Eosinophilic Esophagitis – Medical and Dietary Treatment

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Eosinophilic Esophagitis – Medical and Dietary Treatment
Scientific organizers:

A. Straumann
Olten (Switzerland)

G.T. Furuta
Aurora (USA)

I. Hirano
Chicago (USA)

A. Schoepfer
Lausanne (Switzerland)

H.-U. Simon
Bern (Switzerland)

Text
Dr. Beate Fessler
Medical journalist, Munich (Germany)

Photos
Portraits, impressions
and presentation of poster prizes:
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Eosinophilic esophagitis: A broad field for research

The research on eosinophilic esophagitis is fascinating, because the knowledge about this rare but more frequently occurring chronic inflammatory disease is still limited. If it is detected early on, however, the dreaded fibrostenosis can be prevented and the significant psychological strain reduced in a large number of patients with drug or dietary therapy.

Eosinophilic esophagitis (EoE) is of great interest from a scientific and medical viewpoint because much is still unclear about this “young” disease which we have known about for only 40 years. This applies to the genetic background as well as to the underlying pathomechanisms, the diagnostic issues, particularly with a view towards the course of the disease and therapy, and last but not least, the therapy itself. Scientists conducting basic research as well as clinicians are accordingly taking action in order to increase their knowledge of and experience in EoE and to put together the individual mosaic pieces little by little.

Only when we understand the pathogenesis of EoE better will it also be possible to find relevant biomarkers for monitoring the therapy and establish new therapeutic targets. Here it should be clarified exactly which immunological processes occur in EoE and to what extent food allergens are involved in them. To date, it is only certain that IgE is not very relevant, however IgG4 is possibly relevant. EoE as an autoimmune disease has largely been ruled out. A disrupted mucosal barrier appears to open the door to possible allergens and thus promote the inflammatory process in a sort of vicious circle. Genetics fundamentally appear to play a minor role in the development of EoE; by contrast, environmental factors may play a crucial role.

To ideally prevent EoE from changing from the inflammatory to the fibrostenosing type, early diagnosis is necessary. Here there is still much to be done. The typical symptoms – dysphagia in adults, a refusal to eat and failure to thrive in children – are frequently not given sufficient attention and clarified. Ultimately, a diagnosis based on the symptoms is easy to make as a result of the histological and endoscopic findings. Contrary to initial assumptions, the response to a proton pump inhibitor (PPI) is not suitable for differentiating from gastroesophageal reflux disease.

There are advancements in the therapy for EoE: For patients who do not respond to PPIs, remission induction can be demonstrably achieved with topical steroids not yet approved for EoE as well as with dietary treatment, whereby a food elimination diet according to the step-up principle should be promoted with regard to patient acceptance. There is no head-to-head study between the various forms of therapy. The physician and the patient should come to a decision together. It is not clear how to proceed if all of the therapeutic approaches listed fail. A series of biologics is in the pipeline. However, to date, there have been no drugs which are explicitly approved for EoE available. That is what we actually need.

Prof. Dr. Alex Straumann
for the scientific organizing committee
“Drug – Diet – Dilatation”: Using therapeutic options for eosinophilic esophagitis

Eosinophilic esophagitis (EoE) is a progressive chronic inflammatory disease of the esophagus with increasing prevalence. A typical symptom is dysphagia. Early diagnosis followed by adequate therapy is urgently necessary, not only to prevent bolus impaction but also to reduce the risk of fibrostenosis. The therapy is essentially based on the three “D’s”: Drug – Diet – Dilatation. It is constantly improving and becoming more patient-friendly.

Eosinophilic esophagitis (EoE) is a “young” disease. It was described for the first time in the 1980s. The initial publications on EoE as an independent disease entity followed, independently of each other, in 1993 and 1994 (Attwood SE, et al. Dig Dis Sci. 1993;38(1):109–16; Straumann A, et al. Schweiz Med Wochenschr. 1994; 124(33):1419–29). EoE was then defined in 2011 by an international group of experts as a chronic inflammatory immune-mediated esophageal disease which is characterized clinically by symptoms of esophageal dysfunction and histologically by the infiltration of the esophageal mucosa with eosinophilic granulocytes. The cutoff value was established at ≥ 15 eos/high power field, HPF (normal: 0 eos/HPF). For the patient, the term “asthma of the esophagus” is a fitting description, according to S. Attwood, North Shields (UK).

