

## Treatment of eosinophil associated gastrointestinal disorders: Now what? Is there a cure?

Treatment of eosinophilic disorders will vary based on the location of the eosinophils, severity of symptoms, and other medical problems the child / adult may have. In most cases, there is no 'cure' but dietary measures and medications can significantly improve symptoms and control the underlying eosinophilic disease. Your doctor will help guide you through the various treatment options to find a therapy that is best for you and your family. This review is intended solely to provide information on currently available therapies and is not a substitute for your physician's advice.

### Dietary Therapy

- **Elimination Diets**

Since EGID is commonly associated with allergies, your doctor may recommend testing for food allergies with [skin prick testing](#), [patch testing](#) or both. At least 50% of children with eosinophilic esophagitis (EE) will test positive to multiple foods on skin prick or patch testing. Seasonal symptoms may also occur in patients with EE, suggesting that environmental allergies may play a role. Patients with eosinophilic gastroenteritis can have an allergic component, but less likely than those with EE. Eosinophilic colitis is least likely to present with detectable IgE allergies but allergy testing may be recommended as well. Based on the results of these tests, an 'elimination' diet may or may not be recommended.

**'Elimination' diet means strictly avoiding all foods to which allergy testing was positive.**

While eliminating multiple foods from the diet may seem overwhelming at first, there are many resources available to help you. The Food Allergy & Anaphylaxis Network ([www.foodallergy.org](http://www.foodallergy.org)) offers recipes and information on hidden sources of allergens. Understanding 'hidden' sources of the foods you are to avoid is an important step. For instance, egg may be labeled in foods in more than a dozen different ways. It is very important that all potential sources of all positive foods be eliminated from the diet. Even small amounts of one positive food can be enough to trigger a reaction. Skin prick testing correlates best with immediate type allergies and patch testing best examines delayed type reactions that are thought to be a more common problem in EGID. However, neither test is perfect and false negatives (missed allergies on testing) do occur, which can result in 'failure' of the elimination diet. Please note the value of these tests is still under investigation.

- **Elemental diets**

Sometimes a stricter diet – **an elemental diet** – is needed. Skin and patch testing are used to guide elimination diets, but it only takes one false negative food for the diet to 'fail'. Elemental diets can help clarify if food is indeed the underlying cause of the EGID and allow healing to take place.

- **Elemental diet** means No protein, either in its whole or incomplete (pre-digested or hydrolyzed) form is allowed. Special elemental formulas are made of **amino acids** (the building blocks of proteins), fats, sugars, vitamins and minerals. Amino acids do not cause allergic reactions but whole or partial proteins can.
- Examples of these special **elemental formulas** include Neocate® and Elecare®. These formulas contain man-made (synthetic) amino acids

Some formulas are made from pre-digested (hydrolyzed) proteins. Generally, these are partially hydrolyzed casein or whey proteins (from cow's milk) and are considered easier to digest. While they are hypoallergenic, these formulas can trigger reactions in sensitive individuals. These 'hydrolyzed' elemental formulas are NOT appropriate for most people with EGID because they still contain partial proteins that can trigger a reaction. Nutramigen®, Profylac®, Alimentum®, and Progestimil®, are some examples of partially hydrolyzed formulas. Completely hydrolyzed formulas may be advertised as 'elemental' (Subdue®) but may not be appropriate for people with EGID.

Snacks made only with sugar, salt and artificial flavor may be allowed, including cotton candy, certain lollipops or popsicles. Permitted snacks may vary at different medical centers. Manufacturers may change ingredients, so always check labels, even if you have purchased the item previously. Always check with your doctor regarding exactly what you or your child may eat on an elemental diet. In some situations, even sugars and salts are to be avoided early in the elemental trial.

- Sticking to an elemental diet can be difficult for both children and adults. Many children who need to be on an elemental diet for a long period of time require a **feeding tube** placed in the stomach to get adequate calories and nutrition. More detailed information on feeding tubes can be found in the [“Living with tubes”](#) section.

While the majority of people with EGID have an allergic cause, some do not. The elemental diet can be helpful in sorting out if the symptoms and eosinophils are food-related.

