# Eosinophilic Esophagitis: Many Questions Remain

***The increase in the disorder mirrors the recent rise in the more traditional manifestations of atopy.***

BY BRUCE JANCIN
*Denver Bureau*

KEYSTONE, COLO. — Does the sharp escalation in diagnoses of eosinophilic esophagitis in the past several decades reflect a true emerging epidemic of a relatively new disease, or is it merely an artifact of greater physician recognition?

The truth most likely lies somewhere in between, Dr. David M. Fleischer said at a meeting on allergy and respiratory disease sponsored by the National Jewish Medical and Research Center.

Eosinophilic esophagitis was first described in 1977. Epidemiologic studies suggest the worldwide incidence in both children and adults is climbing and may now exceed that of inflammatory bowel disease.

Eosinophilic esophagitis has been characterized by some as "eczema of the esophagus." And indeed, the increase in the disorder mirrors the well-documented rise in recent decades in the more traditional manifestations of atopy—food allergy, atopic dermatitis, allergic rhinitis, and asthma.

How common is eosinophilic esophagitis? When gastroenterologists at the Karolinska Institute, Stockholm, conducted a population-based study in which they performed esophagogastroduodenoscopy in 1,000 randomly selected adult volunteers, they found 1.1% had 15 or more intraepithelial eosinophils per high-power field (Gut 2007;56:615-20), thereby fulfilling the pathologic portion of the diagnostic criteria for eosinophilic esophagitis.

Pediatric gastroenterologists in Ohio estimated the prevalence of eosinophilic esophagitis in youths up to age 19 years at 4 per 10,000 in 2003 (N. Engl. J. Med. 2004;351:940-1). And a blinded retrospective evaluation of esophageal biopsies at a tertiary pediatric gastroenterology clinic in Western Australia showed a rapidly increasing prevalence of eosinophilic esophagitis, from 0.05 cases per 10,000 children in 1995 to 0.89 per 10,000 in 2004 (Arch. Dis. Child. 2006;91:1000-4).

But with the exception of the Swedish study, these reports are susceptible to ascertainment bias. Moreover, while the annual number of PubMed citations on eosinophilic esophagitis has grown exponentially since 1978, only 29% of them were original studies; the rest were case reports or review articles. That in turn suggests awareness of eosinophilic esophagitis on the part of gastroenterologists, allergists, and pathologists is growing at a considerably faster pace than any actual advance in scientific understanding.

The implication is that increased physician recognition of the GI disorder is contributing—to an as-yet uncertain extent—to the apparent rise in incidence and prevalence, observed Dr. Fleischer, a pediatric allergist at the center.

Although the epidemiology of eosinophilic esophagitis is incompletely understood, it is known that males account for 75%-80% of cases, consistent with the strong male predilection for food allergy. It is clearly an allergic disease. Most affected patients have a personal and family history of allergic disease. Some also display seasonal variation in their GI symptoms.

Moreover, roughly 80% of patients with eosinophilic esophagitis have elevated serum total IgE and display sensitization to food or environmental allergens on skin prick tests, patch testing to foods, and/or RAST testing, Dr. Fleischer continued.

Biopsy specimens of esophageal mucosa in affected individuals show eosinophils, T cells, and mast cells, suggestive of chronic TH-2–associated inflammation. Elevated levels of TH-2 cytokines such as interleukin-5 and interleukin-13 are also present.

Further underscoring the allergic nature of eosinophilic esophagitis is the fact that most affected patients respond to antiallergy therapy, whether it be swallowed inhaled corticosteroids or food elimination or elemental diets, Dr. Fleischer noted. ■

# *Create Individualized Elimination Diets for Eosinophilic Esophagitis*

BY BRUCE JANCIN
*Denver Bureau*

KEYSTONE, COLO. — Use of an elemental diet in patients with eosinophilic esophagitis is extremely effective—albeit draconian, disruptive, and seldom necessary, Dr. David M. Fleischer said at a meeting on allergy and respiratory disease sponsored by the National Jewish Medical and Research Center.

"We don't want to eliminate all foods, because it's hard on the patient. They're more likely to cheat on that diet," according to Dr. Fleischer, a pediatric allergist at the center.

"We don't usually put patients on an elemental diet, because we want them to be able to eat other foods. So we spend the time to find out what foods they can't eat and take them out of the diet," he said.

He and his colleagues rely on skin prick testing and radioallergosorbent tests for meats, grains, eggs, and a limited number of the other major food antigens in constructing individualized elimination diets. Patch testing is utilized at some other centers. The reliability of all of these tests is questionable; results need to be correlated with clinical findings.