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Early therapy prevents fibrostenosis

Intensive research work in recent years has rapidly increased the knowledge about epidemiology, pathogenesis, as well as diagnostic and therapeutic options. According to M. Chehade, New York (USA), EoE occurs more frequently in men aged 30–50 years (sex ratio 3:1), however it can manifest at any age. It is associated with food allergies or atopic diseases, such as bronchial asthma, allergic rhinitis or atopic eczema. The symptoms of EoE vary with age. While dysphagia and bolus impaction are the primary symptoms in adults, children tend to manifest a refusal to eat and a failure to thrive, in combination with abdominal symptoms and vomiting. M. Chehade additionally stressed the progressive course, from the initially inflammatory type to the fibrostenosing type. To ideally prevent progression to the point of fibrostenosis and avoid the need for dilatation, early appropriate drug or dietary therapy is necessary.
Exclusion diet in the step-up regimen

EoE can also be successfully treated with dietary measures, first and foremost with the elemental diet which achieves remission rates of over 90%. By contrast, only 45% of patients go into remission on an exclusion diet based on allergy tests. “An allergy test cannot predict the foods which the patient reacts to,” says A.J. Lucendo, Tomelloso (Spain). The empirical 6-food elimination diet (6-FED), in which the patient, independent of the sensitization pattern, avoids cow’s milk, soy, eggs, wheat, nuts and seafood, is more successful. However, this strategy is a challenge for the patient! For this reason, A.J. Lucendo recommended an FED as a practical application according to the step-up principle in which the patient initially avoids only two foods – milk and gluten. In the 2-4-6 study which investigated this strategy, 45% of patients responded. If there was no response, the 2-FED was turned into a 4-FED with the additional avoidance of eggs as well as vegetables/soy. Here the responder rate was just under 60%. Only if no therapeutic success was achieved is a 6-FED tried. In this way, unnecessary dietary limitations and endoscopies can be avoided and the diagnostic process can be shortened.

Topical steroids as a drug therapy for EoE

With regard to drug therapy, S. Miehlke, Hamburg, initially clarified for which drugs there are no recommendations, namely prednisolone, immunosuppressants and antiallergics. Proton pump inhibitors (PPI) can be initially tried. A therapeutic alternative to induction of remission, especially if there is no response to PPIs, is topical steroids in particular, such as budesonide and fluticasone, which have successfully stood up to the eosinophil-dominant inflammation in randomized, controlled studies but which are not yet approved for EoE. Various meta-analyses demonstrate the benefit of this treatment strategy with regard to histological remission and also to symptom improvement. The formulation is vitally important for the efficacy of the topical steroid, stressed S. Miehlke. A viscous topical pharmaceutical form, such as a suspension or an orodispersible tablet, demonstrates longer adhesion to the mucosa than inhaled pharmaceutical forms which tend to deposit the active substance in the lung. In the randomized, double-blind and placebo-controlled phase III study BUL-1, a highly significant advantage was able to be shown for a budesonide orodispersible tablet (2 × 1 mg/day). The rate of patients with clinical-histological remission after 6 weeks, defined as the primary endpoint, was significantly higher than on placebo (57.6% vs. 0%, p < 0.00001).

The three “Ds” of EoE therapy

D  DRUGS
D  DIET
D  DILATATION

Budesonide orodispersible tablets are highly effective in acute EoE

Exclusion diet in the step-up regimen

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Empirical 6-food elimination diet (6-FED): Omission of the six critical food groups: cow’s milk, soy, wheat, eggs, nuts, seafood
Still unclear: Duration of therapy, rates of recurrence, elimination trials

Many questions are still unanswered. There are only very little data on remission maintenance during long-term topical therapy with off-label steroids. It is also unclear whether mucosal atrophy develops in the esophagus during long-term medication. It is also hardly possible at present to say how long the treatment should last and when it is time for an elimination trial. Even if patients achieve deep remission, the risk of a relapse is high. T. Greuter, Rochester (USA), presented data from the Swiss EoE Research Network, according to which fewer than 10% of patients achieved deep remission over a 6-year follow-up. After stopping topical steroids during deep remission, there was a relapse in 81.8%. The median time to relapse was 22.4 weeks.

“We need approved drugs”

In view of these findings, the therapeutic challenges are evident: “We need approved drugs with which a remission can be induced and maintained,” S. Attwood, North Shields (UK), called for. Other objectives are, in his opinion, reducing the number of endoscopies needed, structuring more tolerable dietary therapies, and generating more information on combination therapies.

Endoscopic findings in eosinophilic esophagitis (EoE)

Figures: © Professor Dr. Alex Straumann, Olten (Switzerland)
Symposium 210

Crossing New Borders in IBD: Thoughts and Demands – From Mechanisms to Treatment

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Scientific Organization
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A. Dignass, Frankfurt (Germany)
The knowledge about EoE is growing little by little – A scientific challenge

EoE has been known for only about 40 years. It is therefore hardly surprising that many questions – about pathogenesis, diagnosis and therapy – remain unanswered. However, the individual pieces of the research puzzle are gradually coming together into a picture which is still incomplete. The researchers’ dedication gives hope to increasingly better diagnostic and therapeutic strategies in the future.

