoE in CCR-3 null mice provide further proof for the critical role of eotaxin-3 in the pathogenesis of this inflammation. Long-term outcomes of this study will hopefully bring novel markers and novel pharmacological interventions.

PATHOGENESIS OF EOSINOPHILIC OESOPHAGITIS

Introduction

The exact pathogenesis of EoE is uncertain. Oesophageal eosinophilia can be seen in a number of conditions including infections, autoimmune diseases, acid reflux disease, eosinophilic gastroenteritis or allergic/hypersensitivity responses.[34] Translational studies examining clinicopathological features of EoE have not identified infectious particles in the epithelium, have measured normal pH monitoring of the distal oesophagus in most patients[35, 36] and have not found evidence of autoimmune diseases. EoE only affects the oesophagus separating it from the more diffuse eosinophilia seen in eosinophilic gastroenteritis. These facts and an increasing body of clinical and basic evidence suggest that EoE is a distinct disease with a pathogenesis related to an immune-mediated response triggered by an exogenous allergen.

Eosinophil life cycle

Eosinophils reside predominantly in three anatomical compartments, the bone marrow, blood vessels and organs with mucosal surfaces. Eosinophils are born from bone marrow progenitor stem cells and mature to a fully granulated state before migration to vascular spaces. This process of proliferation and maturation is controlled by interleukin (IL)-5, IL-3 and granulocyte–macrophage colony-stimulating factor (GM-CSF) with IL-5 being the most specific for eosinophils. In addition to influencing selective differentiation of eosinophils, IL-5 also stimulates release of eosinophils from the bone marrow and extends their survival once in target tissues. Mice lacking IL-5 develop a significant reduction in mucosal eosinophilia whereas mice overexpressing IL-5 show markedly increased peripheral eosinophilia.[37]

Eosinophils tether, roll and diapedese as they leave the vascular space and enter the mucosa. This stepwise journey is orchestrated by Th2 cytokines (IL-4 and IL-13) that pave pathways and serve as chemoattractants providing a nidus for migration. IL-4 and IL-13 induce expression of cell surface ligands of the β-integrin family, such as VLA-4 on the surface of eosinophils surface, and their counter ligands on endothelia that include vascular cell adhesion molecule (VCAM)-1.[38] Eosinophil-specific chemoattractants, such as chemokines (eotaxin-1, eotaxin-2 and eotaxin-3), leukotriene B4 and platelet-activating factor, beckon eosinophil migration along a gradient that is released within local mucosal microenvironments.[39] Eotaxin is produced by a number of different cells including resident cells (epithelium, fibroblasts) and recruited cells (macrophages, eosinophils).[40, 41] Eotaxin binds to the chemokine

receptor CCR-3, a seven transmembrane G-protein-coupled receptor that is primarily expressed on eosinophils. Eotaxin is critical in maintaining eosinophil homeostasis in the gut as evidenced by the fact that eosinophils are absent from the gastrointestinal tract in mice lacking eotaxin-1.

Potential mechanisms of inflammation observed in eosinophilic oesophagitis

To date the pathogenesis of EoE is controversial. Clinical observations suggest that EoE results from an immune-mediated response to a swallowed allergen. For instance, when an amino acid-based formula is administered or specific food proteins are removed from diets, a clinicopathological remission occurs. One case report documents acute exacerbations in the spring and fall when the exposure to known aeroallergens, which may be swallowed, was most significant.[42] Personal and/or family history of allergic diseases including IgE-mediated food allergies, asthma, atopic dermatitis, allergic rhinitis and drug allergy are found in 50–91% of patients with EoE. In up to 90% of selected populations, peripheral eosinophilia can occur. Interestingly, up to 10% of patients with eosinophil gastrointestinal diseases have an immediate family member with the same disease suggesting a genetic predisposition.[43, 44] Despite these observations, the precise immune mechanism(s) that lead to symptoms and epithelial eosinophilia are uncertain.

IgE or non-IgE-mediated response?

An immunoglobulin (Ig)E-dependent mechanism for EoE is supported by clinical observations. For instance, Spergel and co-workers showed that affected patients have IgE sensitization to a wide variety of food including cow's milk, soy, peanuts, chocolate, wheat and egg.[12, 45, 46] In these patients, clinicopathological features of EoE resolve with dietary restriction and an amino acid-based formula.

However, not all patients demonstrate evidence of IgE sensitization, i.e. normal radioallergosorbent test (RAST) or skin prick tests. Spergel *et al.*[46] addressed this issue by performing skin prick and skin patch testing (SPT) in 26 children with EoE. Skin patch testing has been used in evaluations of patients with atopic dermatitis when seeking evidence of a delayed type hypersensitivity response. Skin patch testing consists of placing specific food proteins on the skin, covering it with a small disc and taping the disc in place. About 24–48 h later, the presence or the absence of swelling and measurement thereof is recorded. Results of this study showed that some children with negative RAST and skin prick testing but abnormal SPT for specific foods (see below in Treatment). Upon removal of those specific foods identified by SPT, most children underwent into remission.

