Eosinophilic Esophagitis – Medical and Dietary Treatment

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EOSINOPHILIC ESOPHAGITIS –
MEDICAL AND DIETARY TREATMENT

Berlin, Germany
October 4 – 5, 2017

Scientific Organization:
A. Straumann, Olten (Switzerland)

Scientific Co-Organization:
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I. Hirano, Chicago (USA)
A. Schoepfer, Lausanne (Switzerland)
H.-U. Simon, Bern (Switzerland)
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Session I

Eosinophilic esophagitis: Update 2017
Clinical presentation of EoE in children and adults: Are there new features?

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Eosinophilic esophagitis (EoE) is a chronic immune disease of the esophagus characterized by esophageal eosinophilia and symptoms of esophageal dysfunction. While dysphagia is the most common symptom in adults, EoE symptoms can widely vary in children and can often be non-specific. These include abdominal pain, gastro-esophageal reflux symptoms and emesis. Discerning EoE from acid-induced reflux disease in these patients by history alone can be difficult. Inquiring for associated symptoms such as early satiety and food refusal, and assessing for failure to thrive, can be very helpful. Esophageal endoscopic findings are also different in children and adults, with a higher proportion of adults than children having fibrostenotic features such as rings and strictures.

Race and gender variations in EoE presentations have also been found. A significantly large proportion of white persons than other races were shown to have dysphagia, food impactions and esophageal rings and furrows. A higher proportion of males than females were found to have esophageal strictures, despite similar symptom presentation.

EoE has also been described in patients being followed for other gastrointestinal diseases, including eosinophilic gastritis/gastroenteritis, celiac disease and esophageal atresia. Patients with EoE are also being encountered in other specialty practices. Since atopic diseases such as asthma, allergic rhinitis, atopic dermatitis and IgE-mediated food allergies are common in EoE, allergists need to be able to screen for EoE when suggestive symptoms are present. Similarly, patients with EoE may present to otolaryngologists for swallowing difficulties, especially children. Finally, EoE was found to be highly prevalent in patients with inherited connective tissue disorders. Therefore, rheumatologists need to consider EoE when esophageal symptoms are suggestive.

In conclusion, EoE can have various clinical presentations. Awareness of the various symptoms and associated co-morbidities is of paramount importance to make a timely diagnosis. In addition, given the chronic progressive nature of EoE, patients tend to compensate through behavioral feeding modifications such as prolonged chewing or avoiding hard or lumpy textured foods, to prevent major symptoms such as esophageal food impactions. Therefore, obtaining a detailed history about these feeding behaviors is crucial, to prevent a delay in diagnosis.
Pathogenesis: EoE, an auto-immune disease or a food allergy?

D. Simon
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Eosinophilic esophagitis (EoE) is a chronic disease characterized clinically by symptoms of esophageal dysfunction and histologically by eosinophil-predominant inflammation in association with T helper 2 immune responses. EoE patients frequently exhibit concomitant atopic diseases and immunoglobulin E (IgE) sensitization to food allergens in children as well as to aeroallergens and cross-reactive plant allergen components in adults. Patients with EoE respond well to elemental and empirical food elimination diets. Recent research has, however, indicated that the pathogenesis of EoE is distinct from IgE-mediated food allergy. Although food has been recognized as a trigger factor of EoE, the mechanism by which it initiates or facilitates eosinophilic inflammation is not well understood. The potential role of epithelial barrier defects, dysregulated innate and adaptive immune responses, and of microbiota in the pathogenesis of EoE are discussed. Understanding the pathogenic role of food in EoE is a prerequisite for the development of specific diagnostic tools and targeted therapeutic procedures.
Eosinophilic esophagitis (EoE) is an antigen-mediated disease that causes esophageal eosinophilia and esophageal symptoms, mainly dysphagia, food bolus impaction, heartburn and chest pain. Gastroesophageal reflux disease (GERD) is an acid-mediated disorder, for which proton-pump inhibitor (PPI) are the most effective medical treatment. Until recently, it was widely accepted that resolution of symptomatic esophageal eosinophilia suggestive of EoE with PPI therapy established a diagnosis of GERD and excluded EoE. The recognition of “PPI-responsive esophageal eosinophilia” (PPI-REE), which refers to patients with clinic, endoscopic and histologic data suggestive of EoE who achieve complete remission on PPIs, challenged this dogma. Currently, patients with PPI-REE remain genetically and phenotypically indistinguishable from EoE patients who do not respond to PPI therapy. PPIs have been shown to restore esophageal mucosal integrity, reduce Th2 inflammation and reverse the abnormal gene expression signature in PPI-REE patients in a similar way that topical steroids do in patients with EoE. Additionally, novel anti-inflammatory effects of PPIs independent of acid blockage, have been demonstrated in esophageal cell cultures. Therefore, evolving evidence points towards PPI-REE might be an inappropriate disease descriptor, arbitrarily based on a response to a single drug, for patients that mostly should be considered within the spectrum of EoE. A response to PPIs may neither diagnose GERD nor rule out EoE. In fact, both diseases may coexist. Recent reports of resolution of symptomatic esophageal eosinophilia suggestive of EoE with vonoprazan, a novel potassium-competitive acid blocker different from PPIs, pose the possibility that GERD may be an important triggering factor for a subset of EoE patients. The interacting mechanisms between GERD and EoE remain to be elucidated yet.
Eosinophilic esophagitis (EoE) is a chronic inflammatory disease of the esophagus. Recognized as a distinct entity only two decades ago, the emergence of the disease along with the availability of new technologies have quickly opened new research avenues and outlined the main features of its pathogenesis. Yet, each advance in our understanding of the disease has raised new questions about the previous consensus. Currently, new subsets of the disease challenge our diagnostic criteria. For instance, in four EoE-families, we have identified five patients presenting with EoE-typical and corticosteroid-responsive symptoms, but without tissue eosinophilia. The clinical manifestation as well as the immunological and genetic characterization of these patients suggest a uniform underlying pathogenesis. Therefore, these five members of EoE families did not fulfill the diagnostic criteria of EoE, but suffered from “EoE without eosinophilia”. In conclusion, conventional EoE appears to be only one phenotype of a broader “inflammatory dysphagia syndrome” spectrum. In this light, the role of the eosinophils, the definition of EoE, and its diagnostic criteria must likely be reconsidered.
Session II

Some hot topics
Remodeling in EoE: How to assess and how to manage?

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The primary complications of eosinophilic esophagitis (EoE) arise as a consequence of esophageal remodeling in the setting of chronic inflammation. Manifestations of dysphagia and food impaction are directly related to esophageal luminal compromise resulting from transmural involvement of both inflammation and fibrosis. The most consistently identified clinical predictor of risk of stenosis in EoE is duration of disease. Studies have examined the TGF beta signaling pathway, epithelial mesenchymal transition, and subepithelial fibrosis scores as biomarkers of the remodeling process in EoE. In routine practice, esophageal remodeling is primarily assessed by means of barium esophagram or upper endoscopy. The consequence of esophageal remodeling can now be accurately assessed during endoscopy utilizing the functional luminal imaging probe (FLIP). Measurements of esophageal distensibility have been shown to correlate with clinically relevant outcomes of food impaction and esophageal dilation. Future directions in FLIP analyses are examining the data in the format of graphical depiction of the esophagus at multiple foci.

The treatment paradigm for EoE has evolved over the past two decades. At present, management strategies include medical therapies with swallowed topical corticosteroids that arrest eosinophilic mucosal inflammation, dietary interventions that eliminate causative food triggers, and esophageal dilation that targets the fibrostenotic sequelae of the disease. Numerous studies have reported lasting relief of dysphagia as well as low complication rates with esophageal dilation. Dilation is generally reserved for patients with strictures that do not respond to medical/diet therapy. Dilation, however, can be an effective primary therapy in patients who are unwilling to comply with medications/diet or who have high grade stenosis at index endoscopy, respectively.
Epithelial barrier defects in EoE: The chicken or the egg?

Arjan J. Bredenoord
Academic Medical Centre, Amsterdam, The Netherlands

In eosinophilic esophagitis (EoE) food allergens activate an allergic, Th2 immune response in the esophagus. The normal esophageal epithelium is a tight barrier and does not allow allergens to penetrate. There is increasing data suggesting that the mucosal barrier in active EoE is decreased, allowing food allergens to penetrate. This increased mucosal permeability in EoE is partly reversed by acid inhibition with proton-pump inhibitors, suggesting that acid reflux may play a role in the mucosal barrier integrity changes, similar as seen in reflux disease.

The impaired mucosal permeability seems to be correlated to the degree of activity of the disease, with the more severely inflamed mucosa the more severe mucosal barrier changes. This suggests that measurement of mucosal integrity can predict inflammation to some degree. Complete removal of food allergens from the diet, as being achieved with elemental diet, almost completely restores the mucosal barrier function.

Conflicting data is present about duodenal mucosal barrier changes. Our most recent data does not point toward impaired duodenal mucosal integrity, confirming that EoE only affects the esophagus.

The observed mucosal barrier changes in EoE is relevant, not only from a pathophysiological standpoint but also because it can serve as a marker for inflammation and it mucosal barrier dysfunction can become a target for treatment.
Genetics and epigenetics in EoE: Is this the diagnostic clue?

Carine Gaelle Blanchard
Nutrition and Health, Nestlé Research Center, Allergy Group, Lausanne, Switzerland

The genetic and epigenetic contribution in eosinophilic esophagitis has considerably advanced this last few years. Genetic variants have been identified and shown strongly associated with the disease. However healthy individuals may carry the culprit variants identified and on the other hand, diseased patients may have the variants associated with healthy state thus rendering the use of genetic for diagnosis difficult. Recent study have identify epigenetic marks or changes in affected patients. Yet this predisposing factor can still not explain alone disease onset and numerous studies will be needed. Environmental factors seem to highly contribute to the disease susceptibility as a twins study has emphasized the prominent influence of shared environment (81.0%) compared with additive genetic heritability (14.5%). Yet identifying what are the causative environmental factors and how these influence the genetic and epigenetic marks will be needed to get to a comprehensive genetic diagnosis tool.
Eosinophilic gastroenteritis: Part of the EoE spectrum or a separate disease?

N. Gonsalves
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Eosinophilic gastrointestinal disorders (EGIDs) consist of eosinophilic esophagitis (EoE), eosinophilic gastritis (EG), eosinophilic gastroenteritis (EGE) and eosinophilic colitis (EC). EoE is characterized by eosinophilic infiltration of the gastrointestinal mucosa isolated to the esophagus and is considered a distinct entity from EG, EGE, and EC. While EoE has been rising in both prevalence and incidence, the other EGIDs (EG, EGE and EC) are significantly less common. Recent estimates suggest the prevalence of eosinophilic gastritis and gastroenteritis in the United States is 22 to 28 per 100,000 persons.

In EG/EGE/EC, eosinophils infiltrate the gastrointestinal or colonic tissue and lead to inflammation. The condition is named by the location of the bowel that is affected. Multiple layers of the bowel may be involved: mucosal, submucosal and serosal. The symptoms at presentation often correspond to the layer of bowel involved. The most common symptoms include abdominal pain, nausea, vomiting, early satiety, weight loss and diarrhea. When deeper layers of the bowel are involved, complications such as perforation, structuring or ascites may occur. Other complications include anemia, gastrointestinal bleeding, and in severe cases malnutrition.

While treatment with elimination and elemental diets are highly effective methods at reducing mucosal inflammation in participants with EoE, diet therapy has not been extensively studied in EG/EGE/EC. Instead, treatment for EG/EGE has focused on systemically active immunosuppressive agents such as systemic corticosteroids. While these medications are very effective at reducing eosinophilic inflammation, long-term side effects limit their use for maintenance therapy. Other alternative treatments discussed include crushed budesonide, proton-pump inhibitors, mast cell stabilizers, and immunomodulators. Due to the significant morbidity with these illnesses and paucity of data on effective and safe treatment options, improved therapeutic options are needed. Dietary therapy has been found to be helpful in a small series of children and adults with EG/EGE. Due to the paucity of controlled studies in EG and EGE, the pathophysiology is also not as clearly defined as in EoE, which has been linked to food allergens in both the adult and pediatric populations. Recent studies have suggested that EG/EGE is a systemic disorder involving blood and gastrointestinal tract eosinophilia, Th2 immunity and altered transcriptome distinct from EoE.
Session III

Therapeutic principles 2017 in EoE
Meaningful readouts in EoE: Symptoms, endoscopy, histology, distensibility: All for one or one for all?

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Disease activity of eosinophilic esophagitis (EoE) can be assessed using clinician-reported outcome (ClinRO) measures, such as endoscopic, histologic, and laboratory findings, and patient-reported outcome (PRO) measures, which include symptoms and EoE-specific quality of life. EoE activity should be measured using a combination of PRO and biologic measures which is in accordance to recommendations from regulatory authorities. Major efforts have been undertaken within the last couple of years to standardize assessment of EoE activity. Nowadays validated instruments are available to measure EoE-related symptoms, EoE-specific quality of life, endoscopic alterations, as well as histologic activity. In most clinical trials a combined endpoint of symptoms, histologic activity, and endoscopic activity is evaluated. For the purposes of planning clinical trials it is important to remember that EoE-related symptoms only moderately correlate with histologic and endoscopic activity, as such clinical remission predicts endoscopic and/or histologic remission only with about 60–70% accuracy. Second, biologic endpoints such as histology and endoscopy typically show a quicker improvement than PRO, as such a sufficiently long treatment period should be planned to observe also a relevant PRO improvement. Standard biopsies provide subepithelial esophageal tissue in only half of EoE patients, as such, we are often unaware of the presence and severity of underlying fibrosis which can also contribute to EoE symptom severity. Measurement of the esophageal distensibility using an inflatable balloon can aid in help in understanding the severity of esophageal remodeling processes. Continued efforts from different stakeholders will be necessary to further standardize outcome assessment in EoE for clinical trials and daily practice.
Therapeutic goals in eosinophilic esophagitis: Which is more important, making the patient feel better or helping the tissue look better?

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Therapeutic goals in eosinophilic esophagitis (EoE) include resolution or improvement of clinical symptoms, endoscopic features, and histologic findings. These are the three most common outcomes assessed in controlled trials studying therapeutic agents for EoE. Of these endpoints, clinical response is the most subjective outcome and can be difficult to accurately capture owing to behavioral modifications and adaptive strategies in swallowing. From an EoE patient’s standpoint, the most important endpoint is clinical improvement in symptoms. As EoE patients need to avoid certain foods, eat slower, chew their food more thoroughly, and have concerns about experiencing a food impaction, this condition greatly affects quality of life. Furthermore, impairment in quality of life worsens over time, particularly if the condition is not treated. There are different reasons why EoE patients may experience symptoms. These include reduced esophageal compliance, changes in motility, development of fixed fibrotic rings, dominant strictures, or a diffusely narrow esophagus. Several studies have demonstrated that the major predictor of stricture formation is duration of disease, especially if left untreated or under-treated, and stricture formation is a key risk factor for food bolus impaction. As changes of esophageal remodeling and fibrostenosis are driven by persistent inflammation, the focus should therefore be on treating the underlying pathogenesis. Options for treatment include proton-pump inhibitors, topical steroids, or specialized diets. Following effective histologic response to treatment, clinical improvement should follow. In one recent study, EoE symptoms had positive correlation with histologic and endoscopic activity. In the end, all therapeutic outcomes are important, however the focus should be on treating the disease, rather than the symptom.
Principles of medical treatment: Corticosteroids and beyond?

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According to the recent guidelines (Lucendo et al. UEG Journal 2017) topical corticosteroid therapy is one option (besides dietary interventions and PPI) recommended for the treatment of eosinophilic esophagitis (EoE). So far, nine randomized placebo-controlled trials on topical budesonide or fluticasone for short-term treatment of EoE and several metaanalysis are available providing the largest body of evidence compared to other treatment strategies in EoE. Based on this evidence topical corticosteroids are regarded as effective and safe for induction of histological remission and symptom improvement. So far, only one placebo-controlled trial has investigated low-dose topical budesonide for long-term maintenance treatment of EoE suggesting a clinical benefit. A current focus of research is to develop optimal, esophageal-targeted formulations of corticosteroids and to study in more detail the efficacy and safety of topical corticosteroids for long-term therapy of EoE in adequately designed clinical trials. For example, a recent phase 3 European multicenter trial has shown that budesonide administered as orodispersible tablet was highly effective for induction of clinico-pathological remission in EoE (Lucendo et al. DDW2017).

Beyond topical corticosteroids there is currently not much to offer. Antiallergic drugs or immunomodulators have either failed to show efficacy or were not adequately studied in EoE. Several monoclonal antibodies including anti-IL5 (mepolizumab, reslizumab), anti-IL13 (QAX576) and anti-IgE (omalizumab) failed to achieve clinically meaningful outcome measures. In contrast, a recent phase 2 trial showed for the first time that a monoclonal anti-IL13 antibody (RPC4046) was superior over placebo in achieving histological response, as well as endoscopic and symptom improvement (Hirano et al. UEGW 2016).

While topical corticosteroids are likely to become the mainstay and treatment of choice for most EoE patients, more research is required to develop effective treatment alternatives which could be offered to patients with inadequate response or intolerance to topical corticosteroids.
Principles of dietary treatment

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EoE is currently known to be an allergic condition predominantly triggered by food antigens, which, unlike conventional IgE-mediated food allergy, largely depends on non-IgE delayed, cell-mediated hypersensitivity. Dietary therapy represents the only treatment for EoE which targets the cause of the disease instead of its inflammatory consequences. However, complexity in implementing diets and differences in response rates provided by the different dietary modalities has hold back its implementation in clinical practice, compared to pharmacological therapy.