Close association with bronchial asthma and allergic rhinitis, but also with connective tissue disorders

Eosinophilic esophagitis (EoE) is closely associated with allergic diseases. M. Chehade, New York (USA), pointed out that the risk of bronchial asthma in children and adults is approximately three times as high, for allergic rhinitis, 5.9 and 4.9 times as high, respectively, and for atopic eczema, 2.4 and 2.1 times as high, respectively. Connective tissue disorders (CTD) also occur frequently in patients with EoE and these include Ehlers-Danlos syndrome: “1.3% of patients with CTD also have EoE,” says M. Chehade. By contrast, in the overall U.S. population, the proportion of patients with EoE is 0.06%. For this reason, rheumatologists should keep an eye on the possibility of EoE in their patients. Otherwise, the chance for effective therapy may be lost. Nevertheless, 26% of patients with EoE-CTD benefit from dietary therapy.

No simple IgE-mediated food allergy

Is EoE an autoimmune disease or a simple IgE-mediated food allergy? It is neither, according to the answer from D. Simon, Bern (Switzerland). EoE is indeed associated with atopic diseases and the majority of patients demonstrate elevated IgE levels upon exposure to food allergens and inhaled allergens. However, a focused elimination diet shows no or only a limited effect, as does drug therapy with the IgE antibody omalizumab. “Eosinophilic esophagitis is no simple IgE-mediated food allergy,” summarized D. Simon. However, it is also not a typical autoimmune disease. Autoimmune diseases are indeed more common in families with EoE, however autoreactive T cells are missing, there are no autoantibodies and the cytokine pattern is different. However, D. Simon was able to show similarities with chronic inflammatory bowel disease, including dysfunction of the mucosa barrier and the cytokine spectrum involved in the inflammatory process with the proinflammatory cytokines TNF-alpha, interleukin 1, 18 and 33. However, she was also able to point out differences. Accordingly, Crohn’s disease is a Th1/Th17 inflammation and EoE and ulcerative colitis are forms of Th2-dependent inflammation. Her conclusion: An epithelial barrier disorder and a Th2-dominant inflammation are pathogenetically relevant in EoE.
**PPI response: not suitable from the standpoint of a differential diagnosis**

The primary differential diagnoses for EoE include GERD (gastroesophageal reflux disease). The response to a proton pump inhibitor (PPI) as a distinguishing diagnostic criterion falls short, however. Thus 20% of patients with a reflux disease do not respond to a PPI, but 50% of patients with EoE do. These patients with PPI-responsive esophageal eosinophilia and esophageal symptoms which respond to a PPI do not genotypically and phenotypically differ from EoE patients who do not respond to a PPI, explained J. Molina-Infante, Caceres (Spain). Antiinflammatory effects of PPIs beyond acid inhibition may also be relevant for the effects in the case of EoE. In this way, omeprazole blocks eotaxin-3 expression through esophageal squamous cells in patients with EoE and GERD. “The response to a PPI is an inadequate marker for unambiguously diagnosing GERD or ruling out EoE,” says J. Molina-Infante. Both diseases may also coexist. “The black-and-white concept should be discarded.”

**Also watch out for remodeling**

EoE is not associated with an increased risk of esophageal carcinoma. However, in the course of the disease, remodeling of the esophagus occurs which increases the risk of bolus impaction, esophageal strictures and perforations as well as malnutrition and ultimately it is associated with a significant loss of quality of life. The risk of such complications as a result of fibrostenosis increases during the course of the disease. After 10 years, it affects approximately 70% of EoE patients. The changes to the esophagus can be measured with FLIP (functional luminal imaging probe), a method which investigates the elasticity of the esophagus. In patients with EoE and bolus impaction, the elasticity is significantly less than in EoE patients without bolus impaction (p > 0.05). In the viewpoint of I. Hirano, Chicago (USA), parameters for remodeling should also be recorded during the course of the disease, because: ”EoE activity is more than just counting eosinophils.” A favorable effect on remodeling is achieved with the topical steroids which have not yet been approved. The expression of fibrosis markers such as TGF-beta and pSmad2/3 decreases during therapy with budesonide, as does the mucosal thickness. According to I. Hirano, drug therapy or even dietary therapy may also prevent the need for dilatation in cases of EoE, in keeping with the motto: “A puff (of steroids) a day keeps the dilator away.”

