Eosinophilic Gastrointestinal Disorders

by Loretta Jay

ALLERGY
DIGESTIVE

Jack didn't sleep more than ten minutes at a time during his first eight months of life. He cried constantly until he was two and his screams led his grandmother to refer to him as the 'baby from hell'. Horrible eczema covered his arms, neck and face; his face oozed puss.

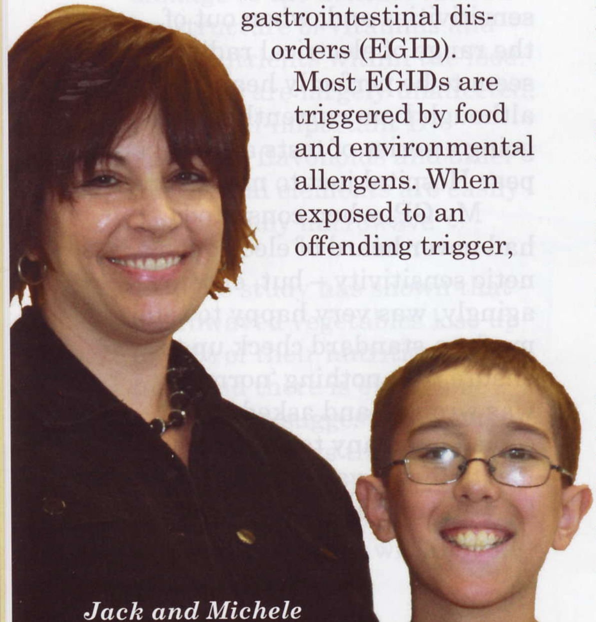
Michele Friedman, Jack's mother, was a practicing psychotherapist. A new mother, but seasoned in life, her gut told her that there was something terribly wrong – that his screams were provoked by pain.

Jack's doctors didn't support this theory, maintaining that he was simply colicky. Even her suggestion that Jack's diet could be the cause was rebuffed. It wasn't until his second anaphylactic reaction, at two years of age, that Jack tested positive for the top eight food allergens, as well as apples and melons. Jack was hurting, and food allergies were responsible.

An increasing number of people are experiencing numerous food allergies: not just nuts and milk or eggs, but many other foods as well.

Some of these people have something called eosinophilic gastrointestinal disorders (EGID).

Most EGIDs are triggered by food and environmental allergens. When exposed to an offending trigger, symptoms resemble gastroesophageal reflux disease (GERD) and irritable bowel syndrome (IBS). Other symptoms include vomiting in children or food impaction in adults.



Jack and Michele

Pathologically, white blood cells called eosinophils develop in the gastrointestinal tract indicating a problem. If eosinophils are present in the esophagus the disease is called eosinophilic esophagitis (EE). Eosinophils in the stomach is called eosinophilic gastritis (EG), and if they permeated the large intestine, eosinophilic colitis (EC). Finally, if eosinophils affect the stomach and/or the small intestine it is called eosinophilic gastroenteritis and eosinophilic enteritis.

EGIDs are a new disease, first identified in the 1970s, and formally recognised only 20 years ago. At that time they were thought to be extremely rare, only affecting one in 20,000-100,000. The diagnosis rate has steadily increased, with EE now affecting one in 2,500 children and adults. It remains unclear whether a growing awareness of the disease is affecting the rate of diagnosis, or if there is an actual increase in the number of people with the disorder.

Symptoms

The varied presentation of symptoms can make it challenging to identify and categorise EGIDs. Symptoms affect different people in different ways.

Jack has anaphylactic reactions to peanuts, eggs, shellfish and garlic. Other foods, including wheat, dairy, chicken and beef give him stomach aches, headaches, vomiting, sore throat, trouble swallowing and gagging. Like many other people with EGIDs, Jack also experiences asthma, eczema and rhinitis symptoms.

Most children experience heartburn and regurgitation and other reflux symptoms that may not resolve completely with acid blocking medications (ie Lansoprazole, Esomeprazole).

Young children who are unable to express how they are feeling may resist eating or refuse food altogether. Nausea, vomiting and stomach aches are also common, as is difficulty swallowing or food getting stuck in the esophagus.

Dysphagia (difficulty swallowing) and food impaction are the most common symptoms for adults with EE.