Elemental diet is the most effective intervention in children and adults, but multiple disadvantages hamper its use. Results for food allergy testing-guided elimination are consistently low in adults and variable in children. By contrast, empiric elimination diets have shown concordant and predictable results among several studies. Initially tested in 2006, six-food group elimination diets (SFGED) lead to clinicohistologic remission in three quarters of children and adults, as consistently demonstrated in studies carried out in USA, Spain and Australia. However, the need of large number of endoscopies during the food reintroduction phase to identify specific triggers for the diseases counteracts its efficacy. After identifying wheat and milk as the major food triggers, followed by egg and soy/legumes, with a minor role for nuts and fish and seafood, a four food elimination diet (FFED) has been proposed as a more convenient option with still an acceptable remission rate over 60%.

A novel steep-up dietary approach consisting in avoiding only milk and gluten (with a 45% histological remission rate), followed by a FFED in non-responders (overall providing a 65% remission rate) and reserving SFED as the final rescue therapy (providing an overall 72% remission rate) has been recently proposed, as able to identify early a majority of responders to empiric diet with few food triggers, avoiding unnecessary dietary restrictions, saving endoscopies and shortening the diagnostic process.

Keys so succeed when implementing dietary therapy for EoE start with selecting the appropriate patient or family since not everyone is able to follow and maintain an elimination diet. In addition, providing patients with written instructions and list of foods and additives will facilitate adherence to the diet. Endoscopies must be scheduled every 6 weeks, and appointments should be strictly fulfilled. Washing periods after food trigger identifications are not required, and in case of doubt about the remission after reintroducing a food, temporarily avoiding its consumption until the result of the biopsies is available appears the most suitable strategy. Patient should find easy to contact with their doctors by e-mail or telephone to resolve the doubts that frequently arise. To consider “diet holidays” when prolonged periods of restriction are required facilitates patients’ involvement. Finally, it is essential to transmit an optimistic attitude to patients: Most of them will respond to dietary treatment; only one or two foods will need to be excluded in the long term in > 90% of cases, and no drugs will be required to maintain disease remission.
Definition of and reasons for refractory EoE: Is it refractory or only pseudo-refractory?

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As discussed during this session, current pharmacologic and dietary treatments for EoE are effective for many patients. However, a sizable proportion of patients with EoE either incompletely respond or do not respond to first line treatments. A conceptual definition of refractory EoE consists of ongoing symptoms, persistent endoscopic findings, and persistent eosinophilic inflammation despite treatment with either swallowed/topical steroids or dietary elimination. At this time, though controversial, failure to respond to a proton-pump inhibitor would not be considered refractory EoE. This presentation will review the nuances of this definition in detail, including what threshold of symptoms, endoscopic findings, and eosinophilic inflammation might support a designation of non-response. Clinical trial and cohort data will be used to examine the frequency of non-response, which for histologic outcomes could range from 5% to 50%, depending on the definitions and treatments used. In addition, it will cover the concept of pseudo-refractory EoE. There are multiple correctible reasons for non-response in EoE that must carefully be assessed from a clinical standpoint. These include incorrect medication dosing, administration, or formulation, suboptimal dietary adherence which could be intentional or inadvertent, persistent or unrecognized esophageal stricturing or remodelling, infections, and an incorrect diagnosis of EoE. In addition, nearly universal response rates with escalation of treatment intensity, either with an elemental formula or with an esophageal-specific drug deposition formula, raises the question of whether EoE can be treated in all subjects, or whether refractory EoE is an artifact of the limitations of currently available treatments.
Session V

EoE a chronic disease
Monitoring of disease activity: What is evidence-based, what is empiric, what makes sense?

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Eosinophilic esophagitis (EoE) represents a chronic, local immune-mediated esophageal disease, characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation. EoE is a young disease and therefore it is understandable that until recently no validated instruments to assess EoE activity existed. Since EoE represents a clinical-pathologic entity diagnosis is based on symptoms and histology results. These two columns, which are essential for an established diagnosis of EoE indicate that total EoE activity includes different point of views. First patient reported outcomes (PRO) und second clinician reported outcome (ClinRO). PRO assess severity of symptoms, quality of life (QoL) and adaption mechanisms to live with dysphagia. ClinRO evaluate endoscopic, histologic and laboratory parameters. For measurement of PRO different, validated or non-validated EoE specific tools have been published. EoE activity Index (EEsAI) is a validated scoring instrument assessing clinical activity in adult EoE patients, Dysphagia Symptom Questionnaire (DSQ) was validated and is currently used in clinical trials, Straumann Dysphagia Score (SDI) is not validated and was evaluated in a natural history study and used in a modified version in a randomized, placebo- controlled trial in 2010, Mayo Dysphagia Questionnaire (MDQ) represents a non EoE specific tool to evaluate dysphagia in patients with different underlying esophageal diseases. ClinRO include endoscopic activity and histologic activity. Recently an endoscopic classification and grading system (EoE Endoscopic Reference Score = EREFS) was evaluated and showed good interobserver agreement. Defining endoscopic remission, mild, moderate, or severe activity of EoE was not yet investigated using the EREFS. For assessment of histologic activity an EoE specific histologic scoring system (EoEHSS) has been recently developed and in-site validated, to provide an standardized method to evaluate esophageal biopsies for features in addition to peak eosinophil count. This scoring system comprises a grading for severity and extent in a 4-point scale for eight EoE associated features and seems to be applicable after minimal training of pathologists. The requirements assessing EoE activity are different in clinical trials and “real life situation”. Until today no EoE specific pharmacologic therapy has been approved worldwide standardized and comparable definitions of clinical outcomes in therapeutic studies using validated scoring systems are needed. A “real world” setting in treating EoE outside of clinical trials requires a simple, fast and easy applicable assessment criteria for EoE activity grading.
Swallowed topical corticosteroids (STC) are highly efficacious in inducing clinical, endoscopic and histological remission in patients with active eosinophilic esophagitis (EoE). In contrast, data on STC’s efficacy in maintaining remission are sparse with so far two maintenance trial conducted (follow-up evaluation after 1 and 2 years, respectively). Beyond two years, data on patients treated with STC are extremely limited. In particular, there is no data on how long patients with EoE should be treated, if in a subset of patients treatment can ever be discontinued, and if there is any potential harm from STC in the long-term. At our Swiss EoE Clinic, a therapeutic concept was therefore developed including an induction phase with 1.0 mg STC bid followed by a maintenance phase with 0.25 mg bid. Patients had annual follow-up visits with clinical, endoscopic and histological disease assessment regardless of clinical symptoms. In patients who had achieved deep remission (DR) defined as long-lasting (> 6 months) clinical (no EoE attributed symptoms), endoscopic (no signs of inflammation) and histological disease remission (peak eosinophil count < 5/hpf), treatment was discontinued and patients attended follow-up visits every 3 months or earlier in case of a relapse. We recently published our results in the American Journal of Gastroenterology showing that only 9.4% (33/351 patients) actually achieved such remission. Median time to DR was 89.0 weeks and a cumulative dose of nearly 300 mg STC was needed. More than 80% of those patients experienced a relapse within a median of 22 weeks. So, only 1.7% of our cohort were able to discontinue STC in the long-term. Those patients had a shorter diagnostic delay and shorter time until clinical remission compared to the patients with an EoE relapse. Despite one of the longest-follow-up reported in EoE literature (median 6 years), no mucosal atrophy or other serious side effects were observed. Most of the candida cases (7/33, 21.2%) were asymptomatic. Taken together, results from this long-term management study are sobering. One possible explanation might be the low maintenance dose chosen. Dose-finding trials such as the ongoing BUL2 are definitely needed. Based on our data, the current understanding of EoE, and the currently available medical treatment modalities, we can neither counsel our patients that EoE is curable nor that a lifetime treatment will be necessary in every single patient. We advocate for a long-term monitoring of EoE patients treated with STC.
Session VI

Oral presentation of awarded posters
Modulation of CD8\(^+\) cells infiltration and activity in eosinophilic esophagitis by six-food elimination diet

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**Introduction:** Eosinophilic esophagitis (EoE) is characterized by a dense intraepithelial inflammatory infiltrate of eosinophils, mast cells, and CD4 and CD8 lymphocytes. Histological and clinical remission after dietary exclusion supports immune-allergic mechanisms as the driving force in EoE. However, the role of CD8\(^+\) cells and CD8-specific cytotoxic molecules, as key contributors to EoE pathophysiology, have not been explored.

**Methods:** Naïve EoE patients (n = 10; age: 33 ± 10 years-old) who responded clinically and histologically to a six-food elimination diet (SFED: milk, cereals, egg, fish, legumes, nuts) and healthy-esophagus controls (C, n = 10; age: 53 ± 20 years-old) were included. Esophageal biopsies were collected in all subjects before and after therapy, and at baseline in controls. Clinical symptoms were assessed and analysed before and after SFED, and food triggers were identified. The number of eosinophils and CD8\(^+\) cells per high-power field (hpf) were quantified after haematoxylin-eosin and immunofluorescence staining, respectively. Expression of eotaxin-3 and cytotoxic CD8-related molecules was assessed by qPCR.

**Results:** Main symptoms reported were dysphagia (70%), and food impaction (70%). The most frequent triggering foods were cereals (70%) and milk (60%). Compared to controls, eosinophils (EoE: 56.80 ± 29.91/hpf vs. C: 0 ± 0/hpf) and CD8\(^+\) cells (EoE: 19.70 ± 12.37/hpf vs. C: 4.9 ± 4.03/hpf) were higher in EoE patients (p < 0.05). SFED significantly reduced cell counts (eosinophils: 3 ± 4.22, CD8: 6.96 ± 7.25/hpf; p < 0.05) in parallel with clinical improvement.

Granzyme A, granzyme B, granulysin and eotaxin-3 gene expression were higher in EoE than in C (1.6 to 26-fold-change; p < 0.05) and decreased to C values after SFED treatment.

Positive correlation was found between eotaxin-3 expression and dysphagia symptoms (r\(_s\) = 0.73), CD8 counts (r\(_s\) = 0.94) and granzyme B (r\(_s\) = 0.75; p = 0.02) and between eosinophils and CD8 counts (r\(_s\) = 0.81; p = 0.06).

**Discussion/Conclusion:** Reduction in CD8 lymphocytes number and proteases expression, in association with clinical improvement after SFED, suggest that CD8-mediated cytotoxic mechanisms are involved in eosinophil recruitment and epithelial damage in active EoE.
The possible pathogenetic role of TSLPR (rs36133495) gene’s polymorphism in eosinophilic esophagitis

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Introduction: Eosinophilic esophagitis (EoE) is a chronic inflammatory disease of immune/atopic genesis, basically associated with mucosal eosinophil accumulation. Genetic background of EoE is based on both similarities with other atopic diseases like asthma or allergic rhinitis, and population studies with dominance of male patients. While the EoE risk is multifactorial and includes environmental and genetic factors, existing database is insufficient. Among the possible candidate genes for EoE, the thymic stromal lymphopoietin receptor (TSLPR), Calpain-14, IL-4, IL-5 attract major attention in terms of development possible future treatment approaches. There is evidence that the TSLP signaling pathway may contribute to the formation of perverted immune response in EoE, while exact polymorphisms and their roles have to be determined.

Methods: We observed 75 schoolchildren with food allergy (FA) based on clinical symptoms and prick skin testing as major criteria for FA. Based on questioning, clinical and laboratory observations, individuals were divided into following groups: 1st group included 68 FA patients with FA without EoE; 2nd group (7 patients, all males) – FA + EoE. Twenty-three practically healthy children formed control group. EoE diagnosed based on symptoms and esophageal endoscopy with biopsies (not less than 15 eosinophils per ×400 hpf in at least one sample). TSLPR gene’s single nucleotide polymorphism (rs36133495) studied in lymphocytes by PCR.

Results: A-allele of the TSLPR gene was detected in 88.89% of group 1, 14.29% of group 2, and 91.30% of controls. Minor G-allele was found in 11.11% of group 1, 85.71% of group 2, and 8.70% of controls, respectively. No GG-genotype carriers observed in control. The likelihood of EoE increases in G-allele carriers of the TSLPR gene (OR = 2.46; 95% CI OR: 0.43–6.16; p < 0.001).

Discussion/Conclusion: In previous studies, it was found that TSLPR participates in the initiation of the Th2-immune response being responsible for multiple atopic conditions. This study shows that the particular rs36133495 (A/G) TSLPR gene polymorphism may be involved into development of EoE and requires further investigation emphasizing possibilities for associated treatment approaches.
Improvement in esophageal distensibility in response to medical and diet therapy in eosinophilic esophagitis

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Introduction: Reduced esophageal distensibility measured via the functional lumen imaging probe (FLIP) is observed in eosinophilic esophagitis (EoE). This study evaluated the effect of medical and diet therapies on esophageal distensibility and the association of changes in distensibility with clinical outcomes in EoE.

Methods: EoE patients completed FLIP at baseline and following therapy without interval dilatation. FLIP analysis was performed to calculate the distensibility plateau (DP). Clinical data included patient reported outcomes, histopathology and endoscopic features. Results were expressed as mean +/- SD unless otherwise stated.

Results: 18 patients (ages 19–54 years; 4 female) treated with topical steroid (8), elimination diet (6), and/or proton-pump inhibitor were included. Follow-up testing occurred at a mean (range) of 14.6 (8–28) weeks. Improvement was observed in DP, 13.9 mm (12.2–19.2) to 16.8 mm (15.8–19.2), p = 0.007) and peak eosinophil count 45 per hpf (29–65) to 23 (5–53), p = 0.042). Nine patients had a positive symptomatic outcome. Six of eight (75%) patients with a DP increase ≥ 2mm had a positive PRO (p = 0.077), while 2/7 (29%) patients that achieved an eosinophil count < 15/hpf had a positive PRO (p = 0.167).

Discussion/Conclusion: Improvement in esophageal body distensibility quantified with FLIP can be achieved with medical and diet therapies without dilation in EoE. Improved DP appeared to be better indicator of symptomatic improvement than eosinophil count, supporting FLIP as a potentially clinically relevant outcome measure in EoE.
Session VII

Outlook
Identification of causative foods: Empiric, serum IgG4, serum FLC’s or other signs of dawn?

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Eosinophilic esophagitis is a chronic immune disease of the esophagus characterized by esophageal eosinophilia and symptoms of esophageal dysfunction. The pathogenesis of EoE remains unclear. It is thought that food antigens trigger disease and cause an esophageal inflammation that is allergic in nature, as the esophagus was shown to display a cytokine profile consistent with that of a Th2-mediated disease. Standard allergy testing to foods however, including measurement of food-specific IgE levels, has not been beneficial in identifying causative foods in EoE. In addition, dietary elimination therapies guided by the results of skin prick tests and atopy patch tests have not been that successful in inducing disease remission. Dietary eliminations based on further refinement of IgE testing, directed by results of IgE measurement to multiple molecular components of important allergenic foods (ISAC testing) did not yield any success either. Empiric dietary eliminations, consisting of removal of foods known to be common allergens in the general population, have demonstrated better results. Therefore, EoE is currently thought to be mostly non-IgE mediated, and a search continues for molecules responsible for disease pathogenesis. IgG4 has been measured in the serum and esophageal tissue of patients with EoE. Finding elevated food-specific IgG4 in the serum of patients with EoE compared to controls, and food-specific IgG4 in the esophageal tissue of patients with EoE, indicates a potential role for IgG4 in EoE pathogenesis. More data is needed to clarify as to whether food-specific IgG4 elevation truly correlates with causative foods in EoE. Other molecules such as free light chains (FLCs) have been investigated in EoE. Immunoglobulin light chains have been shown to be elevated in allergic diseases in an antigen-dependent manner, and independently from serum IgE levels. Serum milk-specific FLC levels were found to be significantly more elevated in children with EoE compared to controls, indicating the potential importance of FLCs in EoE pathogenesis. Larger studies are needed to confirm these findings. In conclusion, several molecules implicated in allergic disease independent of IgE are currently under investigation, some may eventually prove to be useful diagnostic tests for causative foods in EoE.
Biologic agents in eosinophilic esophagitis – Past, present and future

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While eosinophilic esophagitis (EoE) has been in the knowledge and limelight for over two decades, the treatment options have been limited to the three “Ds” namely diet, dilation, and drugs. The last category, drugs, is limited to corticosteroids (CS), fluticasone, budesonide and prednisone, for the most part. Over the years, it has become obvious that the Drugs category needs expanded, and this talk will discuss role of biologic agents in the management of EoE.

Various biologic agents have been considered in EoE with initial reports targeting eosinophils themselves as these are considered to be the main driver of this disease. Early reports focused on anti-IL5 agents namely mepolizumab (pediatric and adult data), reslizumab (pediatric data mainly), followed by case series on anti-TNFα agents and trials of anti-IgE drug called omalizumab. More recently, studies have been conducted on two anti-IL13 agents, QAX576 and RPC4046. Another anti-IL13 drug lebrikizumab has been described but not yet studied in EoE. A dual-agent dupilumab – with anti-IL4 and anti-IL13 properties – recently completed a clinical trial. Other novel therapies being considered include benralizumab, an inhibitor of anti-IL5α receptor.