**Eosinophil infiltration irrelevant for symptomatology**

There are no eosinophils in a healthy esophagus. However, in EoE, the eosinophil-predominant inflammation is the decisive histological criterion (> 15 eos/HPF). There does not appear to be a close correlation with the clinical symptoms. Thus anti-IL5 therapy in EoE patients indeed demonstrates a reduction in eosinophils in the blood and tissues, however it does not have any significant effect on symptoms and also no effect on T cell infiltration. It is different for topical steroids: Topical budesonide (2 x 1 mg/day for 15 days) has been shown to not only reduce the infiltration of eosinophils and T cells but also improve dysphagia and retrosternal pain. For the EoE-associated symptoms, the eosinophil infiltration thus does not appear to be the determining factor, summarized H.-U. Simon, Bern (Switzerland). However, it is possible, according to his assumption, that they increase the inflammatory reaction in destroyed tissue.
Environmental factors more relevant than genetics

A genetic influence on the development of EoE is evident. “EoE patients have a unique gene expression profile,” says C. Blanchard, Lausanne (Switzerland). A comparison with the expression profile in asthma or atopic dermatitis demonstrated similar gene clusters. Even a glance at the family history of EoE patients suggests a genetic component. However, environmental factors are even more relevant. Thus the concordance is only 41% in monozygotic twins, 22% in dizygotic twins and 2.4% in siblings. In the general population, the prevalence of EoE is approximately 0.05%. It is calculated that genetics have an approximately 14% influence on the development of EoE and environmental factors, by contrast, have an approximately 80% influence. C. Blanchard therefore called for the causal environmental factors and their influence on genetic and epigenetic markers to be identified in order to be able to develop a genetic diagnostic tool.

Rarity of eosinophilic gastroenteritis: broad spectrum of symptoms

Eosinophilic gastroenteritis is far more rare than EoE with a prevalence of 6.3/100,000 for eosinophilic gastritis, 8.4/100,000 for eosinophilic gastroenteritis and 3.3/100,000 for eosinophilic colitis. The symptoms of eosinophilic gastroenteritis (EoG) essentially depend on the affected layer in the intestinal wall. Depending on the location and depth of the infiltration, a differentiation is made between the mucosal, muscular and serosal form of EoG. The clinical picture correspondingly varies, ranging from abdominal pain, diarrhea and structuring to anemia and ascites. Because of the rarity of the disease, there are only very limited data on possible therapeutic options, clarified N. Gonsalves, Chicago (USA). Steroids and antihistamines are currently being tried. Similarly to EoE, a good clinical and histological response was able to be demonstrated for the elemental diet. In the opinion of N. Gonsalves, prospective studies to evaluate these data are indispensable.

Epithelial barrier disorder: Chicken or egg?

The permeability of the esophageal mucosa is increased in EoE. It is impossible to determine whether this epithelial barrier disorder is the chicken or the egg in the pathogenesis of EoE, according to A.J. Bredenoord, Amsterdam (Netherlands). Rather, it is “a cycle”: More inflammation leads to increased permeability of the mucosa which opens the door to food allergens and they then further boost the inflammatory process in the mucosa. The mucosal permeability appears to correlate with the disease activity and for this reason, it is also a target for the therapy. The integrity of the esophageal mucosa can be restored with the topical steroids which have not yet been approved. This was shown by a study which compared 10 patients with EoE on fluticasone with 10 untreated EoE patients and 10 control persons. The faulty regulation of “tight junctions” and the dilatation of intercellular spaces could also be corrected, in particular. Even an elemental diet can have a beneficial effect on the barrier disruption.

Epithelial barrier disorder: Chicken or egg?
No linear connection between histology and symptoms

Whether PROs (patient-related outcomes) or biological markers are to be used for evaluating the success of the therapy always also depends on the individual disease. Thus in the case of diabetes with the HbA1c value, a laboratory parameter is the primary concern; in the case of migraines, the focus is on the patient’s pain. The benefits of therapy for EoE can be measured by means of the clinical symptoms, the endoscopy and the histology. There is a wide range of measurement instruments available for measuring PROs, that is, symptoms, changes in behavior and quality of life. The EoE-QOL-A is considered for adults in particular, according to A. Schoepfer, Lausanne (Switzerland) and for children, the Pediatric Eosinophilic Esophagitis Symptom Score (PEESS) to measure clinical activity and the PedsQL module to determine the quality of life. Symptoms and quality of life demonstrate a good correlation. However, there is no linear connection between the biological activity of EoE, measured using histology and endoscopy, and the PROs, that is, symptoms and quality of life. For this reason, the symptoms are only suitable to a limited extent as a measure for remission.

The important thing is to prevent fibrostenosis

“Should the patient be doing better or should the histological and endoscopic findings look better?” F. Moawad, La Jolla (USA) posed this question to make it clear that: “In a perfect world, all three objectives are important.” By contrast, from the patient’s perspective, symptoms and quality of life are paramount. The situation here is hardly satisfactory. F. Moawad referred to a study with 74 adults with EoE whose quality of life was compared with that of the general population, using the Short-Form-Health-36 questionnaire (SF-36). According to this, the patients had a lower quality of life, in particular younger patients and patients whose disease had lasted a longer period of time. This also applies to children in whose case the entire family is additionally affected. During the course of treatment, the disease-related quality of life improved. However, a range of studies shows that there is no direct correlation between the symptomatic and histological response. There are few current studies which come to a different result. F. Moawad left no doubt, however, that, with regard to the course of the disease, it is important, beyond the symptoms, to inhibit inflammation and prevent fibrosis. “It is rather the disease than the symptoms which should be treated.”