"It's more of an art than a science. It can be complicated to figure out what the offending foods are," he conceded.

That being said, modern elemental formula liquid diets don't taste as bad as they used to, and they are nutritionally fairly complete, needing only supplemental calcium and a few other nutrients for long-term use, Dr. Fleischer continued.

Multiple studies demonstrate that the use of an elemental diet in children with eosinophilic esophagitis is effective in 92%-98% of cases. Symptoms resolve in 7-10 days. The esophageal eosinophilia drops from the 15 or more cells per high-power field (HPF) required for the diagnosis to zero cells or close to it in 4-5 weeks.

Elimination diets guided by allergy testing are often nearly as effective.

A low-cost, no-hassle alternative elimination diet has been described by pediatric gastroenterologist Dr. Amir Kagalwalla and coworkers at Northwestern University, Chicago. They dispensed with allergy testing and instead simply removed six of the most common allergenic foods from the diets of 35 children with eosinophilic esophagitis. The excluded foods were milk, soy, wheat, egg, peanut, and seafood.

Upon repeat esophageal biopsy at least 6 weeks later, esophageal inflammation was significantly improved to 10 or fewer eosinophils/HPF in 26 of the 35 children (74%). From a mean baseline of 80 cells, the post-treatment average fell to 13.6 eosinophils/HPF. The histologic response was associated with clinical improvement (Clin. Gastroenterol. Hepatol. 2006;4:1097-102).

But the on-treatment eosinophil count achieved with this approach remained well above normal. That makes Dr. Fleischer uneasy. "We don't know what it means long term. Will it prevent esophageal strictures?" he wondered.

As part of the same retrospective observational study, Dr. Kagalwalla and colleagues assigned 25 children to a liquid elemental diet. Esophageal eosinophilia dropped from a mean baseline of 59 cells/HPF to 3.7 cells/HPF. Of the 25 treated patients, 22 (88%) experienced a significant reduction in esophageal inflammation as defined by a reduction to not more than 10 eosinophils/HPF.

Most patients with eosinophilic esophagitis also respond to antiallergy medication. For example, having patients swallow inhaled corticosteroids so the topical medication coats the esophagus quells their esophageal inflammation. When the regimen is stopped, however, the eosinophilic esophagitis returns. ■

# Potential Pouchitis Tx Wins Orphan Drug Status

BY SHERRY BOSCHERT
*San Francisco Bureau*

SAN FRANCISCO — A clinical phase II/III trial of a potential oral medication for pouchitis will begin this year, following a Food and Drug Administration decision to grant orphan drug status to the experimental compound AST-120.

There are no approved treatments for pouchitis, a problem seen in approximately half of patients who undergo a colectomy and surgical creation of a j-pouch to treat ulcerative colitis. The pouch becomes inflamed and is associated with frequent and severe diarrhea, abdominal cramps, fever, and dehydration.

**AST-120 is also being studied for the treatment of Crohn's disease, fistulizing Crohn's disease, and other GI diseases.**

**DR. FISCHER**

Pouchitis affects fewer than 100,000 patients in the United States, allowing AST-120 to earn its orphan drug status, which is designed to encourage companies to develop medicines for rare diseases. Orphan drug status grants 7 years of exclusive rights to the market of the drug, among other benefits.

Ocera Therapeutics also is conducting studies of AST-120 for the treatment of Crohn's disease, fistulizing Crohn's disease, and other GI diseases, Dr. Laurent Fischer said at a JP Morgan Healthcare conference. Dr. Fischer is president and CEO of the San Diego–based company, which licensed AST-120 from its Japanese developers.

The first 10 patients with pouchitis in an open-label proof-of-concept trial showed significant improvements after 4 weeks of taking 2-g sachets of AST-120 t.i.d., he said. Nine patients completed therapy and one dropped out because of an upper respiratory tract infection. Four patients had complete remission, and five had a clinical response.

AST-120 is an oral spherical adsorptive carbon that may adsorb bile acids and bacterial toxins associated with pouchitis, potentially protecting the intestinal mucosa of the j-pouch from inflammation. AST-120 does not absorb vitamins and digestive enzymes, and is not itself systemically absorbed in the GI tract.

The drug is marketed in Japan as a treatment to delay the time to dialysis and to decrease uremic symptoms in patients with chronic renal failure. AST-120 has been studied in Japan for the treatment of Crohn's disease in more than 2,600 patients, and appears to have a good safety profile, Dr. Fischer said.

A separate, ongoing phase III study in the United States of AST-120 to treat fistulizing Crohn's disease may produce results in time for presentation at the Digestive Disease Week conference in May, he added. ■