In conclusion, a number of biologics have been examined in EoE and newer ones are being described as we advance our understanding of the pathophysiology of EoE. Fortunately no significant safety concerns have been raised in clinical trials to date. However, the enthusiasm about current biologics is tempered by their limited efficacy especially in reducing esophageal eosinophil load as compared to topical corticosteroids, and consistent improvements in clinical course and patient reported outcomes tools. It is postulated that clinical phenotypes and biomarkers might impact therapeutic response as we further define the role of these drugs in EoE management.
Can histology be replaced by molecular testing?

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Eosinophilic gastrointestinal disorders (EGID) are characterized by eosinophil-rich inflammation in GI mucosa. Molecular and genetic studies have illuminated the pathogenesis of some of the esophageal biopsy alterations in eosinophilic esophagitis (EoE), the most extensively-studied EGID, and led to clinical trials testing the efficacy of restricting the activity of important contributors to pathogenesis, such as IL-5 and IL-13, using monoclonal antibodies.

In an effort to improve diagnosis and reduce the amount of tissue required for diagnosis, a 94 gene panel (EoEGP) was constructed based on the results of whole genome sequencing of esophageal biopsies. Since the panel does not examine the entire genome it is inherently biased. Nevertheless, the EoEGP appears useful to distinguish EoE cases from non-EoE controls at baseline, with a variable indeterminate group depending on the cut-off values used, and appears useful to monitor treatment response. Differences in levels of gene expression across the few studies using the panel may be due to use of different array platforms. Studies determining the performance of the EoEGP used peak eosinophil count (PEC) as the sole histologic feature to identify EoE and non-EoE cases, as well as to determine response to therapy. The eosinophilic esophagitis histology scoring system evaluates eight histopathologic features and outperforms PEC to identify untreated vs treated cases, but the correlation between the EoEGP and histopathologic features of EoE other than PEC is unknown. The ability of the panel to detect signs of infection, such as invasive fungal or viral infection, or unexpected tissue alterations following novel therapies is not known. Quantifying cells other than eosinophils that are important in EoE such as Th2 lymphocytes may also require tissue examination. The gene panel does not distinguish patients who have EoE from those who have proton-pump inhibitor responsive esophageal eosinophilia, currently considered a subtype of EoE, suggesting a limitation to distinguish among EoE phenotypes. The role of molecular testing in diagnosis and monitoring treatment response of EGID remains to be determined.
New diagnostic criteria for EoE: How can we diagnose EoE in the post-PPI-trial area?

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Eosinophilic esophagitis is a chronic inflammatory disease requiring symptoms referable to esophageal dysfunction and esophageal eosinophilia. Underlying causes or these findings need to be ruled out prior to making the diagnosis. For the last decade, proton-pump inhibitors (PPIs) have been used as a method to exclude gastro-esophageal reflux as an underlying etiology. During this time, basic studies revealed that PPIs possess anti-inflammatory properties that may can decrease cytokine production from esophageal epithelial cells. In addition, clinical studies determined that a large percentage of patients with esophageal symptoms and dense esophageal eosinophilia resolve both findings with PPI treatment. Thus, new approaches are needed to help make the diagnosis of EoE.
EoE yesterday, today and tomorrow

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EoE, first described in 1989 in abstract form, was slow to become accepted as a new disease entity, because of a perceived low prevalence and failure to understand its unique clinico-pathologic presentation. Despite seminal papers published in the early 1990’s – two very similar case series in adults (1993/4) and a paediatric case series in 1995, it took until the early 2000’s before the disease became regularly identified in routine clinical practice. Developments in Europe and the USA showed diagnostic variations between children and adults and described, in uncontrolled trials, benefits in dietary therapy, topical steroids and endoscopic dilatation. The end of the introductory era of this disease was marked by the very comprehensive Clinical Guidelines first published by Furuta in 2007 and followed up by the broad ranging guidance under Liacouras in 2011.

The era of today is perhaps 2011–2017 most marked by the increasing prevalence of the disease from rare to “not uncommon”. There has been some improved structured approach to the diagnosis and better understanding of the range of treatments. The effects of ppi have been described in some patients, distinct from the contribution of GERD, and development of algorithms that included a role for ppi in therapy and disease. Therapies that have not produced clinically beneficial results are currently biologics but they continue to be investigated.

Tomorrow we expect that the condition of EoE will become even more frequent than it is seen today. More countries around the world will identify disease cohorts, an example being Brazil and other South American countries that have not so far published any disease prevalence of EoE.

We look towards a clearer diagnostic algorithm that will include not just a density of eosinophil infiltration in the esophageal epithelium but also disease markers in the tissue or circulation that can identify EoE specifically from other causes or esophageal infiltration. We hope also to be able to predict natural history identifying those patients with stricturing disease that might better suit more aggressive early therapy, and at the opposite end of the spectrum identify those patients with mild non progressive disease that might not require long term maintenance therapies. In therapy we are very optimistic that we will have licensed therapies in topical steroids, improved dietary strategies that can reduce the burden of repeat endoscopy and ways to improve the quality of life of all patients on therapy for EoE.
List of Chairpersons, Speakers and Scientific Organizers

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POSTER ABSTRACTS

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Increased functional Toll-like receptors in the esophageal mucosa of adult patients with eosinophilic esophagitis

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Introduction: An adaptive Th2-type immune response to food antigens is involved in eosinophilic esophagitis (EoE). However, a role for the innate immunity in EoE has arisen after recognizing changes in esophageal microbiome in EoE patients. Toll-like receptors (TLRs) link innate and adaptive immunities. Therefore, we aim to determine expression of TLRs, pro-inflammatory mediators, transcriptional factors and effectors in esophageal and duodenal mucosal samples of EoE patients compared to controls, and assess changes induced by dietary treatment.

Methods: Esophageal and duodenal samples from 10 adult EoE patients were obtained before and after 6 weeks of treatment with six-food elimination diet. Samples from 10 normal esophagi were also analyzed. Expression levels of TLRs (TLR1, 2, 3, 4, 6, 9), pro-inflammatory mediators (IL1β, IL6, IL8, IL10, TNF-α), NGK2D system regulators, major effectors (iNOS, PRF1, GZMB), transcriptional factors (NF-KB, MYD88) and main mucins (MUC1, MUC4, MUC5B) were assessed by RT-PCR.

Results: A significant upregulation in TLR1, TLR2, TLR4 & TLR9 genes were documented in esophageal (being 2.5, 2.4 & 3.7 fold-increases, respectively) and duodenal mucosa of EoE patients (each one with a 1.5 fold-increase), compared to controls (p < 0.05). After dietary treatment, the expression of TLRs reduced both in esophagus and duodenum. However pro-inflammatory cytokines, transcriptional factors and main effectors were exclusively upregulated in esophageal samples (between 2 to 12.2 fold-increases). Similarly, main mucins were downregulated in esophageal (2 to 21.5 fold-decreases) but not in duodenal samples.

Conclusion: TLR1, TLR2, TLR 4 & TLR9 were upregulated in the esophagus and duodenum of patients with EoE. However, expression of main molecules involved in their pathways and functionality (pro-inflammatory cytokines, effectors, transcription factors and mucins) was only modified in esophagus. Dietary treatment down-regulated gene expression to controls levels. Our result points towards an interplay between dietary components, microbiome and innate immune responses in the pathophysiology of EoE.
11-year-old boy with eosinophilic esophagitis and Asperger’s syndrome – A case report

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Introduction: Eosinophilic esophagitis (EoE) is a chronic immune/antigen mediated esophageal inflammatory disease associated with dysfunction of the esophagus resulting from severe eosinophil-predominant inflammation. It is not characterized by any pathognomonic clinical or endoscopic features. During childhood vomiting and/or abdominal or retrosternal pain are mainly reported, but during adolescence signs of gastroesophageal reflux disease (GERD), dysphagia, and food impaction are the most frequent manifestations. EoE can also present as food selectivity or feeding disorders, especially in children with autism spectrum disorders (ASDs).

Case report: We report the case of an 11-year-old boy with Asperger’s syndrome who was admitted to our hospital due to paroxysmal abdominal pain and diarrhea with blood and mucus. Recently patient’s behavior has also deteriorated. Due to allergic skin rashes, the boy was on a hypoallergenic diet and was treated with antihistamines, but the patient did not take them regularly. Because eosinophilic gastroenteritis was suspected a gastroscopy and colonoscopy were performed. The endoscopic examination of the upper gastrointestinal tract showed esophageal rings of the lower midline of the esophagus and white exudates over the cardia. The remaining part of the gastric and duodenal mucosa as well of that of the large and small intestine was macroscopically normal. All together four biopsies were taken – from both the proximal and distal esophagus. Histological examination of the biopsies revealed eosinophilic infiltration of the esophageal mucosa (> 90 eos/hpf), basal zone hyperplasia and lamina propria fibrosis. There were no microscopic changes in the large and small intestine. Blood test revealed high blood eosinophilia and increased serum IgE levels.

Conclusion: In the present case, there were no typical symptoms from the upper gastrointestinal tract. Abdominal paroxysmal pain with diarrhea suggested rather eosinophilic gastroenterocolitis. Typical endoscopic findings should be always confirmed by esophageal biopsy. Unrecognized eosinophilic esophagitis may contribute to behavioral problems, especially in patients with autism disorders.
**Eosinophilic esophagitis – Diagnostic and therapeutic challenge: A case report**

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**Introduction:** Eosinophilic esophagitis is an immune mediated inflammatory disease with eosinophil-predominant inflammation. The diagnostic clue is histological presence of ≥ 15 eosinophils per high-power field. Therapy is mainly dietary, less often with swallowed corticosteroids.

**Methods:** Here we present 17-year-old boy with history of chronic cough, pain in the left upper abdomen and swallowing difficulties that have been present for 2 years. The boy has allergic rhinitis with proven allergy to certain inhalatory allergens and egg. The upper endoscopy has found pale esophageal mucosa with white exudates, but with less than 15 eosinophils per high-power field (HPF) on histological samples. The therapy with PPI started without adequate clinical response. Repeated endoscopy showed similar macroscopic finding, but with of almost no eosinophils/HPF. The 24-hours-pH-metry showed 200 acid reflux episodes mainly during the day, so a hypothesis of psychogenic cough was made and psychiatric support was started along with PPI treatment with certain clinical response. Six months after stopping PPI, the boy still had same symptoms. The upper endoscopy finding was the same, but with up to 47 eosinophils/HPF. The boy refused the elimination diet and oral budesonide 2 mg daily was started during 8 weeks with minimal response, with > 30 eosinophils/HPF on control upper endoscopy. Finally, empiric elimination diet with avoidance of 6 most commonly accepted food allergens was started, in the beginning without adequate dietary adherence, but after next 8 weeks of strict elimination diet, some clinical response was seen with up to 25 eosinophils/HPF, and elimination diet was continued.

**Discussion/Conclusion:** Eosinophilic esophagitis is a clinical condition with a rising incidence, partly because we are getting more aware of its existence. In this case report we wanted to show difficulties in making the correct diagnosis and the problems with adherence to elimination diet which is especially expressed in pubertal years.
Endoscopic dilation of esophageal strictures in eosinophilic esophagitis

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Introduction: Strictures are a frequent complication of eosinophilic esophagitis (EoE). Their treatment is based on medical therapies such as proton-pump inhibitors and corticosteroids, but, in some cases, it may require an endoscopic approach. The aim of this study was to evaluate the results of endoscopic treatment in eosinophilic esophagitis.

Methods: We conducted a retrospective study including patients with EoE followed in our department between January 2010 and December 2016. Patients with esophageal stricture were listed and their epidemiological and evolutionary features were studied.

Results: We included 15 patients with EoE during the period of study. Their mean age was 28 years, the sex ratio was 2.7 (11 M/4 F). Personal and/or family history of allergies were found in 60% of cases. The diagnosis was suspected because of a history of dysphagia, and it was confirmed based on histological esophageal hyper-eosinophilia found in biopsies. Three of our patients suffered from recurrent episodes of esophageal food impaction. They had a mean age of 32 years and were all males. The esophageal endoscopy showed a single stricture in the distal esophagus in all cases, the mean length of the stricture was 1.8 cm. These patients were treated by proton pump inhibitors for two months without clinical response. An endoscopic dilation using bougienage was performed in three cases. No immediate post-dilation complications occurred, apart from epigastric pain. Two patients achieved clinical remission after first dilation, only one needed a second endoscopic dilation. After a follow-up of 12 months, all patients had a sustained treatment response.

Conclusion: Endoscopic dilation is useful in patients for patients with esophageal strictures in eosinophilic esophagitis which don’t respond to medical treatment with high rates of sustained response.
Prevalence of eosinophilic esophagitis in patients with esophageal symptoms

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Introduction: Eosinophilic esophagitis (EoE) is a rare disease, but its frequency is probably underestimated. We aimed to evaluate the prevalence of EoE among patients with esophageal symptoms.

Methods: Retrospective study including patients with esophageal symptoms, including dysphagia and food impaction, referred to our department between January 2011 and December 2016. The enrolled patients underwent an esophagogastro-duodenoscopy and esophageal biopsies. EoE was diagnosed if esophageal biopsy showed ≥15 eosinophils/high-power field.

Results: A total of 52 patients were enrolled in the study. Three out of 52 patients met the criteria of EoE establishing a prevalence of 5.7%. They were 2 men and one woman. The mean age was 32.3 years. Endoscopic findings were white exudates in one patient and ring-like appearance in one case. One patient had a normal-appearing esophagus despite a severe histologic esophageal eosinophilia.

Discussion/Conclusion: In our study, prevalence of EoE among patients with esophageal symptoms was 5.7%. Clinicians should pay attention to patients manifested with dysphagia and do systematically esophageal biopsies.
The PPI treatment and the elimination diet among patients with eosinophilic esophagitis

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Introduction: Eosinophilic esophagitis (EoE) is a chronic, immune/antigen-mediated esophageal disease, with eosinophilic infiltration limited to the esophagus. Elimination diets and high-dose proton-pump inhibitors (PPI) are advocated as first-line treatments in patients with eosinophilic esophagitis (EoE). A minority of EoE patients respond well to PPI therapy alone, and that condition is labelled PPI-responsive esophageal eosinophilia (PPI-REE). The prevalence of PPI-REE among EoE cases is unknown. We aimed to identify clinical manifestations of EoE, and the proportion of PPI-REE among all EoE cases.

Methods: EoE was diagnosed based on esophageal symptoms and eosinophilic infiltration limited to the esophagus, with ≥15 eosinophils per high-power field. Patients commenced esomeprazole 40 mg twice daily for 8 weeks. Those in histological remission were re-classified as PPI-responsive esophageal eosinophilia. Nonresponders were offered the 6-food elimination diet with a PPI for another month. Once disease control was achieved remission was reassessed at 3 months (all modalities) and an additional 6 months (diet group).

Results: The clinical manifestations of EoE were dysphagia (10 patients), foreign body sensation (8 patients), regurgitation (7 patients), cough (4 patients), heartburn (3 patients), nausea (2 patients), dyspepsia (2 patients). Of 36 patients who completed 8 weeks of PPI, 11 (30%) were PPI-responsive. The other 25 patients (69%) continued with the elimination diet with PPI for another month. 15 patients (60%) had complete remission. Remission was sustained in 72% of patients at 3 months with the 2 treatment modalities. At 9 months, only 9/15 (60%) of patients who responded to the elimination diet with PPI remained complaint and sustained remission. 5 out of the 11 PPI-responsive patients also sustained remission at 9 months.

Discussion/Conclusion: Many patients previously diagnosed with EoE will respond to PPI. Initial response > 50% is possible with the elimination diet plus PPI, but many will cease the diet and relapse.
Endoscopic, histological, clinical and radiological characteristics of patients with eosinophilic esophagitis

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Eosinophilic esophagitis is a chronic disease characterized by esophageal symptoms in an association with a dense eosinophilic infiltrate associated with clinical and endoscopic manifestations.

Introduction: We aimed to determine typical features of eosinophilic esophagitis patients.

Methods: The study included patients with dysphagia and underwent upper endoscopy for eosinophilic esophagitis (≥ 15 eosinophils in at least one high-power field and no response to acid suppressants). Demographic and multiple clinical factors were collected.

Results: A total of 45 patients (80% males, mean age 35 ± 16) met the criteria for eosinophilic esophagitis. Median age at presentation was 31 years (range 18–49 years). 32 patients complained of solid disphagia (71%), and 29 of bolus impaction (64%). 66.7% of eosinophilic esophagitis subjects had either asthma or airway hyperresponsiveness. Total serum IgE was the only biomarker associated with a greater risk of airway hyperresponsiveness (OR = 9.643, 95% CI: 1.633, 56.925). Endoscopic found furrows in 20 (44%), rings in 9 (20%), crepe paper in 12 (27%), whitish exudates/plaques in 7 (13%) and normal findings in 14 patients (31%). Ten patients had proton-pump inhibitor-esophageal eosinophilia (22%). Endoscopic and radiologic stenosis occurred in 20 (44%) and 23 (52%), respectively.

Discussion/Conclusion: Asthma and airway hyperresponsiveness may be more prevalent than previous estimates in patients with eosinophilic esophagitis, and also IgE was the only biomarker associated with a greater risk of airway hyperresponsiveness.
Eosinophilic esophagitis in children: Clinical manifestations and endoscopic findings

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Eosinophilic esophagitis is an allergic inflammatory disease defined by abnormal immune response of the esophageal mucosa to exogenous allergens.