- **Food trials**

Patients who respond favorably to an elemental diet or elimination diet with resolution of the eosinophilic disease may then undergo food trials. Typically, this involves adding back one pure food at a time, starting with those that tested negative (via allergy testing) and are least likely to cause a reaction. The foods may be added back every 1- 3 weeks with re-evaluation after several foods have been resumed. Specifics of food trials vary at different medical centers, so as always, it is best to check with your physician before starting a food trial.

## **Medications**

There are no medications to cure eosinophilic disorders. Medication may suppress eosinophils in the gastrointestinal tract and relieve symptoms of the disease. Not all types of eosinophilic diseases respond to the same treatment and different people with the same disease type may need very different medications. As always, it is important to work closely with your physician and use this information as a resource.

A team approach (doctors, patient, families, nutritionist, nurses, and others) is very important in developing an individualized treatment plan and an optimal result. Potential benefits versus side effects of all medications should be discussed with your health care provider.

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### **Medications known to be effective for eosinophilic disorders:**

- **Glucocorticoids (“Steroids”)**

Steroids are medications that fight (suppress) many types of inflammation. Steroids are not specific for suppressing eosinophils, although eosinophils are particularly sensitive to them. Steroids can be taken intravenously (IV), ingested orally (via a tube, if applicable), or given topically (inhalers). Systemic steroids, those that are absorbed into the bloodstream (oral or IV), are very effective for treating a number of eosinophilic disorders. Unfortunately, the disease may return when the steroids are stopped. For patients with small intestine and or colon involvement, Budesonide (Entocort®) allows delivery of the steroid to the small intestines and upper colon with less absorption (i.e fewer side effects) of the steroids.

### **Side Effects**

Steroids given systemically may have many harmful side effects when used for long periods of time.

Common side effects can include:

- fluid retention (swelling)
- increased appetite
- “moon-face”
- irritability

Serious, but less common, side effects include:

- osteoporosis (brittle bones from bone loss)
- infections
- adrenal insufficiency (body becomes unable to properly respond to illness or stress)
- avascular necrosis (collapse of the bones in a joint, usually the hip)
- stunted growth.

- **Topical Steroids**

Several studies have shown an improvement in both symptoms and eosinophil counts in children with eosinophilic esophagitis (EE) when topical steroids are given. Fluticasone propionate (Flovent®), an asthma inhaler, can be used in this manner. The fluticasone is sprayed in the mouth and then swallowed by the patient. Often the dosage required is higher than the dosage used in asthma. Budesonide mixed with a viscous solution also may be used to treat EE. Always discuss the potential risks and benefits of any therapy with your doctor. Although there is some concern of side effects with fluticasone, they are less problematic than with prednisone or other systemic steroids.

- Thrush (a Candida yeast infection of the mouth) is a potential complication of fluticasone or other topical steroids when used long-term. The esophagus can be affected as well.

Keeping the mouth clean and good dental hygiene are important to prevent thrush. Swallowed Flovent for EE should not be rinsed until 30 minutes after the final spray. Rinsing too soon may wash away the medication from the esophagus.

- **Other medications**

Some medications may improve symptoms in patients with EGID without improving the eosinophil numbers. These include the [leukotriene inhibitors](#). The one most commonly used in the United States is montelukast (Singulair®). These generally have few side effects. Their usefulness in treating EGID is very controversial and not agreed upon by the gastroenterology or allergy community.

Due to potential side effects with medications, dietary measures are the preferred treatment for EGID when effective and tolerated.

### **Treatment of associated illnesses**

Patients with EGID involving the upper GI tract (esophagus and stomach) may benefit from other medications to treat either the complications of EGID or commonly associated illnesses such as gastroesophageal reflux disease (GERD), delayed gastric emptying (gastroparesis), asthma, and environmental/seasonal allergies.

- **Reflux** is a common symptom in people with EE or EGE. The two most common categories of medicine to treat reflux (when acid goes from the stomach back up the esophagus) are H2-blockers and proton pump inhibitors (PPI). H2 – blockers suppress, but do not completely eliminate, stomach acid. PPIs eliminate acid where it is produced in the stomach.

