

# Eosinophilic Gastrointestinal Disease

Patient Information



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# Essays on Gastrointestinal Physiology

# Eosinophilic Gastrointestinal Disease

Eosinophils (e-o-sin-o-fills) are a type of white blood cell that circulate in the blood and are a normal part of the immune system. When triggered by allergies or infection, eosinophils increase in number and become active. In the short-term, this response is important and effective in clearing the body of pathogens. Certain tissues and organs throughout the body are accustomed to eosinophils, including some parts of the GI tract. However, a disease state can occur when eosinophils are present in areas where they don't normally occur on an ongoing basis, resulting in chronic inflammation. This prolonged tissue infiltration and inflammation can ultimately affect the function of that organ.

In recent years, physicians have been diagnosing a rare condition of unknown cause, called eosinophilic gastrointestinal disease (EGID), with increasing frequency in children and adults. EGID is characterized by chronic inflammation in the gastrointestinal (GI) tract caused by a higher than normal number of eosinophils without evidence of other causes (e.g., infections, allergy).

Physicians classify the disease according to the body tissue where the eosinophils accumulate. Each type of the disease requires monitoring. There is currently no cure for EGID.

- **Eosinophilic esophagitis (EoE)** is the most common type of EGID, in which large numbers of eosinophils are found in the esophagus, where normally there are no eosinophils. The esophagus is the tube that carries food from the mouth to the stomach.
- **Eosinophilic gastroenteritis (EG)** affects the stomach and/or the small intestine.
- **Eosinophilic colitis (EC)** is the rarest form of the disease and describes the occurrence of high levels of eosinophils in the large intestine.

EGID can affect people of all ages and ethnic backgrounds, although there appears to be sex and genetic factors associated with the disease. Research has found that 75% of individuals with EoE are male and 70-80% have associated allergic disorders such as asthma, eczema, and seasonal and/or food allergies. Most of the literature is based on EoE and the evidence base for interventions for EG and/or EC is poor and often adapted from EoE studies.

## **Symptoms/Diagnosis**

With eosinophilic esophagitis (EoE), the symptoms vary for each person and can include difficulty swallowing solids (often meats, rice, drier foods like bread), a feeling of food getting stuck after eating, vomiting, reflux, and abdominal and/or chest pain. More subtle symptoms include eating slowly, chewing excessively, and drinking water or other fluids through the meal to help you swallow the bites of food. Younger children may present with poor growth, vomiting, food refusal and difficulties transitioning to more solid foods.

Symptoms of EG are even more non-specific but may include diarrhea, swelling (edema), and or iron deficiency anemia. Symptoms of EC typically involve bloody stools and diarrhea.

Unfortunately, many individuals with EGID can go for years without a proper diagnosis, as the symptoms of EoE are similar to other well-known GI diseases such as gastroesophageal reflux disease (GERD) and the symptoms of EG and EC are similar to Crohn's disease,



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ulcerative colitis, and celiac disease. EGID is a relatively newer condition that has less general awareness and the diagnosis is not always straight forward. You should not initiate treatment prior to consultation with a gastroenterologist, who can diagnose these conditions.

At present, the only way to diagnose EGID is through biopsies from an endoscopy and/or colonoscopy. During an endoscopy, a physician inserts a flexible tube with a light and a tiny camera at the end (an endoscope) through the mouth to examine the esophagus, stomach, and first part of the small intestine. For a colonoscopy, a physician uses a long, flexible tube (a colonoscope) inserted via the anus to view inside the colon. For a biopsy, the physician extracts a tiny piece of tissue for examination under a high-powered microscope. A pathologist reviewing biopsy samples will look for characteristic features of EGID but will also count the number of eosinophils. The combination of relevant symptoms and a high eosinophil count will lead to a diagnosis of EGID.

## **Treatment**

Treatment will vary depending on the part of the GI system affected, but typically includes medication and adjustments to diet after a comprehensive review with your gastroenterologist. The multidisciplinary input of a dietitian and allergist (if you suffer from allergies) can be helpful. The goal of treatment is to reduce your symptoms as well as demonstrate improved histology, which means a reduction and ideally an elimination of the amount of eosinophils in the affected tissue. The treatments do have to be individualized, as what works for one person may not work for the next.

## **Dietary Therapy**

Dietary therapy is one of the primary treatment methods. These can be effective whether or not you have a previously diagnosed allergic type condition.

While not intuitive, eliminating the most common food allergens is more effective than getting testing and removing foods based on the testing (called targeted elimination). The main reason for this is the testing used is designed for identifying immediate allergic reactions, but symptoms in EGID are caused by long-term exposure to a trigger.

A variety of dietary therapy options are available. There are six food categories that make up the most common allergens: dairy, wheat, eggs, soy, peanuts/nuts, and fish/shellfish.

Previous recommendations involved removing all six food groups and adding back foods stepwise if the diet is effective (after biopsy review), but evidence shows that starting with fewer may be sufficient and more sustainable. However, it is important to note that you must eliminate the foods for quite some time, typically 8 weeks, to know whether or not it is effective. Some sets eliminate single food groups such as dairy, or wheat as the first intervention. Another approach has been called the 2-4-6 step-up elimination diet. Step-up therapy involves removing the two most allergenic foods (dairy and wheat), then, if that is not sufficient, removing the four most allergenic (dairy, wheat, eggs, and soy), and if that is still not providing relief, removing all six.