The Center for Pediatric Eosinophilic Disorders at the Children's Hospital of Philadelphia (CHOP) has the largest number of clinical patients with EE in the world. Dr Chris Liacouras, the co-Director at CHOP's Eosinophilic clinic, said that physicians are beginning to see the same symptoms for children and adults. Varied symptoms are now being recognised in different age groups and therefore diagnosed more readily across the spectrum.

Diagnosis

A diagnosis of an eosinophilic disorder requires a physician's confirmation of the symptoms, coupled with an analysis of biopsies taken during an endoscopy. Scoping, as the endoscopy is referred to informally, is performed when a gastroenterologist puts an endoscope (a thin tube with a video camera at the end), through the person's mouth and into the targeted GI area; the patient is sedated during the procedure. Tissue samples, or biopsies, are taken of the different parts of the GI tract. Although a normal esophagus has no eosinophils, the American Gastroenterological Association's consensus recommendation concluded that 15 eosinophils per high powered field is the current criterion for an eosinophilic diagnosis. (*Gastroenterology, 2007;133:1342-1363.*) A few eosinophils may be present with untreated reflux, so patients are typically placed on a reflux medication prior to the scope, to avoid any confusion with GERD.

Eosinophilic food allergies may be IgE-mediated, causing an immediate and sometimes anaphylactic reaction. They may also be cell mediated, resulting in a delayed hypersensitivity. One study (*Assa'ad et al, Journal of Allergy and Clinical Immunology, 2007; 119: 3,731-738*) found a nearly three-year lag between the onset of symptoms and the first endoscopy. The researchers interpreted this to mean that it wasn't the severity of the symptoms that led to the scoping, but their duration.

Some people are able to figure out what foods trigger a reaction for them, and modify their diet on their own – without securing a diagnosis. Dr Liacouras explained that if someone is experiencing EGID, it is important to obtain an accurate diagnosis, and not self-manage by restricting one's diet. For example, he said that about 50% of those with EG have an autoimmune problem, which means that their antibodies are attacking their own body in an attempt to rid it of the toxin. Others may have internal tissue damage due to unknown allergens without any overt symptoms.

If the eosinophilic disorder is identified early, Dr Liacouras believes that the likelihood of long-term problems, such as strictures or morbidity is low. One quarter of those affected have intermittent symptoms, another quarter have long-term or exasperated symptoms, and the rest fall somewhere in between.

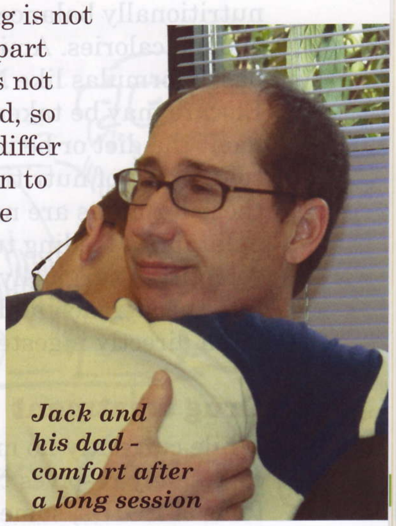
Recurrence

EGIDs are chronic, although patients' state may fluctuate: sometimes they are stable and other times not. A recurrence is defined as the reappearance of symptoms and eosinophils in a patient who was previously stable, with a restricted diet under control and no eosinophilic infiltration apparent in the affected area of the gastrointestinal tract. When this occurs, the cause, or new allergens, must be identified and eliminated. In a patient who is unable to resolve the presentation of symptoms the disease is considered persistent.

Treatment

Because EGIDs affect the gastrointestinal system, but are typically mediated by allergy, they are dually managed by an allergist and a gastroenterologist. The general treatment for EGIDs is removing the offending foods from one's diet. Frequently the challenge is figuring out what the offending foods are.

Skin prick tests are a fairly common method used to identify allergens. Many people don't have an immediate reaction to an allergen, and don't test positive with skin prick testing (SPT). Some eosinophilic research centers in the US are now using atopy patch testing (APT). APT was initially used in Europe for patients with eczema. Spergel et al (*Allergy Asthma Immunology 2005; 95:336-343*) found that 77% of EE patients improved after six weeks on a restricted diet when patch testing was used in conjunction with SPT to determine what the allergens were. Despite this favourable response, Dr Liacouras explained that patch testing is not reliable, in part because it is not standardised, so the results differ from location to location. The testing is conducted by mixing commercially available food product (milk, dried whole egg powder, tomato, corn, etc) with saline to make a paste. After mixing, the food paste is applied to the skin of the upper back and removed and scored between 48 to 72 hours.