Introduction: Allergic responses to food and aeroallergens have been increasingly implicated in the etiology of this disease.

Methods: We describe a retrospective data analysis of pediatric eosinophilic esophagitis patients followed in our Department of Immunoallergology. Were performed a total of 30 esophagogastroduodenal endoscopy in children, diagnosed with eosinophilic esophagitis, aged from 3 and 16 years.

Results: Of the 25 children (22 male, average 10.8 years), 88% had prior history of rhinoconjunctivitis, 76% asthma 48% eczema and 36% food allergy. After evaluation, we identified in 76% and 92% of patients food and aeroallergen sensitization, respectively; 68% had simultaneously food and inhalant sensitization and 96% had at least one positive test to aeroallergens or food allergens. Feeding aversion, vomiting and/or regurgitation were most frequently observed in the younger children, while in older children: abdominal pain, dysphagia and chest pain. Granular mucosa, longitudinal furrows and mucosal rings belong to the findings most often summer, 23% in the fall and 25% in the winter. The time between symptoms onset and the eosinophilic esophagitis diagnosis averaged 17.3 ± 21.5 months.

Discussion/Conclusion: Eosinophilic esophagitis was diagnosed in every age, with more frequently in boys than in girls. A multidisciplinary approach is needed for a correct evaluation and follow-up of these patients.
Association between eosinophilic esophagitis and allergic rhinitis

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Eosinophilic esophagitis has been reported to co-occur with some allergic diseases; frequently associated with other allergic conditions such as allergic rhinitis, allergic dermatitis and eosinophilia.

Introduction: We aimed to evaluate the co-existence of eosinophilic esophagitis at the patients with allergic rhinitis.

Methods: The study group included 113 patients with allergic rhinitis (AR group) and the control group (CG) was formed with 97 cases with dyspepsia symptoms. Symptoms of AR and CG groups were compared in terms of endoscopic and histological findings.

Results: A total of 14 patients of the AR group met the criteria for eosinophilic esophagitis. All patients were males. Median age at presentation was 33 years (range 17–46 years). Blood IgE levels were significantly higher among eosinophilic esophagitis patients compared to those without eosinophilic esophagitis (p = 0.006). Reflux symptoms were more common in patients with eosinophilic esophagitis (71.4%). The presence of H. pylori was similar between groups. Skin prick test (SPT) positivity was present in 85.7 of patients with eosinophilic esophagitis and 50% of the patients without (p = 0.223). The most common endoscopic finding was plaques (46.6%) and other findings were irregular, erosive esophagitis, white exudates, linear furrows, Schatzki ring, ulcers and erythema. Allergens were more likely to be dermatophagoides fariniae and dermatophagoides pteronyssinus in patients with eosinophilic esophagitis (p = 0.084 and p = 0.068).

Discussion/Conclusion: The most common symptom among patients with eosinophilic esophagitis is reflux. In AR patients with reflux symptoms, high serum IgE levels and tests are positive for allergy, endoscopic evaluation may be recommended.
Benefits and side effects of drug therapy in patients with eosinophilic esophagitis

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The medical treatment of eosinophilic esophagitis can have beneficial effects consisting of reducing patient accusations, improving endoscopic and histopathological appearance, but also side effects.

Introduction: The objectives of our study were to investigate the frequency and characteristics of the benefits/adverse reactions of the drug treatment of patients with eosinophilic esophagitis.

Methods: We have examined 38 patients diagnosed with eosinophilic esophagitis who have received treatment with corticosteroids (budesonide and fluticasone propionate) and proton-pump inhibitors (esomeprazole). The data have included the patient’s sex, the environment of origin, the type of corticosteroid treatment used as well as adverse reactions.

Results: Thirty-eight patients have been treated with eosinophilic esophagitis, 18 have received budesonide 2 mg/day, 20 with fluticasone propionate 880 microg/day associated with esomeprazole 40 mg/day for 6 weeks, 28 males and 10 female, 25 of them come from the urban environment and 13 from the rural area, 3 patients have developed oropharyngeal candidiasis as an adverse reaction. The therapeutic success has been recorded in 32 patients by diminishing dysphagia.

Discussion/Conclusion: Drug treatment leads to diminution of dysphagia, and to improved endoscopic and histopathological appearance. Corticosteroids used over a long period of time can cause a number of side effects: diabetes, osteoporosis, hyperphagia, acne.
Dietary management in patients with eosinophilic esophagitis

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Eosinophilic esophagitis is a chronic, immune esophagus which shows the clinical manifestations and symptoms of esophageal disorder and it is characterized by histopathological infiltrated esophageal epithelium with over 15–20 eosinophils/field.

Introduction: The aim of our study was to evaluate dietary treatment in patients with eosinophilic esophagitis.

Methods: We have examined 40 patients diagnosed with eosinophilic esophagitis who have received dietary treatment. It has consisted of removing some diet foods such as soy, eggs, peanuts, nuts, wheat and seafood. All patients have been evaluated through biopsies, endoscopic removal and skin test.

Results: Forty patients have been examined, of which 28 were males and 12 females. In 32 patients who have been excluded from 6 food diet, we have found a reduction in having difficulties in swallowing, 28 have shown an improvement in endoscopic appearance, and 26 of the patients an improvement in histology. 17 patients have experienced allergy to peanuts, to egg white 10 patients, and 8 of them are associated with asthma.

Discussion/Conclusion: More than 50% of the examined patients have suffered from food allergy, most commonly to peanuts, eggs and soy. Eosinophilic esophagitis is increasing as a result of exposure to a variety of allergens, food additives. Elevated eosinophil can also occur in the following conditions: asthma, allergic rhinitis, atopic dermatitis, gastroenteritis/proctocolitis eosinophilia, Loffler’s syndrome, vasculitis, lung aspergillosis, parasitic infestations, such as eosinophilic leukemia and inflammatory bowel diseases.
Eosinophilic esophagitis: Proton-pump inhibitor approach

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Eosinophilic esophagitis (EoE) is an immune-mediated inflammatory disease, characterized by eosinophilic infiltration in the mucosa. A proton-pump inhibitor (PPI) therapy is mandatory in patients with a histopathologic diagnosis of EoE; in those unresponsive to PPI treatment, EoE should be suggested.

**Aim:** To determine the effect of double-dose PPI therapy on symptoms, endoscopic and histological findings in patients diagnosed with EoE (≥ 15 eosinophils/high-power field [HPF]).

**Methods:** We conducted a study that included 19 patients diagnosed with EoE. The patients received a PPI (omeprazol) 20 mg twice daily before meals for 8 weeks. After 8 weeks we evaluated clinical, endoscopic and histological results. The histological response was interpreted as follows: resolution (0–5 eosinophils/HPF), partial improvement (5–14 eosinophils/HPF) or no improvement (≥ 15 eosinophils/HPF).

**Results:** The outcomes of the study revealed histological improvement for 52.6% (10) and complete resolution for 31.5% (6). Similar results were deducted from the clinical evaluation (improvement in 68.4% – 13 patients) and from the endoscopic analysis as well, where signs were normalized for 36.8% (7) and reduced for 57.8% (11). In addition, complete remission occurred for 26.3% (5) both clinically and histologically.

**Discussion/Conclusion:** After receiving 8 weeks of treatment with a double dose of PPI, more than half of the studied patients diagnosed with EoE considerably improved. Our results are in accordance with the published guidelines for recommending a PPI trial prior to diagnosing EoE.


Prevalence of atopic disease in Tunisian patients with eosinophilic esophagitis

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Introduction: Eosinophilic esophagitis (EoE) is an increasingly prevalent chronic inflammatory disease of the esophagus with an immunoallergic etiology. There are a number of etiologic risk factors that have either been identified or hypothesized to contribute to the increase of EoE. One possibility relates to EoE as an allergic disease. The objective of this study was to evaluate prevalence of atopic disease in patients with eosinophilic esophagitis.

Methods: We performed a retrospective study from 2006 to 2016 including patients diagnosed with eosinophilic esophagitis based on typical symptoms, endoscopic abnormalities and infiltration of the esophageal epithelium with ≥ 15 eosinophils/high-power field. Data regarding patient characteristics, history of atopic comorbidities, and allergy test results were collected for analysis.

Results: Nine patients were included (5 male – 4 female). Mean age was 39.5 (28–52 years). Two patients had a family history of atopic disease. Two thirds of patients had a personal atopic comorbidities: asthma (22.2%, n = 2), rhinoconjunctivitis (22.2%, n = 2), atopic dermatitis (11.1, n = 1) and food allergy (n = 1) confirmed by a positive skin test. Forty four of all patients suffered from at least 1 of these 4 diseases and 1 patient suffered from 3 of them. One third of patients have increased numbers of circulating eosinophils 810 elements/mm³ [600–1200]. Total IgE levels are increased in 50% to 60% of patients with EoE in 2 patients (22.2%).

Conclusion: In our study, atopic diseases were associated with the diagnosis of eosinophilic esophagitis in 66% of patients. This high prevalence support the consideration of eosinophilic esophagitis as an atopic disease and underline the important role of allergists in early diagnosis and treatment.
Distinguishing features of eosinophilic esophagitis from gastroesophageal reflux disease

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Introduction: Eosinophilic esophagitis is a chronic, immune disorder mediated largely by food antigens. It have overlapping clinical, manometric, endoscopic and histopathologic features with gastroesophageal reflux disease.

The aim of our study is to define the clinical features of patients with eosinophilic esophagitis, distinguishing it from gastroesophageal reflux disease.

Methods: We performed a retrospective study from 2006 to 2016 including patients suffering from gastroesophageal reflux disease and eosinophilic esophagitis. Eosinophilic esophagitis was diagnosed with epithelial eosinophils ≥ 15 in high-power field. Two groups were compared:

1. First group: patients suffering from eosinophilic esophagitis (n = 9)
2. Second group: patients suffering from gastroesophageal reflux disease (n = 155)

Results: From 164 patients included, nine had a confirmed eosinophilic esophagitis (5.4%). Patients was significantly younger in the first group (mean age 39.5 years versus 53.4 years, p = 0.003). There was no difference between the two groups in the male gender rate (55% in the first group versus 54.2% in the second, p = 0.1). Concerning clinical presentation dysphagia and food impaction were significantly more common in the first group (77.7% versus 40%, p = 0.002; 22.2% versus 7.7%, p < 0.001 respectively). Chest pain was equally found in the two groups (33.3% in the first versus 33.5% in the second, p = 0.6). Endoscopic fixed esophageal rings were more common in eosinophilic esophagitis patients (22.2% versus 0.6%, p < 0.0001) while hiatus hernia was more common in non-eosinophilic esophagitis patients (20.6% versus 11.1%, p = 0.002).

Conclusion: Our study showed a higher prevalence of eosinophilic esophagitis in young population without male gender predominance. The interaction between eosinophilic esophagitis and gastroesophageal reflux disease seems complex but the distinction is important because of different treatment.
Clinical features of eosinophilic esophagitis: A monocentric study

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Introduction: Eosinophilic esophagitis (EoE) is a chronic immune system disease. Once considered a rare condition, it is now one of the most common cause of dysphagia and food impaction in adults. The aim of this study was to analyze the diagnostic, endoscopic, histological and therapeutic features of EoE.

Methods: We performed a retrospective study from 2006 to 2016 including patients diagnosed with EoE based on typical symptoms, endoscopic abnormalities and infiltration of the esophageal epithelium with ≥ 15 eosinophils/high-power field (hpf).

Results: Nine patients were included (5 male – 4 female). Mean age was 39.5 (28–52 years). 2/3 of patients had a personal history of atopic disease. The median duration of symptoms before diagnosis was 36 months (3–60 months). The main symptoms were dysphagia (77.7, n = 7), chest pain (33.3%, n = 3) and food impaction (22.2%, n = 2). 1/3 of patients have increased numbers of circulating eosinophils. Total IgE levels are increased in 50% to 60% of patients with EoE in 2 patients (22.2%). Endoscopic findings were fixed esophageal rings (n = 2), whitish exudates (n = 2), longitudinal furrows (n = 1), edema (n = 1), diffuse esophageal narrowing (n = 1), narrow-caliber esophagus, and esophageal lacerations (n = 2). Mean number of eosinophils/hpf in the biopsy was 63 (range: 20–260). All patients underwent treatment: corticosteroids (n = 4), proton-pump inhibitor (n = 4). For one patient who refused medical treatment, we opted for dietary therapy.

Conclusion: As shown in the literature, EoE affects mostly middle-age atopic males and manifest with dysphagia. Its incidence is increasing justifying that any patient with symptoms of esophageal dysfunction should be biopsied for EoE.
Is there a way to upgrade the diagnosis of eosinophilic esophagitis?

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Introduction: The occurrence of eosinophilic esophagitis has increased recently. It is debatable whether the reason for the recent high prevalence of eosinophilic esophagitis is a real increase in the incidence or increased diagnosis due to increased awareness about the disease. Few series had been reported in the literature. The aim of our study is to describe epidemiological, clinical and endoscopic features of patients with confirmed eosinophilic esophagitis and to try to define a group a patient in whom the esophageal biopsies is necessary.

Methods: A retrospective study from 2006 to 2016 including patients diagnosed with eosinophilic esophagitis based on infiltration of the esophageal epithelium with $\geq 15$ eosinophils/high-power field.

Results: Nine patients were included with a mean age of 39.5 (28–52 years). The sex ratio was 1.25 (M/F = 4/5). Personal history of atopic disease was found in 75% of cases. Most of patients (77.7%) were symptomatic at least 4 years before diagnosis established. Dysphagia was the main symptom (77.7%). All patients had reported a past of gastroesophageal reflux disease of 5.7 years (range 4–9 years) treated for meanly 3.7 years as idiopathic gastroesophageal reflux disease with proton-pump inhibitor with only 22.2% therapy response. Endoscopic findings were strongly suggesting eosinophilic esophagitis in two patients (fixed esophageal rings) while it was nonspecific in the most cases (whitish exudates [n = 2], longitudinal furrows [n = 1], edema [n = 1], diffuse esophageal narrowing [n = 1], narrow-caliber esophagus, and esophageal lacerations [n = 2]).

Conclusion: Neither the symptoms are pathognomonic nor the predictive value of the endoscopic features are sufficient to make a certain diagnosis of eosinophilic esophagitis. That is why biopsy of esophagus should be considered, even when the macroscopic appearance is normal especially in patients with rebel gastroesophageal reflux disease.
Gastric eosinophils in patients with eosinophilic esophagitis: Incidence and clinical impact

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Introduction: Eosinophilic gastritis represents one member within the spectrum of diseases collectively referred to as eosinophilic gastrointestinal disorders. It is less common than eosinophilic esophagitis (EoE).

The aim of this study was to determine the incidence of eosinophilic gastritis in EoE patients and to compare the clinical features and response to therapy between the two groups.

Methods: A retrospective study from 2006 to 2016 including patients diagnosed with EoE, based on infiltration of the esophageal epithelium with $\geq 15$ eosinophils/high-power field. All patients had systematic gastric biopsies and eosinophilic gastritis was defined by $> 10$ eosinophils/high-power field. Two groups were compared:
1. EoE patients with eosinophilic gastritis
2. EoE patients without eosinophilic gastritis

Results: From nine patients included, 1/3 had an eosinophilic gastritis. There was no difference between the two groups in the mean age, sex ratio and the personal history of atopic disease. Concerning clinical presentation, all eosinophilic gastritis patients suffered from dysphagia while it was absent in two cases in non-eosinophilic gastritis patients. No significant difference was noted about chest pain and food impaction ($p = 0.3$ and $p = 0.07$ respectively). Biological findings showed highly significant peripheral eosinophilia and total IgE level in the first group (33.3% versus 16.6%; $p = 0.02$). The endoscopic examination was similar in the two groups. Two patients in each group were treated by corticosteroids. The therapy response was significantly better in EoE patients without eosinophilic gastritis (33.3% versus 16.6%, $p = 0.02$).

Conclusion: Our study showed that the incidence of eosinophilic gastritis in patients with EoE was 33.3% and it was associated to severe clinical presentation and worst therapy response. It is unclear whether patients with EoE and normal gastric biopsies are phenotypically different from patients with EoE and gastric mucosal abnormalities.
Eosinophilic esophagitis presenting with hematemesis in an adolescent with meadow pollen allergy

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Eosinophilic esophagitis (EoE) is presented with vomiting and feeding difficulty. Most of the patients have food allergy while some have inhalant allergies. Here we report an adolescent with meadow pollen allergy who had hematemesis and finally was diagnosed as EoE.

Case report: Sixteen-year-old boy was admitted to pediatric allergy department due to nasal itching, sneezing, nasal discharge. Skin-prick test revealed meadow pollen 20 x 20 mm positive. Besides medical therapy meadow pollen specific subcutaneous immunotherapy was began after 3 month's follow-up. On the 3rd dose of starting protocol the patient had sudden short of breath, hyperemia on the face and body, and itching and finally developed to anaphylaxis. Immediately anaphylaxis was treated in the ER and immunotherapy was stopped thereafter. Seven months later the patient had symptoms of allergic rhinitis and abdominal pain and bloody vomiting and was admitted to hospital. Upper gastrointestinal system endoscopy revealed erosive esophagitis, hyperemic stomach. Pathological evaluation severely elevated showed eosinophils (51/100 HPF). Treatment included PPI, H2-receptor blockers, inhaled fluticasone propionate (250 mcg swallowed BID). The patient’s complaints resolved after treatment. Food and inhalant specific IgE levels were studied and only meadow pollen was found > 100 IU/dl. After meadow pollen season all the medications were stopped. 3 months later meadow pollen specific sublingually oral immunotherapy was started and the patient had very mild symptoms during spring. He is still under our control with very mild symptoms.