In brief

Half of the adult patients complain of retrosternal pain. In children, with EoE, a refusal to eat and failure to thrive are the primary concerns. There may also be stomachache, abdominal pain and diarrhea.
If therapy fails: refractory or pseudorefractory?

If drug therapy with a topical steroid or dietary therapy for EoE fails, the cause should be investigated before the term “therapy-refractory eosinophilia” is assigned, recommended E.S. Dellon, Chapel Hill (USA). Non-compliance or a dosage which is too low can inhibit the response to a topical steroid, as can a suboptimal pharmaceutical formulation of the preparation, persistent allergen exposure, or strictures. In the case of dietary measures, it should be checked whether the determining triggers have actually been eliminated. In a further step, differential diagnoses must also be clarified. In addition to GERD, these also include functional dyspepsia and tablet-induced esophageal injury. The search is all the more important since the treatment options in patients who are actually refractory are limited, says E.S. Dellon. Various biologics are currently undergoing testing, according to S.K. Gupta, Peoria (USA), however they are rather unconvincing because of the limited data to date and their limited efficacy. In the future, he sees, among others, the development of antibodies which induce apoptosis of the eosinophils or even substances which intervene in the signaling pathways of eosinophils such as anti-eotaxins and anti-TSLP (thymic-stromal lymphoprotein).

Missing: Biomarkers to monitor progress

“One cannot rely on the symptoms to assess disease activity in EoE,” stressed U. von Arnim, Magdeburg. They allow only modest statements to be made regarding endoscopic or histological remission. In her opinion, the most meaningful and most objective method is esophagogastroduodenoscopy (EGD) plus biopsy. This invasive method is not a suitable instrument, particularly in children, for reasons including invasiveness, possible complications and, not least of all, the costs. For this reason, non-invasive biomarkers for monitoring disease activity would be important, U. von Arnim stressed. There are still no biomarkers available for clinical practice. Currently, the AEC (absolute blood eosinophil count), a marker which correlates with the histological activity before and after budesonide therapy, is currently being investigated, among others. However, there was no correlation with the endoscopy score and dysphagia. Her conclusion: AEC, ECP (eosinophilic cationic protein) and EDN (eosinophil-derived neurotoxin) could be appropriate for diagnosing EoE. AEC could be appropriate as a biomarker for monitoring if the value is initially elevated.

“An inflamed esophagus must be treated”

In a debate of the pros and cons of the management of asymptomatic patients with an inflamed esophagus, S. Aceves, San Diego (USA), stressed the need for therapy, even if there are no symptoms. If left untreated, there is a threat of the development of strictures. She argued in favor of also treating children since remodeling begins earlier in them. This opportunity should not be wasted. However, A. Straumann, Olten (Switzerland), warned of improper treatments. The infiltration of the esophagus with eosinophils is pathological but not synonymous with EoE. Differential diagnoses would have to be ruled out. In addition to GERD, these also include celiac disease, infections or achalasia. He recommended an accurate history and an endoscopic and histological follow-up after 3–6 months to establish the chronic nature and endoscopic signs of EoE.
Still unclear: What role do IgG4 and FLC play in pathogenesis?

According to current estimates, EoE is not IgE-mediated or is IgE-mediated only to a very small extent. However, there are now indications that argue in favor of involvement of IgG4. Elevated IgG4 levels against specific foods could be found in the serum and in the esophageal tissue in patients with EoE, according to M. Chehade, New York (USA). Whether there is actually a correlation between the IgG4 level and the causal food remains to be clarified. Researchers are also focusing on the immunoglobulin free light chains (FLCs) which are elevated in the case of allergic diseases, independent of IgE. Milk-specific FLCs are significantly increased in the serum of children with EoE. However, M. Chehade had to concede that much still remains unclear. But: “The future is promising!”

Molecular testing instead of histology? It depends!

GERD is the most common differential diagnosis to EoE. Molecular investigations using a 94-gene panel, developed on the basis of gene expression analyses of esophageal biopsies, are currently not able to discriminate between EoE and GERD, according to M.H. Collins, Cincinnati (USA). The same applies to the differentiation between a case of EoE which responds well to PPIs, and one which does not. “The panel appears to not be able to differentiate between EoE subtypes,” says M.H. Collins. On the other hand, it is possible with the panel to differentiate between patients with and without EoE.