Participation of Th2 cytokines

The pathogenesis of eosinophilic oesophageal inflammation has been examined in greater detail in basic animal models. Mishra *et al.* developed a murine model of oesophageal eosinophilia in which nasal and bronchial sensitization and challenge with the ubiquitous aeroallergen *Aspergillus fumigatus*, led to oesophageal but not gastric or small intestinal eosinophilia.[37] With the use of IL-5 and eotaxin null mice, Mishra *et al.*[37] demonstrated that this eosinophilia was IL-5-dependent and partially dependent on eotaxin.

Because of translational studies demonstrating increased expression of IL-13 in patients with EoE and because IL-13 is a critical Th2 cytokine thought to participate in other allergic diseases associated with eosinophilia, Mishra *et al.* and Blanchard *et al.* examined the impact of IL-13 in murine systems. Direct delivery of murine or human IL-13 into the pulmonary tree induced oesophageal eosinophilia[47] a finding that was blocked with antihuman IL-13 antibody,[48] and found to be diminished in IL-13 null mice. Finally, translational studies have shown that the affected squamous epithelium is immunologically rich in Th2 milieu containing increased numbers of CD8 and CD1a lymphocytes, mast cells extensively degranulated eosinophils and prominent expression of IL-5 and IL-13.[28, 49–52]

Taken together, these studies support a role for Th2 cytokines in the development of oesophageal eosinophilia. Future treatments may find basis in targeting specific molecules, such as IL-5, IL-13 or eotaxin-3. In fact, the use of anti-IL-5 antibody improved clinicopathological features in a teenager with EoE.[53]

Link between mucosal systems

Rothenberg and co-workers hypothesized that both skin and respiratory tracts contribute to the development of oesophageal eosinophilia. In the murine model

system of aerosensitization, both the trachea and oesophagus must be exposed to the *A. fumigatus* antigen for inflammation to occur. If *A. fumigatus* is applied only to the oesophagus or to the stomach alone, no oesophageal eosinophilia develops.[37] The skin has also been shown to participate in allergen sensitization in murine oesophageal eosinophilia.[54] Mice receiving skin sensitization to *A. fumigatus* develop oesophageal eosinophilia upon inhalation of the allergen. Together these findings provide evidence that the development of murine oesophageal eosinophilia relies on close relationships between the mucosal immune systems of the oesophagus, lung and skin.

Proposed effector roles for eosinophils in gastrointestinal disease

Previous studies document a potential role for eosinophils as proinflammatory effector leucocytes within mucosal target organs. Eosinophils contain a number of biologically active components including highly charged cationic proteins, cytokines [IL-1, IL-3, IL-4, IL-5, IL-13, GM-CSF, transforming growth factor (TGF)-β, tumour necrosis factor (TNF)-α, RANTES, MIP-1 and eotaxin-1], arachadonic acid mediators and lipid products that are associated with organ dysfunction.[35] For instance, inflamed oesophageal tissues contain increased extracellular deposition of cationic proteins, such as major basic protein and the stool effluent of patients with inflammatory bowel disease contains increased concentrations of granule proteins suggesting that activated eosinophils release proinflammatory mediators at mucosal sites.[10] At concentrations found in human tissues, major basic protein (MBP) can diminish tight junctional molecule expression in epithelial cells,[55] induce organ contraction,[56–58] remodel nerves[59, 60] and stimulate mast cell and basophil degranulation[61–63] in *in vitro* model systems.

While the natural history of EoE remains obscure, the fact that some patients develop oesophageal narrowing and strictures is of concern. Leukotriene C4 is metabolized to LTD4 and LTE4 both of which posses a large profile of actions including increasing mucus secretion and vascular permeability and stimulating smooth muscle contraction. This last action is quite important because obstructive symptoms may be related to dynamic smooth muscle contraction.[64] Alternatively, obstructive symptoms could occur secondary to epithelial proliferation and extracellular matrix remodelling, processes linked to eosinophil-derived TGF-β.[65, 66]

TREATMENT OF EOSINOPHILIC OESOPHAGITIS

Approach to management

No consensus exists regarding optimal treatment of patients affected by EoE. Factors deserving consideration when deciding on the best treatment for an individual patient include the patient's age, impact of symptoms on quality of life, impact of treatments on quality of life and comorbid disease(s). Effective treatments for EoE include systemic[15] or topical corticosteroids,[52, 67–70] specific elimination diets,[46] elemental diets[12, 71, 72] and oesophageal dilation.[6, 8]

Treatment decisions require examination of the impact that EoE has on patient's lives and the expected long-term outcomes. As described previously, children can present with symptoms significant enough to affect growth, development or lifestyle. Although the natural history of this disease has yet to be fully determined, some patients with EoE develop oesophageal strictures. The duration of time that is required for this complication to develop and its potential reversibility with non-invasive treatments are both unknown.