Conclusion: Eosinophilic allergies may flare with inhalant and during seasonal changes. Those patients should be followed by both pediatric allergy and gastroenterology clinics. Immunotherapy should be kept in mind among EoE patients who have inhalant allergies.
Eosinophilic esophagitis: Rationalizing therapy

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Introduction: Eosinophilic esophagitis (EE) is a chronic condition of the esophagus with pathognomonic clinical, endoscopic and histologic features. We aimed to prognosticate which cohort of patients respond best to proton-pump inhibitor monotherapy or topical steroids based on index endoscopy and histology in conjunction with symptoms at presentation and on follow up.

Methods: Patients referred with dysphagia or with an incidental histology finding of > 15 eosinophils/high-power field (eos/hpf) between Feb 2013 and Dec 2015 were analyzed by retrospective case note review and patient communication. Univariate analysis and binary logistic regression was used to identify associations between clinical characteristics subsequent response to treatment. Associations were assessed by Fishers exact test, t-test and Mann-Whitney for nominal, continuous parametric and non-parametric variables respectively.

Results: There was a trend towards a higher eos/hpf in patients who presented with FBO (47 ± 21) compared to dysphagia (38 ± 17) and reflux (38 ± 17) (p = 0.073). Endoscopic evidence of chronic stricturing disease was associated with a higher eos/hpf than those with no strictures (mean 50.3 vs 38.6; p = 0.04). Patients with index features of chronic disease were more likely to be associated with failure of the eosinophilia to normalize regardless of medical treatment compared to those with acute changes (furrows, exudates) (33% vs. 75%; p = 0.02). Furthermore, patients with dysphagia or FBO demonstrated a reduced normalization of eos/hpf following either steroid or PPI therapy compared to those not presenting with these symptoms at a minimum of 3 months (46% vs. 100%; p = 0.03). Regardless of endoscopic findings, patients presenting with dysphagia and/or FBO demonstrated a higher response to steroids than those with reflux symptoms (50% vs 9% p = 0.018) who responded best to PPI (91%).

Patients with chronic EoE findings at initial endoscopy were less likely to respond symptomatically to PPI monotherapy compared to those with normal or acute endoscopic findings (32% vs. 68%; p = 0.003) while they were more likely to respond to steroids (64% vs 36%; p = 0.002. Specifically, the presence of strictures indicated a more likely clinical response to steroids compared to PPI alone. (p = 0.007).

Discussion/Conclusion: A higher eos/hpf was found in patients with chronic features at index endoscopy than those with normal or acute endoscopic signs. In those with normal/acute EoE changes, without dysphagia as a presenting complaint, clinical response was noted with PPI therapy alone. In those with chronic EoE changes or with dysphagia/FBO, steroids appear to be the preferred therapeutic option, although at 3 months follow up a clinical response might precede a histological one.
Modulation of CD8+ cells infiltration and activity in eosinophilic esophagitis by six-food elimination diet

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Introduction: Eosinophilic esophagitis (EoE) is characterized by a dense intraepithelial inflammatory infiltrate of eosinophils, mast cells, and CD4 and CD8 lymphocytes. Histological and clinical remission after dietary exclusion supports immune-allergic mechanisms as the driving force in EoE. However, the role of CD8+ cells and CD8-specific cytotoxic molecules, as key contributors to EoE pathophysiology, have not been explored.

Methods: Naïve EoE patients (n = 10; age: 33 ± 10 years-old) who responded clinically and histologically to a six-food elimination diet (SFED: milk, cereals, egg, fish, legumes, nuts) and healthy-esophagus controls (C, n = 10; age: 53 ± 20 years-old) were included. Esophageal biopsies were collected in all subjects before and after therapy, and at baseline in controls. Clinical symptoms were assessed and analysed before and after SFED, and food triggers were identified. The number of eosinophils and CD8+ cells per high-power field (hpf) were quantified after haematoxylin-eosin and immunofluorescence staining, respectively. Expression of eotaxin-3 and cytotoxic CD8-related molecules was assessed by qPCR.

Results: Main symptoms reported were dysphagia (70%), and food impaction (70%). The most frequent triggering foods were cereals (70%) and milk (60%). Compared to controls, eosinophils (EoE: 56.80 ± 29.91/hpf vs. C: 0 ± 0/hpf) and CD8+ cells (EoE: 19.70 ± 12.37/hpf vs. C: 4.9 ± 4.03/hpf) were higher in EoE patients (p < 0.05). SFED significantly reduced cell counts (eosinophils: 3 ± 4.22, CD8: 6.96 ± 7.25/hpf; p < 0.05) in parallel with clinical improvement. Granzyme A, granzyme B, granulysin and eotaxin-3 gene expression were higher in EoE than in C (1.6 to 26-fold-change; p < 0.05) and decreased to C values after SFED treatment. Positive correlation was found between eotaxin-3 expression and dysphagia symptoms ($r_s = 0.73$), CD8 counts ($r_s = 0.94$) and granzyme B ($r_s = 0.75$; p = 0.02) and between eosinophils and CD8 counts ($r_s = 0.81$; p = 0.06).

Discussion/Conclusion: Reduction in CD8 lymphocytes number and proteases expression, in association with clinical improvement after SFED, suggest that CD8-mediated cytotoxic mechanisms are involved in eosinophil recruitment and epithelial damage in active EoE.
The effect of diet on eosinophilic esophagitis in adult patients

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Introduction: Eosinophilic esophagitis (EoE) is an immune-mediated inflammatory disease, characterized by eosinophilic infiltration in the mucosa. The effectiveness of 6-food elimination diet (SFED) were demonstrated in children with EoE. Our aim was to assess the effects of the SFED followed by food reintroduction on the histologic and clinical response in adults with EoE.

Methods: We conducted a prospective study that included 16 patients diagnosed with EoE. Patients were recommended to SFED for 8 weeks. Clinical, endoscopic and histological (resolution: 0–5 eosinophils/HPF, partial improvement: 5–14 eosinophils/HPF), or no improvement: (≥ 15 eosinophils/HPF) evaluation was repeated at the end of this period.

Results: The most common symptoms of EoE were dysphagia (91%), food impaction (79 %), and heartburn (96%). After the SFED, clinical improvement occurred in 12 (75%) – p < 0.0001, endoscopic signs were reduced in 10 (62,5%) and normalized in 3 (18,75%), and histologically, 6 (37,5%) improved, while 4 (25%) obtained complete resolution. After food reintroduction, symptoms have reappeared, endoscopic signs and esophageal eosinophil counts returned to pretreatment values (p < 0.0001).

Discussion/Conclusion: Dietary interventions are effective in improving endoscopic and histologic features in adults patients with EoE. Food reintroduction re-initiated features of EoE in patients, indicating a role for food allergens in its pathogenesis. In conclusion, diet is a feasible therapeutic option for adult EoE patients.
A presumptive relationship between presence of the allergic asthma and development of the eosinophilic esophagitis

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Introduction: Aim of this study was to determine the predictive factors of eosinophilic esophagitis (EoE) in patients with asthma and to identify the mains relationships between EoE and type of asthma.

Methods: This retrospective study was performed comparatively on two groups of patients: the A group consists of 34 cases with EoE in asthmatic patients and the B group contains 54 patients with asthma without EoE. Diagnosis of EoE was based on clinical patterns and endoscopy with biopsies showing > or 15 eosinophils/hpf. Also we determined allergy evolution consisting of skin testing to allergens and serological tests. In all groups we analyzed age, gender, use of inhaled corticosteroids, type of asthma (allergic vs. non-allergic), peripheral eosinophilia and diagnosis of other atopic disease.

Results: The mean age of the patients was: 33.91 ± 12.33 years in the A group and 41.09 ± 13.28 years in B group. In the whole group majority of patients (55 cases, 62.50%) had allergic asthma: 12 patients had only one allergen, 32 cases present 2–4 allergens and in 11 cases identified more than 5 allergens. The use of inhaled corticosteroids was negatively associated with EoE (p < 0.01) in asthma patients. The negative relationship was strong in patients with allergic type of the asthma. We identified correlations between EoE and peripheral eosinophilia, allergic asthma or allergic rhinitis in patients with asthma. The presence of the allergic asthma was correlated with EoE, but uncorrelated with the count of eosinophils/hpf in the tissue biopsy.

Discussion/Conclusion: The inhalant allergens and the food can represent main factors involved in the development of EoE in patients with asthma. The use of inhaled corticosteroids had a protective effect against EoE in patients with allergic type of the asthma.
The safety and tolerability of the budesonide in treatment of eosinophilic esophagitis

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Introduction: We investigated the efficacy and safety of therapy with nebulized oral budesonide versus corticosteroids in patients with active eosinophilic esophagitis (EoE).

Methods: We studied 36 patients with active eosinophilic esophagitis. Diagnosis was based on clinical presentation and endoscopy with biopsies shorting > or 15 eosinophils/hpf. This comparative study was performed on two groups of patients: the A group composed of 25 patients who received treatment with nebulized oral budesonide (1 mg twice daily for 2–4 weeks as induced remission therapy) and B group consist of 11 patients treated with methylprednisolone (1.5 mg/kg daily, 60 mg/day as maximum). In the A group, maintenance therapy consist of nebulized oral budesonide (0.5 mg twice daily for 6–24 weeks). Pre-treatment and post-treatment disease activity was assessed clinically, endoscopically and histologically.

Results: At baseline the mean values of dysphagia scores was similar in both groups: 3.16 in A group and 3.09 in B group. After six weeks dysphagia scores significantly improved in A group (in 20 cases, 80%) comparative in B group (6 cases, 54%). The dysphagia scores continue to improve in maintenance therapy in majority of cases. At four weeks course of therapy significantly decreased the number of eosinophils in the esophageal epithelium in the A group (from 61.4 to 8.5 eosinophils/hpf) comparative with B group (from 49.8 to 12.7 eosinophils/hpf). The side effects of treatment in B group was: poor growth (5 cases), osteopenia (3 cases), bone marrow suppression (only one case), hyperglycemia (2 cases), cushingoid features (2 cases). In A group esophageal candidiosis was the only adverse effect (2 cases). In B group discontinuation of therapy led to a recurrence of symptoms in 4 cases (35.37%).

Discussion/Conclusion: Treatment with nebulized oral budesonide was highly effective and safe in inducing clinical and histological remission in eosinophilic esophagitis.
Eosinophilic esophagitis: A Tunisian retrospective study

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Introduction: Eosinophilic esophagitis (EoE) is a rare disease that is often misdiagnosed. It is characterized by persistent esophageal eosinophilia. The aim of this study was to report the clinical, endoscopic and histological features of EoE in a Tunisian population.

Methods: We conducted a retrospective study including patients with EoE followed in our department between January 2013 and December 2016.

Results: Eight patients were included. Their mean age was 26 years and the sex ratio was 3 (6M/2F). Only one patient had a personal history of asthma and allergies. The appealing signs were dysphagia in 5 cases, epigastric pain in 2 cases and hematemesis in one case. One patient had an eosinophilic ascites. A high blood count of eosinophils (> 500/mm³) was found in 50% of cases (4 patients). All patients underwent esophageal endoscopy. Esophageal rings with linear furrows were found in six patients, moreover, 3 of them had whitish papules and one had a stricture that needed dilation. In other cases, the esophageal endoscopy was normal. Histologically, esophageal biopsies showed in all cases more than 15 eosinophils per high-power field. All patients were treated by proton-pump inhibitors. Systemic corticosteroids were administrated in case of associated blood hypereosinophilia and topic steroids were given in case of asthma. The patient with a stricture underwent endoscopic dilation. Clinical remission was obtained in 75% of cases. Endoscopic control was performed in 2 cases which had persistent dysphagia, esophageal biopsies showed histological remission in both cases.

Conclusion: EoE should always be evoked in case of unexplained dysphagia, and, since the diagnosis is based on histological features, esophageal biopsies should be performed even in the absence of endoscopic abnormalities.
Benefits of esophageal biopsies in patients with dysphagia and normal upper endoscopy

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Introduction: Dysphagia frequently reveals organic as well as functional esophageal diseases. Endoscopy sometimes shows few signs or even a macroscopically normal esophagus. The discovery of “eosinophilic esophagitis (EoE)” has added immensely to our understanding of dysphagia causes in patients with normal-appearing esophageal mucosa, which led many endoscopists to realize systematic biopsies of a normal esophagus in case of dysphagia.

The aim of our study is to evaluate the importance of systematic esophageal biopsies in patients with dysphagia and normal endoscopy, and report the incidence of EoE which remains a rare entity.

Methods: It is a retrospective descriptive study, collecting all consenting patients who had an upper endoscopy for dysphagia from June 2015 to June 2017. All patients who had an organic malignant or benign stenosis causing dysphagia were excluded and only those with strictly normal esophageal mucosa and esophageal biopsies were included in the study.

Results: Eighty-five patients (40 men and 45 women) suffering from chronic dysphagia with normal upper endoscopy were studied. The mean age of our patients was 56 years old (13 to 88 years old). Fifteen patients (29.4%) had past medical history: 9 (10.5%) with Crohn’s disease, four patients have been treated for a gastroesophageal reflux by proton-pump inhibitors (PPIs), one patient was diagnosed with multiple myeloma and one other patient had Gougerot-Sjögren syndrome.

All patients had normal-appearing esophagus in upper endoscopy and they all had biopsies of esophagus.

Histopathological examination revealed normal esophageal mucosa in 65 patients (76%), non-specific esophagitis in eleven cases (12.9%), reflux esophagitis in 4 cases, Barrett’s esophagus in one patient, and eosinophilic esophagitis was diagnosed in 4 patients (4.7%) with a good outcome with PPI treatment in 3 cases and topical steroids in 1 patient.

Discussion/Conclusion: Our study shows the importance of systematic biopsies in normal esophagus in case of dysphagia as they may enable us to diagnose some rare diseases like eosinophilic esophagitis which can be successfully treated, so that we can avoid many unnecessary costly explorations like manometry. Further studies are to be conducted to confirm the cost effectiveness of systematic biopsies.
Eosinophilic esophagitis: Case reports

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Introduction: Eosinophilic esophagitis (EoE) is a chronic immune system disease. It has been identified only in the past three decades, but is now considered a major cause of dysphagia and food impaction. Many other disorders are accompanied by eosinophilic infiltration in the esophagus, but EoE has become an independent entity which was considered in 1993 by Attwood et al. as distinct clinical condition. The aim of this poster is to report four cases of EoE which remains an important scarce entity to understand and to treat.

Methods: We report 4 cases of EoE diagnosed in patients who underwent an upper endoscopy for dysphagia in our Gastroenterology Department between June 2015 and June 2017.

Results:
Case 1: A thirty-six year-old woman with a past medical history of allergic rhinitis presented with a history of food impaction for 3 months. There was no history of reflux, vomiting, or other gastrointestinal symptoms. Clinical examination was normal. Upper endoscopy showed concentric rings along the esophagus. Biopsies of the esophagus showed a dense eosinophilic infiltrate (> 30 eosinophils per high-power field – HPF). Allergy skin tests were negative and blood count did not show hypereosinophilia. Our patient was treated for EoE with topical steroids (Fluticasone) for eight weeks and elimination diet avoiding all presumed allergens. Symptoms were relieved and our patient remained in remission for a 20-month follow up.

Case 2: A fifty-six year-old man with a past of a coronary heart disease, presented to our division with a history of dysphagia, GERD symptoms and heart burn. His electrocardiogram was normal and his physical exam was unremarkable. The upper endoscopy was normal and biopsies of esophagus showed high eosinophilic infiltrate (> 26 eosinophils/HPF). No allergic tests were conducted and complete blood count did not show high polynuclear eosinophils level. We prescribed proton-pump inhibitors (PPIs) for 8 weeks and dysphagia was completely resolved and he has been in remission for an 18-month follow up.

Case 3: A thirty-two year-old woman with no past medical history presented with dysphagia and vomiting for two weeks. Clinical examination was normal and biology tests were unremarkable. Upper endoscopy showed mucosal longitudinal furrows in the esophagus. Biopsies showed eosinophilic infiltrate of 24 eosinophils/HPF. We treated our patient with PPIs for 8 weeks and we have no information regarding her follow up.

Case 4: A sixty-two year-old woman with a past history of asthma, presented with dysphagia and weight loss. Physical exam was normal. Upper endoscopy showed a normal esophagus. Biopsies from proximal and distal parts of esophagus showed an infiltrate of 24 eosinophils/HPF. She was diagnosed with EoE and treated by PPIs for 6 weeks. Dysphagia was relieved and she was in remission for a 3-month follow up.

