Dr. Justinich Discusses Eosinophilic Esophagitis “EoE”

Eosinophilic esophagitis is a condition that has become more frequently diagnosed in the last 15 years. Before that time there was an occasional case that was probably eosinophilic esophagitis, often this occurred in the context of eosinophilic intestinal disease affecting the stomach, small bowel or even colon, something that we call ‘eosinophilic gastroenteritis’ or ‘eosinophilic enteropathy’. For reasons that are not understood we are seeing more and more children now with EoE, a condition that is confined to the esophagus and does not affect other parts of the bowel.

**Diagnosis of EoE**

- **Eosinophils** are white blood cells that help fight parasitic infections, and are also the cells that are implicated in allergic type of inflammation

- In biopsies of the normal esophagus, eosinophils are never seen under the microscope

- In EoE, eosinophils are markedly increased within the surface lining of the esophagus

- For purposes of diagnosis, by convention, many experts agree that there should be more than 15 eosinophils per high power field under the microscope and that most of the time this affects the lower, middle and upper part of the esophagus equally

- The area is a little confusing, however, because eosinophils are seen with acid reflux disease in children. This eosinophilic inflammation is are usually located more in the lower part of the esophagus where more acid exposure would occur, and often there are smaller numbers of eosinophils (<15 per field)

**What are the characteristics of EoE patients?**

- EoE occurs predominately in boys; approximately 75%

- Seventy to eighty percent of patients have associated allergic disorders such as asthma, atopic dermatitis (eczema), seasonal allergies and sometimes coexisting food allergies

- Associated allergic disease is often not severe
What symptoms do patients experience?

Patients who get EoE seem to form two separate groups:

1. Young children (infants and toddlers) who often come with reflux symptoms, spitting up, vomiting and refusing to eat often leading to problems with weight gain. Some of these children then need tube feeding to help maintain their nutrition.

2. The second group tends to be older (pre-teen, teens and adults) who have trouble swallowing, sometimes getting food stuck in the esophagus (food impaction). Many of these patients eat very slowly, or need to constantly drink while eating, otherwise they have trouble swallowing.

Allergy in Eosinophilic Esophagitis

- Food allergies are increasing and eosinophilic esophagitis appears to be increasing as well.

- It has been reported by some that food allergies cause eosinophilic esophagitis and that removing food allergens from the diet will make eosinophilic esophagitis better. This is still a controversial issue in my mind. Environmental allergies may also be involved in EoE. We have information from both patient and animal studies.

What we know:

A) Experimental animal studies

(We do not do animal studies ourselves; most information comes from allergy research at Cincinnati Children’s Hospital). Animal models may not be the best indicator of human disease and under the microscope, similarities and differences with human EoE are seen. However, the mice models may offer some insights and raise questions about how EoE may occur.

- Animal studies have been done using mice strains that are prone to develop allergy
- If these mice are made allergic to a food, and then are fed this food, they do not get EoE; they may get allergic disease in the small intestine
• If animals are made allergic to a food and then the food is put in the nose or put into the air that they breathe, they develop signs of nasal allergy or asthma and then seem to develop EoE
• Non-food or environmental allergens (eg dust, fungus) may also lead to EoE in mice in this way

B) Human EoE and Allergy

I believe this area to be the most controversial aspect of EoE. As stated the majority of patients (especially pediatric patients) have some allergic disease (asthma, 'atopic dermatitis' or eczema, environmental or food allergies.

In my way of thinking, if a patient were allergic to food and developed an allergic reaction or response within the esophagus, then this should also occur in the stomach, small bowel or even the colon (similar to the mouse models). However, most of our patients do not show signs of allergy in these other areas. Most patients who are allergic to milk protein, for example, would have inflammation with eosinophils in the stomach or the small intestine when eating milk protein in the diet. This would get better when milk is removed and most of these patients would not have any disease in their esophagus.

• Patients taken off food protein in the diet and fed with an elemental diet (formula made with the building blocks of protein-'amino acids', EoE tends to resolve in most cases, but will reappear when foods are reintroduced into the diet

• This means that the patients are allergic to foods that we cannot identify or that elemental diet can help with allergic inflammation in the GI tract in some other indirect way

• Some patients do not improve with dietary therapy, implying that at least some patients’ disease is not directly or indirectly influenced by food

• Elemental diets were first used in young infants typically requiring tube feeding for EoE

• Elemental diet may help older patients with EoE but tube feeding special formula with patients not eating food is difficult and requires a highly motivated patient and family

• How can skin testing help??
  o Regular skin prick testing correlates quite well with immediate reaction to food (usually within minutes) such as hives or breathing difficulty
Patients with this type of allergy and positive skin tests are often avoiding those food when diagnosed with EoE meaning the foods are not causing the disease

Some patients may be eating foods without a reaction, but skin test positive; we then restrict these foods if the patient has EoE (this may or may not help the EoE)

What is seen in the esophagus appears more like a ‘delayed’ reaction to food so some allergists have advocated the use of skin ‘patch’ tests to look for evidence of delayed reaction to food. Patch tests are done by placing the food on the skin for a period of 48 hours and reading the test after 72 hours to look to see if there is redness or inflammation in the site where the food has been placed. A research group at the Children’s Hospital of Philadelphia have reported that almost sixty percent of patients with EoE have positive patch tests for food and if these foods are removed the EoE improves. However this has not been the experience at our center or in other centers in North America so the role of patch tests is still in question.