Thus, clinical experiences and the published literature support a stance that children with EoE should receive nutritional or medical treatment. On the other hand, personal experiences and clinical reports suggest that a substantial fraction of adults benefit more from oesophageal dilation than from medical or nutritional treatment. This must be performed with extreme caution as oesophageal rupture and shearing can occur as a complication[73, 74] (see Figure 2).

Nutritional treatments

Two types of nutritional management demonstrate effectiveness in the treatment of EoE. The effectiveness of these treatments relies on the fact that specific or dietary antigens that invoke this eosinophilic response are removed. Kelly *et al.* were first to identify the successful impact of elemental diets on clinicopathological features of EoE.[72] In this study, 10 children with EoE received amino acid-based formula. At the end of treatment, all patients had resolution of symptoms and significant improvement in oesophageal eosinophilia. Likewise Markowitz *et al.* demonstrated the effectiveness of an elemental diet in 51 patients with EoE. Within 8.5 days patient's symptoms and histopathology improved significantly.[71]

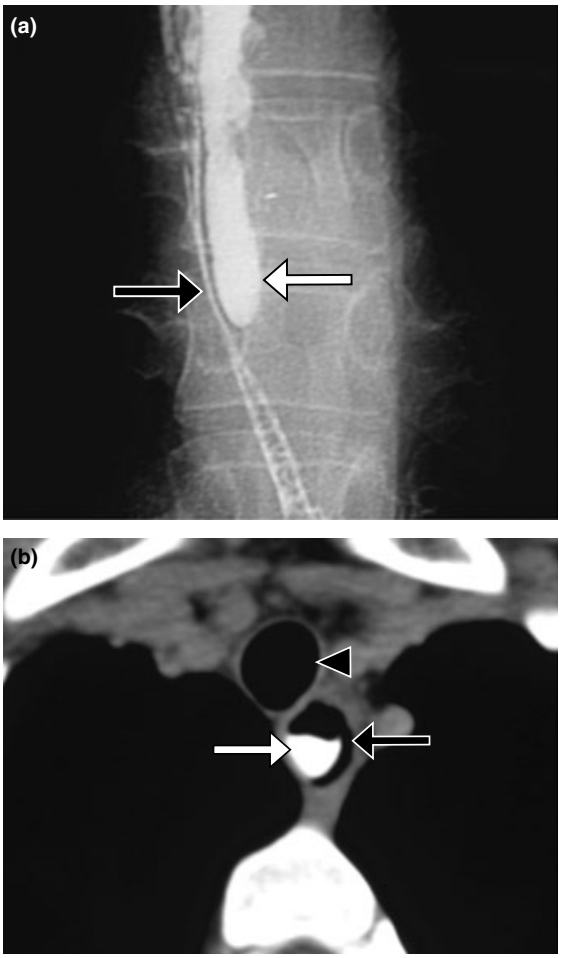

Figure 2. (a) Oesophagography from a 35-year-old female patient, suffering from dysphagia for 15 years. This radiograph was performed immediately after an attempt to remove an impacted food bolus by rigid oesophagoscopy and shows a long dissection of the oesophageal wall. Laceration, dissection and perforation are well known complications of the inflammation-induced remodeling of the oesophageal mucosa. White arrow: oesophageal lumen; Black arrow: dissection channel. (b) CT scan from the same patient, performed after an attempt to remove an impacted food bolus showing a dissection of the oesophageal wall. White arrow: oesophageal lumen; Black arrow: dissection channel; White arrowhead: trachea.

Subsequently, Spergel and Brown-Whitehorn, have demonstrated the utility of SPT in identifying potential allergenic foods.[12] SPT relies on a delayed response (non-IgE-mediated) to an allergen. In this study, 51 children with EoE were treated with an amino acid-based formula and all but two showed a clinical response within 9 days and mean oesophageal eosinophil counts decreased from 33 to 1 per HPF. Forty-eight of 51 patients required a nasogastric tube for administration or the formula.

In the largest series to date, Liacouras *et al.*, recently reported their findings in 381 patients with EoE.[16] They identify significant impacts of treatment with an elemental formula and dietary restriction in children with EoE. It should be noted that three of the above studies originated from the same institution. Additional studies to examine the utility of SPT, quality of life related to treatments and disease, and long-term outcomes of medical and nutritional treatments will be important in the future.