Discussion/Conclusion: EoE has become a certain cause of dysphagia. Endoscopists should be aware of the importance of esophageal biopsies if clinical and endoscopic features of this rare entity are present.
Diagnosis and management of eosinophilic esophagitis: A 13-year retrospective review in a pediatric population in the Netherlands

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Introduction: Eosinophilic esophagitis (EoE) is an increasingly recognized, chronic, immune-mediated disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation (> 15 eosinophils/HPF). The symptoms vary from frequent vomiting to food refusal in young children to refractory GE reflux, dysphagia or even food impaction in older children and adolescents. In 2007 international consensus recommendations were published on the diagnosis and treatment of EoE and in 2013 the ESPGHAN published practical guidelines on EoE in children and adolescents. The aim of our study was to determine the diversity in diagnosis and management of EoE in pediatric patients in the Netherlands in comparison to the international consensus recommendations.

Methods: The medical records of 151 children < 18 years old with biopsy proven EoE treated from 2000 to 2013 by pediatric gastroenterologists in the Netherlands were reviewed. Patient characteristics, clinical, endoscopic, and histologic findings were recorded and analyzed using SPSS.

Results: EoE was diagnosed from 1 to 24 in 13 years, the majority being diagnosed after 2008. 69% were male and the median age at diagnosis was 9.3 years (range 3 months to 18 years). In 67.5% symptoms of refractory GE reflux or dysphagia was the indication for endoscopy, in 18.5% was this even food impaction. In 74% macroscopic findings as granular mucosa, longitudinal furrows, white plaques and trachealization were present. The initial treatment consisted of local (42%) or systemic (6%) corticosteroids, elemental or elimination diet (31%), a combination of diet and corticosteroids (15%) or no treatment (6%). The amount of endoscopies during the diagnostic process varied from 1 to 12 per patient.

Discussion/Conclusion: Eosinophilic esophagitis is increasingly diagnosed in the pediatric population of the Netherlands. The diagnostic process and treatment varies significantly. An even better recognition and more uniformity in the management of EoE is necessary.
Pediatric eosinophilic esophagitis: Results of the retrospective pediatric eosinophilic esophagitis registry (RetroPEER)

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Objectives: Recommendations for diagnosing and treating eosinophilic esophagitis (EoE) are evolving, however information on clinical practice is lacking. This study aimed to assess the practices of European pediatric gastroenterology centers diagnosing and treating EoE and to identify the allergens reported to trigger EoE.

Methods: Pediatric gastroenterologists from 25 centers in 13 European countries submitted retrospective anonymous patient information to an online database. Patient inclusion criteria were: Diagnosis with EoE below the age of 18, completion of the diagnostic work up prescribed by the treating physician, and were on stable medical or dietary interventions. Patients responsive to proton-pump inhibitors (PPI) were excluded.
**Results:** In total, 410 patients were analyzed. The most frequent indications for endoscopy were: dysphagia (26.8%), gastroesophageal reflux symptoms (22.1%), foreign body or food impaction (19.7%), and failure to thrive (6.4%). PPI trials were performed in 70.5%, with higher rates of PPI testing noted in more recent cases (p = 0.005 for trend) as new guidelines were published. In patients who had undergone any form of elimination diet, the allergens reported as causative for EoE were milk (35%), egg (17.4%), wheat/gluten (9.3%), and peanut (8.1%). Elimination diets were used exclusively in 145/410 (35.3%), topical steroids without diets in 57/410 (14%), both elimination diet and topical steroids in 183/410 (44.6%), systemic steroids in 22/410 (5.4%), while esophageal dilation was performed in 7/410 (1.7%). Patient refusal, a shortage of endoscopy/anesthetist time, and physician reluctance to perform numerous endoscopies in a single patient were noted as primary factors justifying deviation from guidelines recommending repeat endoscopies following food re-introduction.

**Conclusions:** In this cohort, milk and egg were the most common allergens triggering EoE in children. While performance of PPI trials has increased, it is still not universal. Measures to overcome barriers faced by patients and physicians and improve the implementation of guidelines are needed.
Eosinophilic oesophagitis – Adherence to oesophageal biopsy recommendations to optimise diagnostic yield

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Introduction: Eosinophilic oesophagitis (EoE) is a chronic inflammatory disorder with a variety of clinical presentations including dysphagia and odynophagia. Diagnosis is established by histological confirmation of > 15 eosinophils per high-power field in at least one sample from the oesophagus. Recommendations state a minimum of six biopsies should be taken from at least two separate locations of the oesophagus, typically distal and proximal sites, even if the oesophagus appears macroscopically normal. The aim of the study was to investigate adherence to current oesophageal biopsy recommendations.

Methods: A retrospective study was conducted at Northumbria Healthcare NHS Foundation Trust. All endoscopy reports for patients undergoing a Gastroscopy for indications of dysphagia and odynophagia during a 3 month period from 1st January 2016 to 31st March 2016 were reviewed.

Results: A total of 139 patients underwent a Gastroscopy during the study period for investigation of symptoms of dysphagia (137 patients) and odynophagia (2 patients). In 134 patients the symptoms were unexplained by endoscopic findings. There were 49 males and 85 females, with an age range from 28 to 92 years (median 64.5 years). Oesophageal biopsies were taken in only 33 of these patients (24.6%), with no biopsies taken in 101 patients (75.4%). Of the 33 patients biopsied, only one (3%) had the minimum recommended six biopsies taken, and this was the only histologically confirmed case of eosinophilic oesophagitis.

Discussion/Conclusion: Our study demonstrates a lack of compliance with current recommendations for taking oesophageal biopsies in patients presenting with symptoms of unexplained dysphagia or odynophagia. The one patient diagnosed with eosinophilic oesophagitis was a patient in which guidelines were adhered to, with six oesophageal biopsies being taken. Our study demonstrates the need for greater awareness and implementation of eosinophilic oesophagitis guidelines among endoscopists to optimise diagnostic yield.
Five patients with eosinophilic esophagitis and the pronghorn

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Introduction: Eosinophilic esophagitis (EoE) coinciding and associated with other immunopathologies – case reports presented by an immunologist.

Methods: This work presents a group of five patients with EoE monitored for a number of years at a department of allergology and clinical immunology. Given the diagnosis of EoE, we primarily focused on excluding IgE and non-IgE mediated food allergies. However, these patients were also monitored and treated for other allergic and immunopathological problems. The progress of eosinophilic esophagitis was monitored in cooperation with gastroenterologists and histopathologists. This work details the case report of a child with atopic dermatitis, a food allergy and a respiratory allergy who was ultimately found to also have celiac disease (sprue) and eosinophilic esophagitis. Data regarding the other patients is summarized in a table. A partly analogical example from the animal kingdom is presented in order to illustrate the evolutionary context of the genetic predisposition to increased reactivity of the immune system (pronghorn).

Results: All patients manifested an increased reactivity of the immune system with a propensity not only to allergic manifestations but also to autoimmune diseases or other disorders associated with chronic non-infectious inflammations, disruptions of the skin and most probably mucosa barrier functions too. These disorders have also been observed in the relatives of these patients. We confirmed the high efficacy of treating eosinophilic inflammation of the oesophagus using a viscous suspension of budesonide.

Discussion/Conclusion: It is absolutely essential for patients with EoE to be treated and monitored by a gastroenterologist. An examination and potential follow-up and treatment by an allergologist and immunologist may be beneficial in the case of many such patients, not only in order to search for potential food triggers of the eosinophilic inflammation in the oesophagus.
Can eosinophilic esophagitis be easily treatable disease?
A case report

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Introduction: Eosinophilic esophagitis is an immunologically mediated inflammatory disease of the esophagus with eosinophil prevalence. The incidence is rising. It is most common in people who already suffer from some allergy mediated diseases such as asthma or allergic rhinitis. Management of EoE is multidisciplinary and involves consultation with gastroenterology and allergy specialists and it can be very demanding. It includes dietary, pharmacologic and sometimes endoscopic intervention. Patient collaboration is very important.

Methods: Here we present 16-year-old girl with history of pain in the upper abdomen and heartburn that have been present for several months. Pain occurs independently of meals, sometimes she also complains about the pain in the stomach during the night and she can’t sleep. EGD has proved eosinophilic esophagitis. Proton-pump inhibitor (esomeprazole) therapy has been performed for 8 weeks. Considering the persistence of the discomfort despite therapy, we have started an elimination diet without gluten, cow’s milk, nuts and soy for three months. As a result of the change in the diet, there was a noticeable improvement with the regression of symptoms, therefore the elimination diet continued over the next 8 weeks. In the control endoscopy, the histological findings in comparison to the previous one are in significant improvement, the number of eosinophils is within the physiological limits in all tissue samples. The patient feels good now, without any kind of symptoms.

Discussion/Conclusion: Eosinophilic esophagitis is a recently recognized disease with increasing diagnosis, resulting in part from growing awareness of the condition. Treatment is based on the elimination diet of potential nutritional allergens which can sometimes be very demanding due to the difficulty in adhering to the dietary diet regime. In this case, we wanted to show how treatment with the patient’s close cooperation can be successful and relatively fast.
Eosinophilic colitis

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Eosinophilic colitis (EC) belong to category EGID (eosinophilic gastrointestinal disease) together with eosinophilic esophagitis and eosinophilic gastroenteritis. EC is rare diagnosis and still rarely diagnose. Diagnostic standard are not exactly defined, belong to abnormal gastrointestinal symptoms (abdominal pain, diarrhea, with or without blood, with or without loss of weight), histopathology report is infiltration colon with eosinophils more then 20/HPF, exclude another diagnosis (infection, autoimmunity diseases, drugs, hypereosinophilic syndrome).

In our cause we would like to introduce a patient with anamnesis 15 years colon irritable with normal finding on colonoscopy, she was treated in another department. We took care about the patient and did a new colonoscopy in our department with normal finding, we did multiple biopsies and histopathology finding was eosinophilic colitis. After complete treatment and exclusion secondary etiology of eosinophilia we classify finding to primary EC.

The patient was treated by MMX budesonid with perfect outcome, all of her difficulty subside. Now, we perform prospective study how multiple biopsy is helping in therapy of patients with colon irritable, we attempt to discover patients with EC and give them adequate therapy.
Clinical and endoscopic features of eosinophilic esophagitis

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Introduction: Eosinophilic esophagitis (EoE) is a disorder characterized by a severe isolated eosinophilic infiltration of the esophagus. We aimed to determine the clinical manifestations and endoscopic characteristics of EoE in Tunisian patients.

Methods: We conducted a retrospective study including all patients with EoE between January 2006 and December 2016. The diagnosis of EoE was considered if eosinophils ≥ 15 per high-power field (HPF) were identified in mucosal biopsies. Clinical symptoms, demographic data and endoscopic findings were recorded and evaluated.

Results: A total of 7 patients (57.1% male, age 38.2 ± 3.2 years) were diagnosed with EoE. These patients presented with dysphagia (4/7, 57.1%), gastroesophageal reflux disease (GERD)-like symptoms (2/7, 28.6%) and abdominal pain (1/7, 14.3%). Endoscopically, the most common finding was white plaques or exudate (4/7, 57.1%), and other findings were linear furrows (1/7, 14.3%), ring-like appearance (1/7, 14.3%) and erosion (1/7, 14.3%).

Discussion/Conclusion: In this series, EoE was mostly manifested with dysphagia and GERD-like symptoms with endoscopic findings of white plaques. Clinicians should evoke the diagnosis of EoE in the presence of such features.
Multidisciplinary approach in pediatric patients with EoE

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Introduction: Eosinophilic esophagitis (EoE) is a chronic, immune/antigen-mediated esophageal disease. Findings of esophageal rings, linear furrows of mucosa, white exudates and narrowing of the caliber of the esophagus are suspected for EoE but not pathognomonic. The most common symptoms are vomiting, dysphagia, abdominal pain and food impaction. The diagnosis of EoE is based on histopathological findings (HF) of esophageal eosinophilia (Table 1). If the esophageal eosinophilia persists after 8 weeks of proton-pump inhibitors (PPIs) therapy the diagnosis of EoE can be made. EoE is a gastrointestinal manifestation of food allergy but allergy testings are positive in only 15–43% of patients. Elimination diet (ED) is a primary therapeutic option (Table 2).

Case report: A 17-year-old girl presented with epigastric pain and haematemesis. We performed esophagogastroduodenoscopy (EGD) and HF was indicative for EoE. The allergy testing was positive on dairy, peanuts, soybeans, rice, rye and wheat. 8 weeks of PPIs therapy was conducted. After the second EGD the EoE diagnosis was confirmed. The nutritionist gathered data about the girls’ eating habits. An education about ED was performed and adequate diet was recommended in order to meet nutritional and energy needs for a girl of her age. Through further follow-up no weight loss and no nutritional deficit was registered.

Conclusion: With this case report we wanted to show the importance of a multidisciplinary approach in pediatric patients with EoE in order to prevent the development of nutritional deficit and to ensure healthy adult life of this vulnerable population.

Key words: eosinophilic esophagitis, esophageal eosinophilia, food allergy, elimination diet, nutritionist

Table 1: Histological findings in EoE

| Presence of 15 eosinophils per high-power field |
| Eosinophilic microabscesses with papilar elongation |
| Basal zone hyperplasia |
| Extracellular eosinophil granules |
| Superficial layering |
| Lamina propria fibrosis |

Table 2: Elimination diet

| Amino acid-based formula |
| Targeted elimination diet |
| 6-food elimination diet: dairy, soy, eggs, wheat, peanuts and fish |
Eosinophilic esophagitis and eosinophilic gastroenteritis, two diagnoses with similar symptomatology in young patients with a different therapeutic effect

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Introduction: Eosinophilic esophagitis (EoE) is caused by intense eosinophilic inflammation within the esophageal wall. It is a chronic abnormal Th2 type immunological response. Typical symptoms in adults are dysphagia and food impaction. Esophageal dysfunction is caused by the fibrous remodeling of its wall. The histological finding is characterized by the presence of eosinophils in the number of 15 or more per high-power field (HPF) and the existence of eosinophilic microabscesses. Eosinophilic gastroenteritis (EGE) is a rare and idiopathic group of diseases characterized by eosinophilic infiltration in one or more parts of digestive pipe (20 or more per HPF) and so the symptoms are not specific. For eosinophilic inflammation of the digestive tract is typical relationship to atopy and especially food allergies.

Methods: We performed endoscopy of the upper gastrointestinal tract in patients aged 15, 19, 22 and 43 years for dysphagia and a food impaction with similar endoscopic and histological findings.

Results: EoE was demonstrated in two elderly patients and both promptly responded to proton-pump inhibitors (PPI) therapy (a dose of 40–80 mg per day), correlating with improvement in histological findings. Eosinophilic gastroenteritis with esophageal disorder has been confirmed in two younger patients. In both, PPI therapy was inadequate with the need for topical corticosteroid application (fluticasone at a dose of at least 0.5 mg per day) to improve esophageal symptoms.

Discussion/Conclusion: EoE and EGE in our patient group have a relationship to atopy. From the clinical point of view, it is important to distinguish these units mainly because of the different response to therapy. From our experience, EoE is more effective in treating by PPI however, there are also forms that are resistant to this therapy. Diagnosis and therapy of eosinophilic gastroenteritis is more complex and treatment with topical or systemic corticosteroids is necessary.
In vivo model of the eosinophilic esophagitis

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Introduction: Contamination of food by mycotoxin Fumonisin B1 (which is produced by fungi Fusarium moniliforme and some related species and contaminates the cereal around the world) causes the esophageal carcinoma in human. In rodents, Fumonisin provokes other tumors. Our investigations of Fumonisin on mice have revealed its immunological effects (polyclonal activation of B cells, autoimmune disruptions, T cell receptor changes, etc.). Our next experiments elucidated the inflammatory action of Fumonisin on mouse esophagus. Detailed study of this phenomenon in mouse allows us to recognize how some food contaminants may initiate an eosinophilic esophagitis in human.

Methods: Fumonisin B1 ($M_{721}$) (0.01–10 mg/kg bw) was administered to male mice (BALB/c, DBA) per os daily. Control groups received physiological solution. Mice were killed using guillotine on 1, 4 or 28 days (n = 8 per group). Esophagus was removed, cells were isolated and investigated by flow cytometry. Proteins were measured by RT-PCR. Levels of cytokines were estimated by ELIZA. Statistic analysis provided by ANOVA.

Results: Analysis of cells isolated from esophagus revealed the time-dependent gradual changes in cell population. 24 hours after first Fumonisin exposure some proteins connected with kinase mTOR. Cyclins, cdk, and another cell-cycle dependent molecules were disrupted. T cell receptor changes were consistent with our previously data and indicated the specific differentiation of subpopulations. On 4th day the plasma cell infiltration were recorded in esophagus as well as accumulation of basophils, eosinophils, mast cells. T cell subpopulations were changed significantly. Levels of pro-inflammatory cytokines (proteins and mRNA) were elevated. On 28th day after beginning of Fumonisin administration the polyclonal activation of B cells in esophagus was maintained almost at the same level as on 4th day. Inflammation was recorded as significant. T cell activation markers were elevated. The ratio of immune cell populations was been violated. Levels of basophils and eosinophils were increased. Markers of autophagy and apoptosis directly pointed the activation of these processes in esophagus.