Diagnosing EoE in the “post-PPI trial” age

In the initial decades after EoE was described, PPIs were used to differentiate between EoE and GERD. Since it is clear that PPIs also have antiinflammatory properties and a percentage of patients with EoE respond to PPIs, this method does not apply. The diagnostic criteria must be rewritten. As a new definition of EoE, G.T. Furuta, Aurora (USA), presented the combination of symptoms of esophageal dysfunction and at least 15 eos/HPF (or about 60 eos/mm²) in the biopsy. Other causes of esophageal eosinophilia, also including GERD, must be ruled out. For G.T. Furuta, this means the following diagnostic algorithm: If EoE is clinically suspected, an EGD with biopsy must be performed. If the findings are positive, possible differential diagnoses should be ruled out, in particular diseases which are associated with esophageal eosinophilia. Only then can the diagnosis of EoE be made.
XXV International Bile Acid Meeting: Bile Acids in Health and Disease 2018

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Medicine thrives on the successful involvement of scientists who are hungry for knowledge. Following a long tradition, young scientists were also honored at Symposium 208 by the Falk Foundation e. V. for their excellent research work.

The first prize was awarded to A. Zalewski, Chicago (USA), together with her research team, for studies on the elasticity of the esophagus during drug and dietary therapy: “Improvement in esophageal distensibility in response to medical and diet therapy in eosinophilic esophagitis”.

The second prize was awarded to L.P. Sydorchuck, Chernivtsi (Ukraine) and colleagues for investigations in the pathogenetic role of TSLPR polymorphisms: “The possible pathogenetic role of TSLPR (rs36133495) gene’s polymorphism in eosinophilic esophagitis”.

The third prize honored M. Fortea, Barcelona (Spain), with her working group for their investigations in immunological changes on a six-food elimination diet (6-FED): “Modulation of CD8+ cells infiltration and activity in eosinophilic esophagitis by six-food elimination diet”.

Left to right: Dr. R. Greinwald for the Falk Foundation, Prof. S. Aceves, Dr. J. Molina-Infante, A. Zalewski, M. Fortea, L.P. Sydorchuck, Prof. A. Straumann
“Difficulty swallowing solid foods always calls for an endoscopy”

Patients with eosinophilic esophagitis suffer greatly. Why the chronic inflammatory disease is still underdiagnosed and undertreated and how this can change was explained by Prof. Dr. A. Straumann, Olten (Switzerland), scientific organizer of the Symposium 208.

Editorial staff: Prof. Straumann, which symptoms should the doctor be aware of and specifically ask about with regard to EoE?

Prof. Straumann: Whenever a patient reports typical symptoms of dysphagia, eosinophilic esophagitis (EoE) must be considered. In these patients, solid foods, such as meat and bread, become stuck in the esophagus or undergo delayed transport towards the stomach. Patients frequently gag when consuming solid foods. These symptoms always need to be clarified. At best, they may be due to inflammation but possibly also to esophageal carcinoma. From my viewpoint, the question regarding swallowing belongs with the systemic history just as much as the question about blood in the stool. Physicians should regularly dig deeper here, including pediatricians. In children, the symptoms vary much more widely, however. I would consider refusal of food and the child dropping off the growth curve in terms of weight and length to be alarm symptoms.

How should the diagnosis be confirmed when EoE is suspected, based on history?

The first step of clarifying dysphagia is always an upper panendoscopy: The general practitioner should always ask the gastroenterologist to take a structured biopsy, even when mucosa is unremarkable. The diagnosis is confirmed if the typical symptoms are present as well as eosinophil-dominant inflammation and, if applicable, the typical changes in endoscopy with furrows, white exudate, edema and rings.

The most common differential diagnosis of EoE is gastroesophageal reflux disease (GERD). How do you differentiate the two clinical disease pictures?

Reflux patients typically have burning pain and acid reflux but rarely dysphagia for solid foods. By contrast, EoE patients may have burning pain which is not rising however, but rather localized. The typical signs of reflux disease – hiatus hernia, erosive inflammation, redness in the lower esophagus – can be seen on endoscopy. However, there are also definitely areas of overlap. Differentiation is then the task of the specialist. I would give a proton pump inhibitor without hesitation only in cases of a history of typical reflux and upper abdominal symptoms. Difficulty swallowing solid foods always calls for an endoscopy. If there is blood in the stool, it is also not enough to treat it with a hemorrhoid ointment.
At present, there are, among others, two fundamentally different therapeutic options available: drug therapy, for example with topical steroids which have not yet been approved, and dietary therapy. According to which criteria do you make a decision?

Dietary treatment is, from a theoretical perspective, very attractive. It does not require any drugs and it is more causal because it omits the triggering allergen. However in practice, it is difficult to implement because we still do not have a good instrument to identify the triggering foods. We have to take a slow, careful approach by omitting one food category after the other. It is tedious and requires repeated endoscopies until the causal foods are found. The patient needs to be highly motivated, because the diet significantly interferes with his or her lifestyle habits. One only has to get used to drug therapy. For these reasons, dietary therapy is of interest above all in centers which have correspondingly trained dietitians and in the case of motivated patients. But that is the exception.

Would it nevertheless be preferable to start dietary therapy in children in view of the adverse effects of steroids?