To summarize, the nutritional management requires testing to identify offending food allergen(s). In close collaboration with the consulting allergist, suspected foods are removed from the diet and the child is followed to see if symptoms abate and histopathology improves. In some cases, an elemental diet formula is required to induce a remission. Individual foods are subsequently reintroduced into the diet, while symptoms and histopathology are again closely observed.

In adults, the effectiveness of elimination diet and elemental diets has not been properly determined. Straumann *et al.*[6] performed a preliminary trial, including six adult patients with active EoE and sensitization to several food allergens. Patients remained on a selective elimination diet for 6 weeks. The elimination diet failed in reducing disease activity, as symptoms as well as endoscopic and histopathological findings remained unchanged (unpublished data). Whether these findings will be confirmed in future studies are yet to be determined.

Medical treatments

Medical treatments focus on the use of corticosteroids. Systemic corticosteroids clearly impact both symptoms and eosinophilia as shown by Liacouras *et al.* in 21 children.[15] In an attempt to reduce the systemic side-effects and target-affected tissues, Faubion *et al.* used the gavage from a metered dose inhaler (MDI), e.g. fluticasone. Children sprayed actuations into the mouth and swallowed steroid preparations to provide a theoretical topical application to the affected oesophageal mucosa.[69] The mouth was closed around the MDI (no spacer was used) and children did not eat or drink for 30 min following actuations. Results demonstrated clinical remission in all four patients studied.

Topical steroids have been used in over 70 adults[67, 70] and children[52, 68, 69] and have shown clinicopathologi-

cal remission in most. In older children a dose of fluticasone of 220 μg per actuation, two puffs twice a day for 2 months has been used successfully.[4] A potential side-effect includes oesophageal candidiasis.

Other medical treatments, such as cromolyn (mast cell stabilizer) and montelukast (leukotriene antagonist) can affect symptoms (personal communications). As mast cells in affected tissues, cromolyn may offer an impact but no reports supporting their role have been published. Eosinophils are rich sources of leukotrienes, molecules known to induce smooth muscle contraction. Thus, montelukast was administered to 12 adults with EoE. While a clinical impact was observed with supra-physiological doses, oesophageal eosinophilia persisted.[75]

Recently, two open-labelled studies with various hypereosinophilic disorders (including one patient with EoE) report beneficial effects from mepolizumab, a humanized anti-IL-5 antibody.[53, 76] As discussed previously, basic evidence supports such an approach because murine models of allergen-induced oesophagitis are IL-5-dependent and translational studies demonstrate increased expression of IL-5 in the affected human oesophageal epithelium. In this report, an adolescent boy with significant upper oesophageal narrowing whose symptoms were refractory to all medical and nutritional management received mepolizumab and developed both symptomatic and histological remission.[53] The role of this medication in the management of adults and children with EoE awaits further study and definition.

The ultimate goal of treatment was to provide symptomatic relief, and, in the opinion of these authors, to significantly improve mucosal inflammation. As long-term outcomes suggest that some patients develop strictures, we currently provide dietary or topical steroid treatment until symptoms resolve, and then repeat the endoscopy to ensure that mucosal healing has occurred. Alternative approaches include monitoring for symptoms and evidence of stricture (Barium swallow).

Dilation treatment

Dilation, either performed with Savary bouginage or with balloon dilators, is an established procedure in the treatment of stenosing oesophageal diseases. However, it is important to realize, the underlying process is not influenced by this manoeuvre. Dilations are often quite painful with symptoms sometimes persisting for several days. Following dilation, it is critical to re-examine the mucosa because the often rigid and inelastic mucosa can experience longitudinal splitting, a quite impressive finding[6] (see Figure 2). While the risk of a deep perforation is unlikely, two cases with perforation have been reported (see Figure 2).[77] Nevertheless, the procedure is efficient and dysphagia disappears usually for several months.[6] Thus, we recommend careful dilation in patients who fail medical treatment for obstructive symptoms with defined oesophageal narrowing(s).

CONCLUSION AND FUTURE DIRECTIONS

Eosinophilic oesophagitis represents a relatively new clinicopathological disease that can mimic symptoms and findings associated with GERD. Studies to date suggest an allergic aetiology with an overriding Th2 phenotype. Present treatments include dietary restrictions and corticosteroids with targeted immunomodulation as potential new opportunities. The identification of the natural history and the verification of basic knowledge in translational studies are future goals. How many children go on to develop oesophageal strictures? Will non-invasive markers be able to predict eventual outcomes? If the rhino-pulmonary tree is protected from allergen exposure, will this impact feature of EoE? What are the best ways to monitor for long-term complications? What is the best therapeutic approach to maintenance therapy? Answers to the questions will follow as adult and paediatric gastroenterologists, allergists and pathologists work together.

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