Discussion/Conclusion: This mouse model may elucidate an initiation of eosinophilic esophagitis in human and explain the immunological disruptions under this condition.
The difficulties of eosinophilic esophagitis diagnosis in case of combined pathology (gastroesophageal reflux disease & eosinophilic esophagitis): Case report

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Introduction: Eosinophilic esophagitis (EoE) is a chronic immune/antigen mediated esophageal inflammatory disease associated with esophageal dysfunction resulting from severe eosinophil-predominant inflammation. Gastroesophageal reflux disease (GERD) is a clinical manifestation of the excessive reflux of gastric contents into the esophagus causing various degree of symptomatic irritation or injury to the esophageal mucosa. Typical symptoms of GERD include heartburn, regurgitation and dysphagia. The prevalence of GERD among the adult population in Ukraine is up to 40%. EoE is one of the rare chronic diseases. In our case the combination of these two diagnoses made difficulties in patient management.

Methods: 31-year-old male patient admitted to our clinic with complaints of dysphagia (difficulty in the passage of solid food and no problems with the passage of liquid food) and heartburn. Dysphagia lasted approximately 19 years. Laboratory tests revealed that; Hb, WBC, RBC, PLT, ESR, ALT, AST, GGT, AP are in normal range, eosinophils 10,0%, total IgE 271.9 IU/ml. Instrumental examinations: abdominal US showed no abnormalities, at previous few EGDSs – hyperemic gastropathy, erosive reflux-esophagitis LA-A. After long use of PPI therapy heartburn had disappeared, but dysphagia remained. PPI refractory GERD was suspected and during 19 years he was treated permanently for this diagnosis. For the purposes for second opinion upper endoscopy was done in our clinic and features of EoE were detected. Multiple biopsies (6 particles) from middle third of esophagus were performed. Histological conclusion was EoE; morphometry: > 300 eosinophilic granulocytes/mm².

Results: At the base on upper endoscopy picture and morphological assessment of the biopsy samples the final diagnosis in this case was EoE. Liquid budesonide in dosage – 2 mg per day, per os was recommended with duration 8 weeks and plus hypoallergic diet also. After the first week of treatment, patient’s condition improved. We continue the observation of patient till FU endoscopy will be performed.

Discussion/Conclusion: Esophageal symptoms preservation, despite the PPI long-term use, requires thorough examination and mandatory morphological assessment for the verification of another esophageal disease. More exactly – persistent dysphagia has to be regarded as an alarm symptom. There is need for a careful examination and clarification of another reason of complaints.
The prevalence of eosinophilic esophagitis in patients with asthma

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Eosinophilic esophagitis (EoE) and asthma are chronic immune-mediated diseases characterized by inflammatory changes in mucosa and submucosa with a characteristic infiltration of eosinophils. There are some similarities between the two diseases such as their pathogenesis. Aim of our study was to evaluate the prevalence of EoE in patients with asthma.

Methods: We included 54 patients with asthma, 20 males and 34 females, mean age 46 years ± 6.3. All patients reported at least one symptom such as dysphagia, chest pain, heartburn, regurgitation, upper abdominal pain or food impactation in the last 2 months and no/slight response to treatment with PPI for 1 month. We practiced upper endoscopy in all patients and took multiple esophageal biopsies, from different levels, even if the mucosa appeared to be normal. We took 4–8 biopsies, 4 in patients with normal mucosa and 6–8 samples in patients with esophageal lesions. A minimum of 15 eosinophils per high-power field were required to consider the diagnosis.

Results: 46 patients had endoscopic features such as: edema mild/moderate, furrows, white exudates, strictures and 8 patients had endoscopically normal-looking esophagus. We didn’t find any patient with concentric rings. 16 patients had only edema, 5 patients associated edema with white exudates, 8 had edema and furrows, in 10 we found edema, furrows and white exudates and 7 patients had strictures. Only in 5 male patients we found more than 15 eosinophils on the pathologic samples and we considered the diagnose of EoE in these patients. Endoscopic findings were edema mild/moderate and white exudates in EoE patients. Clinical symptoms in EoE patients were dysphagia, chest pain and 1 patient accused food impactation.

Conclusion: In our study 9.25% of patients with asthma associated EoE. All of them were males, younger than the others (from 31 to 38 years) but we did not find any characteristic symptom or endoscopic lesion compared with the other patients from the study group.
Prevalence of eosinophilic esophagitis in obese with GERD

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Gastroesophageal reflux disease (GERD) represents a pathophysiologic event associated frequently with esophageal eosinophilia and it is common in obese patients. Eosinophilic esophagitis (EoE) is a chronic immune-mediated disorder characterized clinically by esophageal dysfunction and histological by eosinophilic infiltrate in the squamous epithelium. Aim of our study was to evaluate the prevalence of EoE in obese with GERD compared with normal weight patients with GERD.

Methods: We included 138 obese patients (40 males) – group A and 125 patients with normal weight (37 males) – group B, mean age was similar in both groups, without diabetes mellitus or obesity due to endocrine disease, non-smoking. Major symptoms in both groups were dysphagia, regurgitation, heartburn and chest pain. In all patients we measured BMI, waist circumference (WC), hs-CRP and leptin, as an inflammatory markers and all of them underwent upper endoscopy with multiple biopsies from different levels of the esophagus. The diagnosis of EoE was based by presence of at least 15 eosinophils/HPF in biopsy specimens.

Results: BMI in obese group was 33.84 ± 7.23, and in group B was 23.32 ± 1.25, WC was 99 ± 5 cm in group A and 79 ± 5 cm in group B. EoE was diagnosed in 18 patients (13%) in group A and in 5 patients in group B (4%) with significant statistical difference between two groups. EoE correlated statistical significant with WC but not with BMI in group A, also CRP and leptin level were significantly higher in EoE subgroup patients from group A. In group B, the presence of EoE correlated, also with WC but not with BMI. In this group we have noticed 21 patients with normal weight but large WC. In group B leptin and CRP level were higher than normal in 42 patients but without relationship with EoE.

Conclusion: In our study EoE is not a frequent disease in normal weight population with GERD, but in obese with GERD we found a high prevalence. In both groups EoE correlated with WC but not with BMI. Leptin and C reactive protein correlated with EoE only in obese group.
Experience of combined inhaled budesonide and leukotriene receptor antagonist use in adult eosinophilic esophagitis

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Introduction: Global incidence of eosinophilic gastrointestinal diseases is growing since beginning of 1990th. Eosinophilic esophagitis (EoE) seems to be similar to many other allergic diseases including asthma. Naturally, leukotriene receptor antagonists (LRA), effective in particular forms of asthma were expected to have treatment potential in EoE. However, existing scientific database shows absent or minimal effect of LRA in EoE. Following this findings LRA’s were excluded from all existing recommendations. At the same time fluticasone and topical budesonide appears to be effective for treating eosinophilic esophagitis. The aim of this study is to extend the knowledge database of combined LRA and corticosteroids use in adult EoE.

Methods: Four adult patients, all males, participated in the study. EoE was diagnose based on recurrent clinical symptoms, negative or minor PPI efficacy and endoscopic examination with multiple biopsies (not less than 15 eosinophils per ×400 hpf in at least one of 6 [3×2] bioptates). Diet was not or partially obeyed in all cases due to behavioural reasons or multiple food allergens. LRA montelukast was given orally starting with 10 mg daily then titrated up to 40 mg. Budesonide was given using a nebulizer with swallowing in a daily dose of 0.5–1 mg. The primary endpoints of the study were speed of symptoms alleviation compared to previous exacerbation episodes (control, 2 mg topical budesonide), endoscopic and histologic picture (esophageal eosinophilic inflammation).

Results: Duration of symptoms alleviation with lower budesonide + LRA was insignificantly (p = 0.083) longer compared to higher dose of single budesonide. General term of in-hospital stay with controlled diet was quite similar. However, in each exact case results vary. One patient had 5 days lesser period of clinical symptoms improvement while 3 others had it longer. Both endoscopically and histologically, changes occur significantly faster under higher budesonide (control), compared with budesonide + LRA.

Discussion/Conclusion: Higher topical budesonide is more effective in controlling esophageal inflammation compared to lower dose budesonide + LRA. While this study shows no clear benefits of additional LRA therapy, there may be individual positive response for LRA associated treatment.
Eosinophilic esophagitis or gastroesophageal reflux disease?

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**Introduction:** Our goal was to highlight the importance of the differential diagnosis between eosinophilic esophagitis (EoE) and gastroesophageal reflux disease (GERD) in patients who are unresponsive to the classical treatment of GERD.

**Methods:** Five patients admitted to the Gastroenterology Department within Sf. Spiridon Hospital, Iasi, Romania presented with typical persistent GERD symptoms. They were treated with maximal therapy including proton-pump inhibitors and antacids, without symptoms reduction. Further, esophageal biopsies were taken.

**Results:** The histopathologic exam showed important eosinophil infiltration for all patients, which raised the suspicion of EoE. Even though GERD may cause the increase in eosinophil counts, in case of refractory disease and marked eosinophilic infiltration, the diagnosis of EoE should be considered as it responds better to corticosteroids. This may prevent unnecessary surgery for GERD.

**Discussion/Conclusion:** Before calling for the surgical cure in patients with refractory GERD symptoms, the diagnosis of EoE should be considered.
Effectiveness of 6 weeks targeted food elimination diet in adults with eosinophilic esophagitis (EoE) and esophageal food bolus impaction

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Introduction: EoE is recognized as one of the most common cause of dysphagia and food bolus impaction in adults. The aim of this study was to identify the effects of 6 weeks targeted food elimination diet on clinical and histological outcomes in adults with EoE and food bolus impaction.

Methods: We have conducted a single-center clinical retrospective study. 35 patients presenting with swallowing difficulty and acute dysphagia secondary to esophageal food bolus impaction were studied. Demographic, clinical characteristics and laboratory findings were collected from medical records. All patients underwent upper gastrointestinal endoscopy. Protocol biopsies from both proximal and distal esophagus were performed. Skin prick tests (SPTs), prick-prick tests (PPTs) and atopy patch tests (APTs) were performed in all patients with EoE using a panel of 25 allergens.

Results: Of 35 patients, 10 (7 male, mean age 40.42, 70% with atopy) were diagnosed with EoE based on histological biopsy evaluation. The most common food allergies identified after SPTs, PPTs and APTs were to legumes, fruits, nuts, tomato, seafood and eggs. After 6 weeks of targeted food elimination diet, 3 patients (30%) showed significant reduction of eosinophils (Eos) level from an average of 108 Eos/high-power field (hpf) to normal values (< 15 Eos/hpf). 2 patients had an increase in Eos level but with clinical improvement. Five patients did not achieve either a clinical or histological response. After gradual food reintroduction (1 food group every 2 weeks), the most common antigen associated with EoE was wheat (40%) followed by milk (20%) and eggs (20%). Prior SPTs, PPTs and APTs showed no relationship with food-reintroduction results in 80% patients.

Discussion/Conclusion: Our study suggests that only a small proportion of adult patients might obtain benefit from a 6 weeks targeted food elimination diet. The contribution of skin testing in guiding dietary interventions is very limited. The results of our research are limited by the small number of patients enrolled in the study.
Interleukin-13 investigation in eosinophilic esophagitis and inflammatory bowel disease

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Introduction: In many cases, eosinophilic esophagitis (EoE), Crohn’s disease (CD) and ulcerative colitis (UC) are well differentiated clinically and histologically but the molecular mechanisms involved are not been established. It is considered that EoE is associated with the T helper type 2 response but CD is characterized by Th1 dominance and Th17 cytokine. It has been shown that IL13 blocking antibody prevent esophageal eosinophilia and inflammation in mice. We have proposed to study levels of serum cytokine IL13 in eosinophilic esophagitis and inflammatory bowel disease-IBD (CD and UC), in an attempt to identify a possible modulation of IL13 production.

Methods: We studied 12 adult patients with clinical manifestations of EoE (the majority atopic), 16 with UC, 18 with CD and 20 healthy persons (controls). The patients and control persons were studied from the hematological, histopathological and immunological point of view. The serological investigations were performed by quantitative determination of IL13 using the ELISA Invitrogen Corporation (Camarillo, CA, USA) kits.

Results: We found that only the biopsies of patients with EoE showed an increased number of eosinophils (over 26 eosinophils/field), mast cells and intraepithelial T lymphocytes. Serum IL13 production did not differ significantly between IBD and control subjects. In EoE patients were found the highest significantly IL13 values (137.2 ± 31.1 pg/ml) comparing to IBD patients (34.08 ± 10.3 pg/ml) and controls (26.16 ± 4.64 pg/ml).

Discussion/Conclusions: Based on experimental observations, scientific publications and our results, we make the following remarks:

- the differential diagnosis in EoE and IBD relies on a multidisciplinary approach as clinical evaluation, tissue or serum biomarkers study, histopathological examination;
- significantly elevated IL13 concentrations, found in patients with EoE, are possible a good target for anti-IL13 monoclonal antibodies as therapeutic strategies in the treatment of this disease;
- in view of the fact that CD and UC patients produced low amounts of IL13, our study suggests that anti-IL13 monoclonal antibodies would not have an appropriate therapeutic effect in inflammatory bowel disease.
Predictors of response to proton-pump inhibitors and glucocorticoids in patients with eosinophilic esophagitis

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Introduction: The aim of the study was the search for predictors of response to proton-pump inhibitors (PPI) and glucocorticoids (GCs) in patients with eosinophilic esophagitis (EoE).

Methods: The study included 35 adults with EoE, 2B-2C (22–35 years old, female – 11, male – 24). Diagnosis was based on clinical symptoms, the endoscopic and histological findings with biopsies of esophagus, food allergy testing. Response to therapy was determined histologically by the number of eos/hpf. Proteomic analysis of esophageal mucosa: 2DPAGE, MALDI-TOF-MS/MS, the identification of sequences (MASCOT Search), the molecular interactions (STRING 10.0 database). The management of EoE included dietary therapy (4–12 weeks), PPI’s therapy (rabeprazol, 20 mg/day, 8 weeks), swallowed oral viscous budesonide (OVB) 2 mg/day (6 weeks) if no improvement occurs in patients. Control group – 20 healthy persons. Statistical analysis was performed by “Statistica 12.0”.

Results: In 35 patients was 75 eos/hpf before and 74 (p > 0.05), 53 (p < 0.0001), 7 eos/hpf (p < 0.0001) after dietary, PPI’s, OVB therapy. There were 100% non-responders after dietary + PPI’s therapy; 85.7% responders, 2.8% partial responder, 11.5% non-responders after OVB therapy. The mean symptom score fell from 6.8 to 0.9 (p < 0.0001) after OVB therapy vs from 7.1 to 6.8 (p < 0.01) after dietary + PPI’s, the mean endoscopy score from 3.9 to 0.8 (p < 0.0001) after OVB therapy vs from 4.5 to 3.9 (p < 0.01) after dietary + PPI’s. The decrease of IgG4, Eotaxin-3, Rock 1, MBP1, ECP, EDN, galectin-10 expression in esophageal mucosa was revealed after 6 weeks OVB therapy in 30 EoE patients vs 6 EoE patients after dietary + PPI’s.

Discussion/Conclusion: We documented the impact of novel biomarkers in esophageal mucosa that can be predictors of response to PPI’s and GCs in patients with EoE.
Demographic and clinical profile in patients with eosinophilic esophagitis

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Introduction: Eosinophilic esophagitis (EoE) is a chronic immune-mediated disease of the esophagus with increasing prevalence in children and adults. This study aimed to examine the demographic and clinical profile of patients with eosinophilic esophagitis in a tertiary center from North Eastern Romania.

Methods: We conducted a single-center clinical retrospective study over a period of 8 years (January 2009–January 2017). 21 patients with confirmed diagnosis of EoE were enrolled in the study. Demographic (age, sex), clinical characteristics and laboratory findings were collected from medical records. All patients included underwent upper gastrointestinal endoscopy.

Results: Mean age at diagnosis was 42 years, with highest prevalence (43%) at age 20–39. The most common symptom was dysphagia (62%), followed by food impaction (29%), chest pain (5%) and epigastric pain (4%). Of 21 patients, 48% had allergy or atopy: 35% had asthma, 55% had allergic rhinitis and 10% atopic family history. Endoscopic findings included ringed esophagus (65%), esophageal strictures (18%) and normal esophagus (17%). 11 patients were treated with topical fluticasone, with clinical improvement in all 6 patients who were seen in follow-up.

Discussion/Conclusion: Dysphagia or food impactation in middle age men may suggest EoE. The endoscopic appearance is not always specific. Patients with eosinophilic esophagitis should be referred to an allergist for optimal management.
A rare cause of retroperitoneal fibrosis

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Introduction: A 69-year-old gentleman presented with a five week history of abdominal distension. He has a past history of diabetes and myocardial infarction, is an ex-smoker with no significant history of alcohol intake. Examination demonstrated a distended non tender abdomen with shifting dullness, no organomegaly and no signs of chronic liver disease.

Methods: Investigations included ultrasound scan of abdomen, ascitic tap, CT abdomen/pelvis and CT guided biopsy.

Results: Ascitic tap revealed chylous ascites with high SAAG (serum ascites-albumin gradient) of > 1.1 g/dl indicating a nonperitoneal cause of ascites. Cytology revealed no evidence of malignancy. CT abdomen revealed a mildly enhancing soft tissue mass encasing the mesenteric and renal vessels and the upper abdominal aorta and also the left peritoneal space; appearances were suggestive of lympho-proliferative disorder. CT guided biopsy showed reactive changes consistent with retroperitoneal fibrosis. Immunohistochemistry done at University College of London showed no evidence of Ig4 disease. Patient was commenced on prednisolone and azathioprine. He failed to tolerate azathioprine which was then stopped. Treatment with Prednisolone failed to slow the rate of re-accumulation of the ascites, and he continued to require frequent abdominal paracentesis.