In the case of steroid drug therapy in children, we must of course be more careful and follow up more frequently, in view of the adverse effects of steroids. But a strict diet also poses serious risks for the child: It can lead to stigmatization, for example, in school. In my opinion, that is an important factor which we must bear in mind.

What is your therapy management like?

I present the therapeutic options to the patient and let him or her choose. If someone is interested in a diet, we try this strategy for a limited amount of time, for 2–3 months, with support from a dietitian. In this process, we perform endoscopic check-ups regularly. If he or she prefers to start medication, this is also possible within the scope of off-label therapy. We currently do not have any head-to-head studies which show which of the two options is the better one.

How long do you treat when you give steroids?

The goal is to achieve complete freedom from symptoms. The patient should be able to eat completely normally. If this goal is achieved, I would perform a follow-up endoscopy on him or her after one year. After a fundamental change in therapy, such as to another drug or from a diet to steroids, I perform a follow-up after 3 months. What is important is that the patient has a hotline which he or she can call if dysphagia recurs. We still have the problem that we lack a true long-term prognosis. However, we can draw analogous conclusions here to chronic inflammatory bowel disease, where we have various disease courses. This appears to be similar in the case of EoE. The therapy is then also based on this. I do not tell my patients that they need to be on lifelong treatment.

When do you feel an endoscopic dilatation is indicated?

Dilatation, in my opinion, is a second-line therapy since the inflammation and thus the fibrosing trigger cannot be eliminated. In the case of a severely symptomatic patient with a significantly inflamed esophagus, I always provide anti-inflammatory treatment first, generally drug treatment. If the symptoms have disappeared after 3 months, even if the esophagus is somewhat narrow, I do not perform dilatation. If the symptoms remain, I check the clinical picture endoscopically. If the patient has symptoms although no more inflammation is present, I perform dilatation.

Over the next year, the approval of topical steroids explicitly for EoE is expected. What do you expect from this?

The situation is unsatisfactory at present. We treat off-label by using preparations which were developed for the topical therapy of respiratory diseases. That’s why the patients must be given accurate instructions on how they are to use these preparations. With the newly approved preparations, the therapy becomes much easier. And they have one more significant advantage: They are being investigated in phase III studies and we thus have solid information on the effects, adverse effects and safety. Our impression is also that, as a result of the adapted pharmaceutical formulation, the efficacy is better than that with the off-label formulations.

Professor Straumann, thank you for the discussion!
HALF A CENTURY OF PROMOTING MEDICAL EXCHANGE

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We would like to offer our deepest thanks to everyone who has participated, and we look forward to further advancing scientific dialogue as we continue to advocate for more knowledge sharing and therapeutic progress!

Allow us to welcome you to the Falk Foundation symposia – now and for many years to come!
Speakers, moderators and scientific organizers

Prof. Dr. Seema Aceves
Center for Immunity, Infection, and Inflammation
Rady Children's Hospital, San Diego
University of California
3020 Children's Way
San Diego, CA 92123, USA
saceves@ucsd.edu

Prof. Dr. Stephen Attwood
North Tyneside General Hospital
Rake Lane
North Shields NE29, United Kingdom
seaattwood@gmail.com

Dr. Luc Biedermann
Gastroenterology
Zurich University Hospital
Rämistr. 100
8091 Zürich, Switzerland
luc.biedermann@usz.ch

Dr. Carine Blanchard
Nutrition and Health
Nestlé Research Center Allergy Group
PO Box 44
1000 Lausanne, Switzerland
carine.gaelle.blanchard@rdls.nestle.com

Dr. Arjan J. Bredenoord
Department of Gastroenterology and Hepatology
Academic Medical Centre
PO Box 22700
1100 DE Amsterdam, Netherlands
a.j.bredenoord@amc.uva.nl

Mirna Chehade, M.D.
Associate Professor of Pediatrics and Medicine
Icahn School of Medicine at Mount Sinai
Mount Sinai Center for Eosinophilic Disorders
The Mount Sinai Hospital
New York, NY 10029, USA
mirna.chehade@mssm.edu

Margaret H. Collins, M.D.
Professor
Division of Pathology
Cincinnati Children's Hospital Medical Center
3333 Burnet Avenue
Cincinnati, OH 45229-3039, USA
margaret.collins@cchmc.org

Evan S. Dellon, M.D.
Gastroenterology and Hepatology
University of North Carolina
Bioinformatic Bldg.
130 Mason Farm Road
Chapel Hill, NC 27599-7080, USA
edellon@med.unc.edu

Marina Fortea, Ph.D.
Translational Mucosal Immunology Lab
Digestive Diseases Research Unit
Vall d’Hebron Institut de Recerca
Passeig Vall d’Hebron 119-129
08035 Barcelona, Spain
marina.fortea@vhir.org