Jack and his dad - comfort after a long session

Allergen prevalence

The children in Assa'ad et al's 2007 study had as many as 62 food allergens and 11 indoor and outdoor environmental allergens, as identified by SPTs. With so many potential allergens, trial and error is not a realistic method to figure out the problematic foods. It is hoped that in three to five years APT will be commercially manufactured so that its results will be consistent and it can be widely used.

While some people with EGIDs have many allergens, others may have only one or two. If testing is not conclusive, other methods to identify the allergens are needed. One such method is an elimination diet, where the patient's food intake is limited to five or six foods. Very gradually, one food at a time is introduced. After each food introduction the patient is scoped, to check for eosinophils.

Depending on the number of determined allergens, a patient's diet may be severely restricted and he may have a difficult time getting a

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nutritionally balanced diet, or enough calories. Amino-acid based formulas like Neocate or Elecare may be taken to supplement the diet or be used as a sole source of nutrition. Since these formulas are not very palatable a feeding tube is sometimes surgically implanted into the stomach and the formula directly ingested.

Drug treatment

While currently no medication completely resolves the symptoms of EGIDs, some drugs do help. Antacids and proton pump inhibitors that treat GERD alleviate some symptoms. Systemic (prednisone) and topical (inhaled through a metered dose) corticosteroids have resolved acute symptoms of EE, but when the medication is discontinued the disease's signs return. (*Gastroenterology, 2007*)

Jack, now a charming 12 year old boy, is an articulate and animated speaker. During the interview for this article he conveyed a positive outlook toward the bi-monthly endoscopies. Jack is clearly a partner in the team made up of his family and physicians. He is currently on a trial of an intranasal corticosteroid; he'll be scoped again to determine if the medication alleviated his symptoms presumably caused by environmental allergens. After the medication's effectiveness is determined, a food challenge is planned: apples. Six to eight weeks eating apples and he'll be scoped again.

Support

The emotional toll of EGIDs on a patient and his or her family is great. It is tough for someone to manage one or two food allergies. Challenges increase with each additional forbidden food. Creativity in the kitchen is a must, as is support from friends and family. Fortunately, today there are support groups, chat rooms and a gradual increase in awareness.

Beth Mays knows how important support and awareness are. When her son, Charlie, was diagnosed with EG his doctor told her there was nothing credible to be gained from consulting the Internet. Beth took the challenge and in 2001 she founded the **American Partnership for Eosinophilic Disorders (APFED)**.

Now with 875 members from more than 10 countries, the organisation provides accurate information to members, advocates for education and awareness of EGIDs, and raises money for research. APFED's website receives 1,500 hits a day and its 400 pages translate into 14 languages.

APFED successfully sought legislation to declare the third week of May National Eosinophilic Awareness Week in the USA. The group was the driving force behind the currently pending proposal in the United States to develop unique ICD-9 codes for EGIDs. Dedicated ICD-9 codes allow physicians to standardise patient diagnosis. This information greatly enhances re searchers ability to classify, track and report patients with EGIDs, and consequently to develop new treatments and improve awareness.

Research

Disbelief that there was no cure for the disease that was affecting her daughter, Ellyn Kodroff was driven to establish the **Campaign Urging Research for Eosinophilic Diseases** (CURED) in 2004. CURED recently raised over $600,000 USD, all earmarked for research. Cincinnati Children's Hospital Medical Center, a recipient of some of these funds, will pursue the identification of eosinophilic markers in the digestive system; their goal is to support diagnosis via blood work instead of an endoscopy.

Dr Liacouras said that researchers continue to explore whether those with eosinophilic disorders are predisposed genetically, if there is a trigger that causes the disorder to kick into gear or if people are born with the disease. The disease's progression is also being explored, including tissue changes such as fibrosis (scar tissue formation). Medications to treat the effects, such as anti-IL5, are also on the horizon. Researchers in Australia have been involved with clinical research for several years, and in Italy, Spain and England they are just starting to get interested. With growing interest in EGID, those on the forefront of the disease are optimistic that the research and increased awareness will yield positive results.

Support groups

APFED - Support, awareness, education, research, chat room
www.apfed.org

CURED
Research and awareness
www.curedfoundation.org

FABED
Support, awareness, chat room for families in the UK
www.fabed.co.uk

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