Discussion/Conclusion: Chylous ascites has rarely been reported as a presenting feature of retroperitoneal fibrosis. [1] Retroperitoneal fibrosis may be an idiopathic in 70% of cases or secondary condition. The incidence of idiopathic form is 0.1 per 100,000 person-years with a prevalence of 1.4 per 100,000 population. [2] The primary modality used for diagnosis of retroperitoneal fibrosis is CT imaging, biopsies are performed in cases of unusual presentation and to exclude malignancy and IgG 4 related pathology. Treatment of retroperitoneal fibrosis in most cases depends on whether it is idiopathic or secondary. The mainstay of treatment is corticosteroids and if no response, immunosuppressive therapy can be used. Case series data is present which has shown that high dose corticosteroids like prednisolone are effective in reducing the chronic inflammatory response caused by retroperitoneal fibrosis; however there is a high rate of recurrence once the steroids are withdrawn. Mycophenolate mofetil in addition to corticosteroids has shown reduced duration of steroid use without affecting the efficacy and reduces disease recurrence rate.
Subepithelial collagen deposition in pediatric patients with eosinophilic esophagitis: Pathomorphological study

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Introduction: During the past decade, the increasing prevalence of eosinophilic esophagitis (EoE) – a chronic immune-mediated disorder – has been recognized. Recent literature reports show that both pediatric and adult patients with EoE experience esophageal remodeling marked by increased collagen deposition. The main aim of the current research was the assessment of subepithelial collagen deposition in esophageal biopsy specimens in pediatric EoE.

Methods: Histological and histochemical studies of esophageal specimens were performed on biopsy material obtained from 12 children aged between 1–18 years (10 boys and 2 girls) with EoE. Collagen deposition in the lamina propria (LP) was assessed in tissue sections with the aid of the Masson trichrome technique. The diagnosis of EoE was based on esophageal eosinophilia ≥ 15 eosinophils per high-power microscopy field. EoE results were compared among samples from control subjects with healthy esophagi. In all study cases, pathomorphological analysis of esophageal biopsy specimens was performed in the Department of Medical Pathomorphology, Medical University of Bialystok.

Results: Children with EoE exhibited a dense subepithelial collagen deposition that was significantly higher than that observed under normal conditions. The intensity of this collagen deposition correlated positively with eosinophil density in the epithelial stratum and in the LP in affected esophageal mucosa.

Discussion/Conclusion: A deeper knowledge of the fibrous esophageal remodeling morphogenesis in children with EoE may provide new insights into potential treatments for this disease.
The cytokines profile in eosinophilic esophagitis depending on interleukin-4 (rs 2243250) genetic mutation

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Introduction: The eosinophilic esophagitis (EoE) is commonly associated with different atopies. Various studies have suggested that EoE occurs in association with Th2-cells allergic responses, yet the local and systemic expressions of relevant cytokines has not been well characterized. IL4, IL10, IL13, IL1β and TNFα appear to be particularly important in EoE since they have multiple ties with Th2-cells and regulate different mechanisms of atopic diseases. As already described in other Th2-associated diseases, EoE development is likely to be associated with allergen sensitization in predisposed individuals, focusing further studies on probable genetic background of the disease. Among the EoE candidate genes, Eotaxin-3 (CCL-26), Calpain-14, thymic stromal lymphopoietin (TSLP) and its receptor genes, are the most commonly studied. Following involvement of both genetic predisposition and cytokines in EoE pathogenesis we hypothesized associations of IL4 genetic variants and cytokines profile in EoE.

Methods: We observed seven schoolchildren, all males with food allergy and EoE. Twenty-three practically healthy children formed control group. EoE diagnosed based on symptoms and esophageal endoscopy with biopsies (not less than 15 eosinophils per ×400 hpf in at least one sample). The tumor necrosis factor α (TNFα), IL1β, IL4, IL10 and IL13 levels in pg/ml were detected in blood plasma by ELISA. Genetic polymorphism of IL4 gene studied by PCR: TT genotype – 195 bp, CC – 177 and 18 bp, CT – 195, 177 and 18 bp).

Results: EoE patients had higher IL4 (41.57 ± 3.91 pg/ml), IL10 (40.21 ± 5.26 pg/ml), and IL13 (32.52 ± 3.06 pg/ml) with lower IL1β (21.24 ± 2.23 pg/ml) and TNFα (22.85 ± 2.56 pg/ml) compared to control (24.61 ± 7.25 pg/ml, 22.57 ± 7.36 pg/ml, 30.45 ± 4.82 pg/ml, 33.22 ± 7.91 pg/ml, and 29.01 ± 6.38 pg/ml, respectively). An imbalance of the immune response in children with EoE is characterized by inhibition of cellular Th1 immunity with Th2 humoral activation: hereditably determined by low production of TNFα and IL1β in C-allele carriers of the and IL4 hyperproduction in TT-genotype carriers of the IL4 gene.

Discussion/Conclusion: This work defines specific genetic associations between EoE and rs 2243250 polymorphism in the IL4 gene. T-allele of IL4 gene is a predisposition factor for EoE determining imbalance between Th1 and Th2 mechanisms.
The possible pathogenetic role of TSLPR (rs36133495) gene’s polymorphism in eosinophilic esophagitis

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Introduction: Eosinophilic esophagitis (EoE) is a chronic inflammatory disease of immune/atopic genesis, basically associated with mucosal eosinophil accumulation. Genetic background of EoE is based on both similarities with other atopic diseases like asthma or allergic rhinitis, and population studies with dominance of male patients. While the EoE risk is multifactorial and includes environmental and genetic factors, existing database is insufficient. Among the possible candidate genes for EoE, the thymic stromal lymphopoietin receptor (TSLPR), Calpain-14, IL4, IL5 attract major attention in terms of development possible future treatment approaches. There is evidence that the TSLP signaling pathway may contribute to the formation of perverted immune response in EoE, while exact polymorphisms and their roles have to be determined.

Methods: We observed 75 schoolchildren with food allergy (FA) based on clinical symptoms and prick skin testing as major criteria for FA. Based on questioning, clinical and laboratory observations, individuals were divided into following groups: 1st group included 68 FA patients with FA without EoE; 2nd group (7 patients, all males) – FA + EoE. Twenty-three practically healthy children formed control group. EoE diagnosed based on symptoms and esophageal endoscopy with biopsies (not less than 15 eosinophils per ×400 hpf in at least one sample). TSLPR gene’s single nucleotide polymorphism (rs36133495) studied in lymphocytes by PCR.

Results: A-allele of the TSLPR gene was detected in 88.89% of group 1, 14.29% of group 2, and 91.30% of controls. Minor G-allele was found in 11.11% of group 1, 85.71% of group 2, and 8.70% of controls, respectively. No GG-genotype carriers observed I control. The likelihood of EoE increases in G-allele carriers of the TSLPR gene (OR = 2.46; 95% CI OR: 0.43–6.16; p < 0.001).

Discussion/Conclusion: In previous studies, it was found that TSLPR participates in the initiation of the Th2-immune response being responsible for multiple atopic conditions. This study shows that the particular rs36133495 (A/G) TSLPR gene polymorphism may be involved into development of EoE and requires further investigation emphasizing possibilities for associated treatment approaches.
Possible connections between eosinophilic esophagitis, food allergy, and bronchial asthma

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Introduction: Although eosinophilic esophagitis (EoE) is becoming more and more frequently diagnosed, many important aspects of this disease remain unclear including its etiology, pathogenesis, and dietetic/treatment options. While EoE is comparatively infrequent, often in childhood food allergy (FA) is associated with bronchial asthma (BA). Possible connection of these conditions is based on probably common pathogenesis and etiology. The aim of the study is to find possible common and distinguished aspects of EoE, BA and FA.

Methods: We observed 131 schoolchildren with food allergy. Based on meticulous questioning, clinical and laboratory observations, individuals were divided into 3 groups: 1st group included 72 FA patients (1A group (65 FA + BA) without EoE; 1B group (7) – FA + EoE; 2nd group consisted of 59 BA patients without FA), 50 practically healthy children formed control. EoE diagnosed based on symptoms and esophageal endoscopy with biopsies (not less than 20 eosinophils per ×400 hpf in at least one sample). Following parameters were used for research purposes: IgA, IgM, IgG, general and trophallergen specific IgE, CD3, CD4, CD8 lymphocytes subpopulations, IL4, CRP.

Results: In all patients of the 1A and 1B groups’ trophallergen specific IgE was found (63.0 ± 6.8% to ovalbumin; to seafood proteins in 20.0 ± 5.6%; to milk hydrolyzates in 48.0 ± 7.1%). In 2nd group patients specific IgE was found only to eggs' protein in 4.0 ± 2.7% (p < 0.001). Polyvalent allergy was found in 1st group (more than 3 trophallergens in 60.0 ± 6.9% cases). BA and EoE exacerbations by food allergens has reliable connection with concealed FA: attributive risk (AR) = 81%; relative risk (RR) = 17.2 (95% CI: 8.6–34.3), χ² = 32.7, p < 0.001; sensitivity (Se) = 45.0%, specificity (Sp) = 92.5%, positive foreseen value – PV(+) = 86.0%, PV(-) = 62.3%, accuracy (Ac) = 68.5%. Indices of epidemiologic risk and diagnostic value in relation to CD4 (33.7%) were higher than average group in determination of FA (AR = 51.0%; RR = 3.04 [95% CI: 1.9–4.7]; OR = 9.2 [95% CI: 4.2–20.1], χ² = 63, p < 0.01; Se = 75.8%, Sp = 74.6%, PV[+] = 75.8%, PV[-] = 74.6%, Ac = 75.2% and Prev [spread] = 51.2%). No reliable differences between groups 1A (FA + BA) and 1B (FA + EoE) were observed.

Discussion/Conclusion: The study shows possible relationship between EoE, BA and FA. Similar results obtained in FA + EoE and FA + BA groups may indicate significance of trophallergen testing in diagnosing EoE. However, this study has limitation emphasizing the number of EoE patients participating in it.
Dysphagia as a symptom of eosinophilic esophagitis in adults – Is it all that simple?

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Introduction: Eosinophilic esophagitis (EoE) is a chronic, immune-mediated disease, characterized clinically by symptoms of esophageal dysfunction and histologically by eosinophil-predominant inflammation, typically not, or only partially, responsive to proton-pump inhibitors (PPIs). EoE occurs most frequently in patients with the atopic constituency. It’s necessary to distinguish EoE from gastro-esophageal reflux disease (GERD) and esophageal eosinophilia corresponding to the therapy of PPIs.

Methods: Case report.

Results: We herein report a case of a 52-year-old male, presented to gastroenterology division with a history of dysphagia and heartburn, started two years earlier. Upper endoscopy revealed weaker esophageal motility with an irregular Z-line and inflammatory reactions (GERD A/B). Biopsy specimens from multiple locations of the esophageal mucosa have shown remarkable infiltration of eosinophils, more than 15 eosinophils per high-power field in the squamous mucosa. Bacterioscopic study of biopsy materials, obtained from gastric antral mucosa, was positive on H. pylori infection. A standard triple therapy for eradication of H. pylori infection was administered, with the PPIs in a double daily dose for eight weeks. With regard to clinically still present dysphagia after three months, complete gastroenterological processing, including allergy and immunological testing, was performed. The upper endoscopic appearance was EoE characteristic, including concentric rings (trachealisation). Allergenic tests were negative, with no other immune disorders. Topical steroid therapy has been initiated (fluticasone a 250 mg 2 x 2 – upon retention in the mouth before swallowing) and in consultation with a nutritionist, we conducted empirical eliminating diet. Good clinical response was observed after the applied therapy, while the endoscopic finding and histological response were in partial improvement.

Discussion/Conclusion: The combination of empiric elimination diet and topical steroids has proved to be successful in our case. EoE remains a complex disorder that still poses clinical challenges and requires a team approach between gastroenterologists, allergists, dieticians, and even speech pathologists to optimize management.
The data of children with eosinophilic esophagitis in a single center

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Background: Eosinophilic esophagitis (EoE) is getting more common as the population gets more developed. It is a chronic, immune/antigen-mediated, esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation.

Aim: We report the data of our patients diagnosed with EoE.

Methods: We reviewed the data of patients with EoE from 2012 to 2017. The diagnosis was made according to ESPGHAN/NASPGHAN criteria.

Results: There were 11 children, 1 girl and 10 boys; aged between 3–15 years (8.8 ± 4.6). Mean weight and height were 34.54 ± 17.16 kg and 136.45 ± 29.14 cm most common complaint was vomiting in 7 patients 2 had haematemesis. The rest had abdominal pain (n = 4) and swallowing difficulty (n = 2). All children had history of either allergy or asthma, dermatitis. Blood eosinophil count ranged between 0.0–13.3%, serum IgE levels were 93.11 ± 136 IU. Endoscopy revealed white lining in the esophagus in 4 children, hyperemia in 6 children, severe erosions in 2 and trachealisation in 2 children. Esophageal tissue eosinophil count was 15–70 cells/HPF (35.45 ± 15.36). Skin prick test was performed in 6 patients and revealed aeroallergens in 3 patients, and nuts, chestnut, in 1, cow meat in 1, olive in 1. Serum specific IgE revealed cow’s milk in 3 patients. 2 patients had negative tests for allergens. All patients had no parasites in stool. The patients were treated by PPI, Sucralfate in serious cases, oral budesonide. Seven patients underwent control endoscopy and all had improvement. The rest 5 patients had clinical improvement but not complete recovery.

Conclusion: EoE is getting more common among children. Most children are male as in adults. The most common symptom is vomiting. We suggest male children who present with vomiting, having a history of some kind of allergy be evaluated also for EoE.
Elevated IgG4 expression in patients with eosinophilic esophagitis compared to gastroesophageal reflux disease patients

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Introduction: Eosinophilic esophagitis (EoE) is a chronic immune disease of the esophagus, presented by esophageal dysfunction and histologically characterized by predominant eosinophilic inflammation. EoE is seen as an atopic condition and recently an association with IgG4, but not with IgE has been reported. Here, we measured serum IgG4 and IgE levels of EoE patients before and after topical steroid therapy, correlated them to IgG4 immunohistochemistry of esophageal biopsies and compared them to gastroesophageal reflux disease (GERD) patients.

Methods: Serum levels of IgG4 and IgE of 19 EoE patients were measured before and after eight weeks of therapy with budesonide (1 mg twice/day). Biopsies were taken from the esophagus before and after therapy for histological and immunohistochemical evaluation. 14 patients with GERD without histological proof of eosinophilic granulocyte infiltration were taken as control group.

Results: Serum IgG4 levels of EoE patients were significantly higher than in GERD patients (121.0 mg/dl vs. 71.2 mg/dl, p = 0.034). No significant difference of IgE levels in EoE and GERD patients were measured. In EoE patients, the number of eosinophilic granulocytes in histology was decreased significantly after topical steroid therapy (51.9 eosinophils/high-power field [hpf] vs. 6.4 eosinophils/hpf, p < 0.001). After therapy lower serum levels of IgG4 were measured (121.0 mg/dl vs. 104.2 mg/dl, p = 0.019), whereas IgE levels didn’t differ. In EoE patients high expression of IgG4 was seen in plasma cells: in 18 evaluated biopsies a mean of 27.4 IgG4-positive plasma cells was counted. In GERD patients, no plasma cell infiltration was detected.

Conclusion: In EoE patients higher systemic IgG4 serum levels but not of IgE levels compared to GERD-patients can be seen. These elevated levels normalize under effective topical steroid therapy. Also local IgG4 expression in plasma cells is high in EoE patients. These findings are proof for a possible association of EoE with IgG4.
Improvement in esophageal distensibility in response to medical and diet therapy in eosinophilic esophagitis

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Introduction: Reduced esophageal distensibility measured via the functional lumen imaging probe (FLIP) is observed in eosinophilic esophagitis (EoE). This study evaluated the effect of medical and diet therapies on esophageal distensibility and the association of changes in distensibility with clinical outcomes in EoE.

Methods: EoE patients completed FLIP at baseline and following therapy without interval dilatation. FLIP analysis was performed to calculate the distensibility plateau (DP). Clinical data included patient reported outcomes, histopathology and endoscopic features. Results were expressed as mean ± SD unless otherwise stated.

Results: 18 patients (ages 19–54 years; 4 female) treated with topical steroid (8), elimination diet (6), and/or proton-pump inhibitor were included. Follow-up testing occurred at a mean (range) of 14.6 (8–28) weeks. Improvement was observed in DP, 13.9 mm (12.2–19.2) to 16.8 mm (15.8–19.2), p = 0.007) and peak eosinophil count 45 per hpf (29–65) to 23 (5–53), p = 0.042). Nine patients had a positive symptomatic outcome. Six of eight (75%) patients with a DP increase ≥ 2 mm had a positive PRO (p = 0.077), while 2/7 (29%) patients that achieved an eosinophil count < 15/hpf had a positive PRO (p = 0.167).

Discussion/Conclusion: Improvement in esophageal body distensibility quantified with FLIP can be achieved with medical and diet therapies without dilation in EoE. Improved DP appeared to be better indicator of symptomatic improvement than eosinophil count, supporting FLIP as a potentially clinically relevant outcome measure in EoE.
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October 4 – 5, 2017
Maritim Hotel Berlin
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Abstracts
Poster Abstracts