Glenn T. Furuta, M.D.
Professor of Pediatrics
Gastroenterology, Hepatology & Nutrition, B290
The Children’s Hospital
13123 East 16th Avenue
Aurora, CO 80045, USA
glenn.furuta@childrenscolorado.org

Nirmala Gonsalves, M.D
Associate Professor
Division of Gastroenterology & Hepatology
Northwestern University
Arkes Family Pavilion Suite 140
676 North St. Clair Street
Chicago, IL 60611, USA
n-gonsalves@northwestern.edu

Thomas Greuter, M.D.
GI Research Unit
Mayo Clinic
200 First Street SW
Rochester, MN 55905, USA
th_greuter@mayo.edu

Sandeep K. Gupta, M.D.
Professor of Clinical Pediatrics and Internal Medicine, Pediatric Gastroenterology, Hepatology and Nutrition
Department of Pediatrics
College of Medicine
Children’s Hospital of Illinois
University of Illinois
North Building Room 6646
530 NE Glen Oak Avenue
Peoria, IL 61637, USA
skgupta@uic.edu

Ikuo Hirano, M.D.
Professor of Medicine
Northwestern University
676 North St. Clair Street
Chicago, IL 60611, USA
i-hirano@northwestern.edu

David Katzka, M.D.
Division of Gastroenterology
Mayo Clinic
200 First Street SW
Rochester, MN 55905, USA
katzka.david@mayo.edu

Dr. Alfredo J. Lucendo
Department of Gastroenterology
Hospital General de Tomelloso
Vereda de Socuéllamos, n/n
13700 Tomelloso, Spain
lucendo@hotmail.com

Prof. Dr. Stephan Miehlke
Gastrointestinal Center
Eppendorf Medical Specialist Center
Eppendorfer Landstr. 42
20249 Hamburg, Germany
prof.miehlke@mdz-hamburg.de
Speakers, moderators and scientific organizers

**Fouad Moawad, M.D.**
Division of Gastroenterology
Scripps Clinic
Anderson Medical Pavilion
9898 Genesee Ave
La Jolla, CA 92037, USA
Fmoawad@hotmail.com

**Dr. Javier Molina-Infante**
Department of Gastroenterology
Hospital San Pedro de Alcantara
Avenida Pablo Naranjo, s/n
10003 Cáceres, Spain
xavi_molina@hotmail.com

**Dr. Ekaterina Safroneeva**
Institute of Social and Preventive Medicine
University of Bern
Finkenhubelweg 11
3012 Bern, Switzerland
ekaterina.safroneeva@ispm.unibe.ch

**PD Dr. Christoph Schlag**
Klinikum rechts der Isar
Technical University of Munich - Med. Clinic II
Ismaningerstr. 22
81675 Munich, Germany
christoph.schlag@mri.tum.de

**Dr. Alain Schoepfer**
Department of Gastroenterology
University Hospital Lausanne
CHUV
1011 Lausanne, Switzerland
alain.schoepfer@chuv.ch

**Prof. Dr. Dagmar Simon**
Department of Dermatology
Inselspital University Hospital
3010 Bern, Switzerland
dagmar.simon@insel.ch

**Prof. Dr. Hans-Uwe Simon**
Institute of Pharmacology
University of Bern
3010 Bern, Switzerland
hus@pki.unibe.ch

**Prof. Dr. Alex Straumann**
Chairman Swiss EoE Clinic
Römerstr. 7
4600 Olten, Switzerland
alex.straumann@hin.ch

**Prof. Dr. Larysa P. Sydorchuk**
Family Medicine Department
Bukovinian State Medical University
Theatre Sq. 2
58000 Chernivtsi, Ukraine
rsydorchuk@ukr.net

**Dr. Ingrid Terreehorst**
Department of Allergy
Academic Medical Centre
PO Box 22700
1100 DE Amsterdam, Netherlands
i.terreehorst@amc.uva.nl

**Prof. Dr. Michael Vieth**
Pathology
Bayreuth Hospital
Preuschwitzer Strasse 101
95445 Bayreuth, Germany
vieth lkpathol@uni-bayreuth.de

**Dr. Ulrike von Arnim**
Gastroenterology/Hepatology
University Hospital
Otto-von-Guericke University
Leipziger Str. 44
39120 Magdeburg, Germany
ulrike.vonarnim@med.ovgu.de

**Angelika Zalewski**
Feinberg School of Medicine
Northwestern University
676 North Saint Clair, Suite 1400
Chicago, IL 60611, USA
angelika.zalewski@northwestern.edu
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July 6 – 7, 2018

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Symposium 213
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Milan, Italy
October 5 – 6, 2018

FALK FOUNDATION e.V.
Leinenweberstr. 5
79108 Freiburg
Germany

Congress Department
Tel.: +49 (0)761/1514-125
Fax: +49 (0)761/1514-359
E-Mail: symposia@falk-foundation-symposia.org
www.falk-foundation-symposia.org

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