While there isn't a perfect way to do the eliminations, trial of food elimination followed by endoscopy and biopsies are a must.

The most effective dietary approach is an elemental diet, which involves only drinking a specialized balanced formula that has no intact proteins. This option is restrictive and difficult to follow because it involves receiving nutrition from an amino acid formula instead of eating food. Most individuals would require a feeding tube, since most people do not like the taste of the formula. It is also extremely expensive. Elemental therapy is not meant to be a long-term treatment and is done under exceptional circumstances.

Although a dietary approach may be appealing because it potentially offers an effective treatment without medication, there are important factors, such as affordability and cost, which those affected by EGID need to consider. Physicians do not recommend eliminating foods beyond the six food groups stated above, as this could result in poor nutrition. Being unable to afford to see a dietitian, or having to pay for the elemental diet formula, might be financially difficult, depending on your healthcare plan.

Dietitian counselling services in Canada can quickly become a huge cost to individuals who need ongoing advice. As the number of individuals with this disease continues to increase, it will be important to address

the access issues to publicly-funded dietitian support to ensure patients are receiving adequate nutrition. Provincial governments should also reconsider their eligibility criteria for public coverage of all medically therapeutic formulas, such as elemental formula. For example, individuals living in Ontario aren't eligible for this coverage if they are able to tolerate some solid food.

## **Medication**

There is currently no medication specifically approved by Health Canada for this disease. However, certain medications can reduce the number of eosinophils and improve symptoms.

For individuals with EoE, proton pump inhibitors (PPIs) such as omeprazole (Losec®), lansoprazole (Prevacid®), pantoprazole sodium (Pantoloc®), esomeprazole (Nexium®), rabeprazole (Pariet®), pantoprazole magnesium (Tecta®), and dexlansoprazole (Dexilant®) might be effective. In the past, physicians used PPIs to exclude a diagnosis of EoE, as they thought that positive response to PPIs meant that symptoms were a result of gastroesophageal reflux disease (GERD) rather than EoE. However, new research shows that PPIs might also treat EoE. There are multiple potential mechanisms for this, including anti-inflammatory effects from PPIs or reduced esophageal damage in those who have both GERD and EoE.

Swallowed (topical) steroids, have been borrowed from approved asthma treatments, and adjusted to deliver to the GI tract to treat EGID. These are swallowed instead of taken through inhalation. Different forms of topical steroids are available, including fluticasone (Flovent®) and budesonide (Pulmicort®). Individuals administer fluticasone via a metered-dose inhaler, by puffing the medication into the mouth and then swallowing. For those using budesonide, a pharmacist can mix it for you, otherwise you can mix it at home. Typically, you open a small, sealed container (ampoule) of the drug and mix it with multiple packages of a sugar substitute, such as Splenda®, and then swallow it. Alternatives to Splenda® have been demonstrated helpful, including Neocate® Nutra, a hypoallergenic nutritional supplement more commonly found in food products such as apple sauce, honey, or maple syrup.

Oral thrush is a common side effect of swallowed



corticosteroids so it is best to rinse your mouth and spit after taking your medication. For the medication to have greatest effect, it is important to not eat or drink for at least half an hour after taking the medication.

Oral steroids, such as prednisone, can successfully reduce the number of eosinophils. However, there are concerns with this type of non-targeted medication and its widespread side-effects, including immunosuppression. They should only be used for short periods of time if you are not responding to other treatments and your symptoms are severe.

Other medications that have been less studied, such as anti-histamines (e.g., ketotifen), which are used frequently for conditions such as hay fever, asthma, and eczema, have also been used to help relieve the symptoms of EGID by stopping the body from reacting to allergens.

Whether an individual is able to control the disease through diet and/or medication, it is important to note that symptoms frequently return after discontinuing treatment. There is no right or wrong with regard to choosing medication vs. dietary elimination and your personal input is important.

## **Outlook**

Ongoing care for individuals with EGID is required, including the likelihood of additional endoscopies to assess how the digestive tract is responding to specific treatment. Untreated EGID may lead to malnutrition, poor growth, and anemia. In some individuals, EoE is complicated by the development of narrowing in the esophagus (strictures) that can cause further issues with swallowing and choking. It is not clear how long EoE has to exist before strictures form but generally it occurs gradually with years of uncontrolled inflammation.

The general principle is to control the inflammation to prevent complications such as strictures. If strictures are present and an individual has been on effective treatment (typically medication), esophageal dilation (stretching with balloon or dilator) may be indicated. It is important to keep in mind that dilation is not treating the underlying inflammatory condition but rather helps reduce symptoms and further risk of food impaction.



Looking forward, researchers are studying new potential treatments for EGID. Several biologics are underway with active clinical trials with results anticipated in the next couple of years. Dupilumab (Dupixent™) is a monoclonal antibody (biologic medication) that is currently in use to treat certain allergic diseases. Early research shows that this is a potential treatment option for EGID. Studies found that it was effective, well-tolerated, and might even improve esophageal function in those with EoE.

The long-term prognosis is unclear and there is much work required to find a cure, including plenty of research. We need increased awareness of this condition, which is still not common at the primary care level to get individuals diagnosed in a timely manner. Once diagnosed, Canadian guidance and recommendations regarding diagnostic and therapeutic algorithms both in children and in adults could be of great benefit, because every gastroenterologist should be competent in managing this condition.

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