We do attempt patch tests to try to identify other foods to which the patient may be allergic

Treatment of EoE

The cause of EoE is not known; as discussed above, there may be food or environmental allergies that lead to EoE, or in some cases there may be no triggering allergy. This occurs in other allergic diseases such as asthma – some asthmatic patients have allergy to dust or pollen, for example, and benefit from control of these factors. Other asthmatics have no allergies but have lung disease that resembles allergy.

A) No Treatment

- We see patients who have very little in the way of symptoms and choose to be followed without diet or medicine treatment
- The underlying principle is that we do not want treatment to be worse for the patient than the disease itself
- We continue to follow these patients for worsening of disease or complications
B) Diet Treatment

Diet treatment should be done under the direction of an experienced dietician to avoid both nutritional problems and to make sure that the foods are being totally eliminated.

- If food allergies can be detected we usually start by eliminating these foods.
- If patients want to try diet therapy when the skin tests are negative, we can remove all milk protein first (the most common food allergy) or try the “six-food elimination diet” avoiding milk, soy, egg, peanut, wheat and corn, some people also avoid shellfish. These are very restrictive diets requiring high motivation, reading labels etc, but may work in some people.
- After a period of at least 8 weeks, foods can be re-introduced slowly, one at a time to see if any of these cause symptoms.
- If the patient has very infrequent symptoms, food removal and re-introduction can be difficult to assess, and follow-up endoscopy may be needed.

C) Medicine Treatment

If no food allergies can be found from skin prick or patch tests, or if the patients do not want to accept removing major food allergens from the diet (this can make the diet very restricted) then we often use medication.

- Corticosteroid “steroid” medicine can make the eosinophils go away.
- Six months after stopping treatment the EoE often has returned.
- Prednisone – works for this disorder but this is a pill that is taken by mouth that is absorbed into the blood stream and may have widespread side effects that are associated with systemic medicine.
- People then have studied the use of topical steroids, that don’t enter the blood stream in large amounts. The researchers used asthma medication, but instead of inhaling it into the lung the patients swallow it into the esophagus.
- Fluticasone (Flovent®) inhalers – have been used for this and also Budesonide or (Pulmicort®) liquid which can be mixed with a thickener and swallowed at night. Side effects of corticosteroids that are given this way are minimal. The major side effect is that of “candida” or yeast overgrowth in the esophagus that occur in some patients. Brushing the teeth and rinsing the mouth after taking the medicine can help prevent this, but no liquids should be swallowed at night after the medicine is given allowing the medicine to stay in the esophagus longer.
• EoE will often relapse when the steroid treatment is stopped, so we can use the steroids on a chronic basis, and perhaps reduce the use to every other night or twice a week (this has not been studied, but may be enough to prevent relapse)

• Montelukast (Singulair®) – another asthma medicine that is taken as a pill at night may help prevent the recurrence of EoE or may help control symptoms of swallowing problems or vomiting. It appears that the doses that are needed are two or three times the doses that are typically recommended for asthma. Side effects of Singulair include problems with sleeping and there are some behavioural effects of the medicine that many people think are related to the sleeping difficulties

• Monteleukast (Singulair®) may allow patients to stop steroid medications

• Antacid treatment may help control symptoms in some patients, usually the strong antacids known as proton-pump inhibitors (PPI) are used. It is not known whether patients who get better on PPIs also have acid reflux disease together with EoE or if the PPI has other effects that might help EoE

Long Term Follow-up

There are a few long term follow-up studies available on EoE. We worry that patients might get scar tissue within the esophagus causing narrowing (strictures) and this is probably the biggest long term worry about this disorder. There is no evidence that EoE can lead to Barrett’s esophagus, a condition which is pre-cancerous and generally thought to be related to chronic acid reflux disease but this is not completely known. There are rare adult patients who have both Barrett’s and EoE but these diseases are likely unrelated and just occurring within the same patient. The vast majority of our EoE patients do not have Barrett’s.

We continue to study this disorder and we do re-endoscope patients at intervals to see the status of their disease in the hopes that we might be able to recognize and prevent complications from occurring.