Examples of H2 blockers include Tagamet® (Cimetidine), Zantac® (ranitidine), Pepcid® (famotidine), Axid® (nizatidine) and others. Examples of PPIs include Prilosec® (omeprazole), Prevacid® (lansoprazole), Protonix® (pantoprazole), Aciphex® (rabeprazole), and Nexium® (esomeprazole). PPIs may cause diarrhea in some individuals. Drug interactions with other prescription medications can occur with both the H2 blockers and the PPIs. Consult your physician about potential medication interactions.

- **Gastroparesis** (delayed or slow emptying of the stomach) or severe reflux may be treated with the anti-nausea medication Reglan® (metoclopramide) or with the antibiotic erythromycin (stimulates the stomach to empty). These medications can produce diarrhea and may interact adversely with other medications.
- **Asthma, environmental allergies or eczema** are also common in individuals with eosinophilic disorders. Treating other allergic disorders is important in controlling EGID

Commonly used asthma medications include the beta-agonists (albuterol, levalbuterol, metaproterenol, pirbuterol), leukotriene inhibitors (Singulair® and Accolate®) and steroid inhalers (Flovent®, Pulmicort®, QVAR®, Advair®, Asmanex®). More severe forms of asthma may require nebulizers (mist) or oral steroids (such as prednisone) to control the disease. [Antihistamines](#) (H1- blockers like diphenhydramine, Claritin®, Zyrtec® and Allegra®) and nasal steroids are an important adjunct to treating seasonal or environmental allergies.

### **Future Directions**

Therapies in development for treatment of eosinophilic disorders are directed at reducing the production or stimuli that attract the eosinophils. These include:

- IL(interleukin)-5 inhibitors
- anti-eotaxin
- CCR3 (chemokine receptor) antagonists

- For those with allergic IgE disorders, medications that block IgE (Xolair® or Omalizumab) are being studied.

Links to [ongoing clinical trials](#) can be found in the ‘clinical trials’ section.

### **Medications used for autoimmune diseases or other types of inflammatory bowel disease**

We have included this section because on rare occasion, some physicians may prescribe medications that are typically used for inflammatory bowel disease (IBD), such as [Crohn’s disease](#) and [ulcerative colitis](#) (UC), to treat EGE or eosinophilic colitis. Crohn’s disease and ulcerative colitis are autoimmune diseases in which the body’s immune system attacks and injures the small bowel (upper intestines) and colon (lower intestines). These diseases share some similarities with the immune types (non-allergic) of eosinophilic colitis (EC) and eosinophilic gastroenteritis (EGE). The benefits of Crohn’s and UC medications for treating people who have EGE/EC are not known. As with all treatments, the potential benefits of therapy must be weighed against the potential risks and toxicity.

**Your doctor can best help you make individual decisions.** The following descriptions serve merely as a guide and source of information.

#### **Anti-inflammatory medications**

- Asacol is used for mild to moderate ulcerative colitis and for maintenance of remission in both Crohn’s disease and UC. It is available as a tablet, enema and a suppository. Asacol contains mesalamine and sulfapyridine components. It can cause hypersensitivity (allergic) reactions in the intestines, lungs or other parts of the body.
- Gastrocrom®, Sodium cromoglycate (SCG) or Cromolyn sodium are anti-inflammatory medications. They are non- absorbable mast cell stabilizers (prevent release of histamine and leukotrienes). They may benefit some patients with active ulcerative colitis but are of limited benefit. Gastrocrom is commonly prescribed in adults and may not be completely beneficial.

#### **Immunosuppressive medications**

These medications suppress the immune system and are used for autoimmune diseases or prevention of rejection in solid organ transplant recipients. Close monitoring is essential, as side effects can be significant.

- Azathioprine (AZA) and 6-mercaptopurine (6-MP)
- Methotrexate
- Cellcept® (Mycophenolate mofetil or MMF)
- Calcineurin inhibitors include cyclosporine (Neoral®, Sandimmune®, Gengraf®) and tacrolimus (Prograf®).

These medications are described in more detail in the section on [Hypereosinophilic syndromes](#)

More detailed information on the treatment of Crohn’s and ulcerative colitis can be found on the CCFA website <http://www.cdfa.org/>

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APFED, Revised 3-22-06, Author: Wendy Book, [mail@apfed.org](mailto:mail@apfed.org)

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