EOSINOPHILIC ESOPHAGITIS (EE)

EE is among a basketful of named diseases offered to us by the medical profession --- a basket that includes Eosinophilic Esophagitis, Eosinophilic Gastritis, Eosinophilic Gastroenteritis, and Eosinophilic Colitis. They are really all the same disease mechanism --- the only difference being the location in the G.I. tract where the tissues are immune-reactive. These Eosinophilic infiltration pathologies in the gut show the same immune system reactivity pattern as do the Eosinophilic infiltration conditions of the Respiratory tract --- namely, Eosinophilic Rhinosinusitis and Eosinophilic Bronchitis.

[In our other articles on related topics we have referred to Eosinophilic Rhinosinusitis as Eosinophilic FUNGAL Rhinosinusitis --- also known as Dennis-Robertson Syndrome. The reason for that is what Dennis and Robertson called a "Super-Antigen Response" to mold spores and mold toxins is so often a trigger to the various Eosinophilic infiltration diseases. Much of what is written below about EE applies equally well to all the G.I.-related and Respiratory-related Eosinophilic conditions.]

EE is associated with excess activation of Lymphocytic T-helper-2 (Th2) cell activation. The Th2 antigen-driven response elicits Mast Cell and Basophil activation. The Th2 inflammatory cytokines involved are Il-4, Il-5, Il-13. These inflammatory cytokines cause dysfunction of the involved tissue's Eosinophil barrier. Eosinophil infiltration of the tissues, if extreme and prolonged, will eventually cause remodeling and fibrosis of the now pathological tissues.

The progressive remodeling of the esophageal tissues is evidenced by furrows, rings, white plaques, and decreased lateral diameter due to strictures.

What are the causes or predisposing factors? What triggers the Th2 antigen-driven inflammation? Consider…

- Early Life Antibiotic Use is currently established as a risk factor.

- Curiously, EE incidence is inversely associated with H. pylori.

- There is a typical abnormal microbiota in EE. The microbiota of the saliva and the esophagus differs significantly, with excesses of certain bacterial and fungal species and lower numbers of other species, when compared to healthy controls.

- Immunoglobulin-E activation is NOT required to trigger EE symptoms. This finding ties in well with the Dennis-Robertson thesis that these

Eosinophilic infiltration conditions (whether the Respiratory tract or G.I tract) involve an Immunoglobulin-G Super-Antigen Response to mold.

- Esophageal Candidiasis is the most common cause of infectious EE.

- Food antigens are extremely common as a trigger. By far the most common food sensitivity in EE is Cow milk. Also common are wheat, egg, soy, peanuts and tree nuts, and fish/shellfish. (In children with concomitant nocturnal enuresis, milk sensitivity is almost assured.)

How is EE diagnosed and monitored? The only definitive diagnosis comes from Endoscopy --- with esophageal tissues showing an elevated level of Eosinophils. What symptoms justify an Endoscopy? Many of the symptoms resemble those of GERD --- pressure or pain or burning in the midline of the chest. Typically, there is dysphagia, and food often gets stuck before reaching the stomach. When those symptoms present, and are frequent and severe, an endoscopy is justified.

The clinician during the Endoscopy must be aware that a differential diagnosis needs to be made between GERD and EE. The examiner must be aware that Candida and other fungal infections of the esophagus are very common.

To avoid the discomfort of the invasive endoscopy, an alternative has been developed --- the Esophageal String Test (EST). This test is shown to be just as accurate as an Endoscopy, and is minimally uncomfortable. The EST should be used routinely for follow-up testing to monitor the Eosinophil presence in the Esophagus.

Since there is so commonly an immune reactivity to foods in EE, it has conventionally been assumed that the food sensitivities can be determined by skin prick tests or skin patch tests. But positive findings on those tests do not correlate at all with the foods that trigger the Th2-driven EE symptoms. The diagnostic failure of skin testing is simply because there is no IgE response required to elicit EE symptoms. This is almost an entirely IgG-mediated condition.

How is EE treated? As of this writing, the standard care is a combination of PPI Drugs and topically swallowed steroids. This combination is frustratingly disappointing for many patients. Studies show that only 30-50 percent "respond clinically" to two months of high dose PPI Drugs. The topical swallowed steroid (using an inhaler, usually Fluticasone as used in asthma) temporarily controls the inflammation, but does not consistently show long-term benefits. And, there are 2 major problems with these steroids. The first is that so often they cause Oral and Esophageal Candidiasis --- one of the primary causes or predisposers to EE. Second, when used in children, corticosteroids can cause adrenal insufficiency.

More recently a drug (Dupilumab) has been approved to treat EE. It involves weekly subcutaneous injections for 8-12 weeks. The drug specifically blocks the action of the inflammatory cytokines Il-4 and Il-13.

The most successful clinical effects come from addressing the dietary triggers. One approach is to use the Elemental Diet. This is a concoction of foods broken down into simple amino acids, maltodextrins, and short chain fatty acids --- staying on that diet, and eating that and only that, liquid diet for 8-12 weeks. The Elemental Diet almost always benefits, and sometimes gives a permanent remission of, EE. However, compliance with the Elemental Diet is very poor since the person must abstain from any real food for at least 2 months.

The more successful dietary approach is the Elimination Diet. The 6 foods listed above as potential triggers are strictly (strictly!!!) avoided for 6-8 weeks. The Elimination Diet has shown a 74 percent success rate in children. After the 6–8-week Elimination Diet, symptoms are evaluated and an Endoscopy or Esophageal String Test is performed to check the Eosinophil count in the Esophageal tissues. Assuming there is significant improvement, then each of the offending foods is reintroduced one at a time, and the reaction monitored.

Since there is abnormal microbiota in EE subjects and since that microbiota is supporting a Th2-driven immune reactivity, supplementation with the appropriate pre- and pro-biotic is essential.

Since mold exposure is known to cause a Super-Antigen response in 1 out of 6 people, mold remediation of the living environment is essential.