Eosinophils are a type of white blood cell that are important to our immune system because they help us fight off certain types of infections. Many different problems can cause high numbers of eosinophils in the blood, including allergies (food and environmental), parasitic infections, and certain cancers (leukemia), to name a few.

**WHAT IS AN EOSINOPHIL?**

**WHAT CAUSES HES AND WHO IS AFFECTED?**

To date, there are five known categories or variants of HES:

- **Myeloproliferative HES (M-HES):** Accounts for an estimated 15% of all HES cases. This variant is most frequently associated with a genetic deletion causing the chromosomal rearrangement of two genes (PDGFRA and FIP1L1). M-HES is not inherited.
- **Lymphocytic HES (L-HES):** Accounts for approximately 10-15% of all HES cases. This variant is associated with an increase of clonal T cells that drive eosinophil production and become active.
- **Associated HES:** Accounts for approximately 10% of all HES cases. A secondary and treatable cause of the HES can be identified in this category.
- **Overlap HES:** Accounts for approximately 10-15% of all HES cases. This category includes disorders with single organ disease (e.g., EGID) or clinical overlap with HES (e.g., eosinophilic granulomatosis with polyangiitis).
- **Idiopathic HES (I-HES):** Approximately 50% of estimated prevalence is considered idiopathic. This category does not have a defined cause.

Both men and women may be affected by HES, although the disease is most often seen in males ages 20-50. While it is more commonly diagnosed in adulthood, it has also been diagnosed in children.

U.S. prevalence estimates range widely, from 1,000-20,000 people affected. In 2004, the European Medicines Agency estimated the prevalence of HES to be 1.5 in 100,000 people, which extrapolates to 5,000 people in the U.S. Since this estimate was made, the definition of HES has changed, therefore the current prevalence is not known.

**WHAT IS HYPEREOSINOPHILIC SYNDROME (HES)?**

Hypereosinophilic Syndrome (HES) is a group of rare disorders in which high numbers of eosinophils are found in the blood and tissue and cause clinical symptoms.

While most people have blood eosinophil levels of less than 500/microliter, those with HES typically have levels of greater than 1,500/microliter. Having a continuously high number of eosinophils in the blood can result in tissue inflammation and progressive organ damage.

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WHAT ARE THE SYMPTOMS OF HES?

The symptoms of HES vary widely, depending on the part of the body that is affected. Symptoms may include:

- Dizziness
- Memory loss or confusion
- Wheezing
- Abdominal pain, nausea/vomiting
- Fever
- Fatigue
- Coughing
- Mouth sores
- Chest tightness
- Shortness of breath/difficulty breathing
- Skin rashes

The nature and severity of the symptoms can vary widely among patients, and even within the course of an individual’s life.

The symptoms of HES are also common in many other medical problems (e.g., autoimmune diseases, allergic disease, cancer, drug reactions), making HES difficult to diagnose.

HOW IS HES DIAGNOSED?

Many different problems can cause high numbers of eosinophils in the blood; therefore, a higher than normal blood eosinophil number alone does not mean an individual has, or will develop, HES.

Tests needed to diagnose HES include:

- Complete blood cell count (including eosinophil count)
- Blood samples for liver and kidney function
- Blood tests for Vitamin B12 and tryptase
- Bone marrow biopsy
- Peripheral blood eosinophilia (high numbers of eosinophils in the blood, greater than 1,500/microliter)
- End-organ (e.g., heart, lungs, GI tract, brain, skin) involvement with eosinophil tissue infiltration (invasion) and injury
- Exclusion of other known causes for the eosinophilia, such as allergic reactions and certain bone marrow/blood diseases.

A bone marrow biopsy is also recommended, to measure eosinophil levels in the bone marrow. Depending on symptoms and test results, other studies (e.g., molecular and flow cytometric tests, ultrasound or echocardiography of the heart, chest x-ray or CT) may be performed.

HOW IS HES TREATED?

When treating HES, the goal is to reduce the eosinophils in the blood, prevent organ damage, and slow disease progression.

Treatments vary based on organs involved, disease severity, and other medical issues and may include:

- Corticosteroids (e.g., prednisone) are the current standard of care for HES. Most L-HES and I-HES patients can be maintained on oral corticosteroids for long periods of time with fairly good success. Corticosteroids fight inflammation and decrease the number of eosinophils. However, the eosinophils and symptoms generally return once steroids are stopped. Long-term steroid use (especially at doses greater than 10 mg/day) is associated with serious side effects such as adrenal insufficiency, avascular necrosis, osteoporosis, infections, and stunted growth.
- Interferon alpha (IFN-α) injections are used to suppress symptoms related to HES. Most patients experience flu-like symptoms from these injections (e.g., fever, chills) and therapy may need to be discontinued due to side effects.
- Cyclosporine suppresses the immune system. In some patients, there may be evidence that the immune cells have a role in supporting HES, and cyclosporine may have a role as a therapy.
- Anti-neoplastic agents or chemotherapy (e.g., chlorambucil, cladribine, cyclophosphamide, etoposide, hydroxyurea, methotrexate, vincristine) kill fast growing cells, such as eosinophils in HES. These therapies provide an alternative approach for severe/advanced cases of HES. These agents have potentially harmful side effects.
- Imatinib mesylate is a tyrosine kinase inhibitor for controlling malignant cell growth. M-HES is typically treated with imatinib. Approximately 10-20% of patients with M-HES have a genetic abnormality involving tyrosine kinase that causes their HES. Genetic testing can help determine if a patient might benefit from this therapy.
- Monoclonal antibody therapy involves lab-created antibodies that are designed to target and destroy specific cells. Mepolizumab and reslizumab are drugs that target interleukin-5, the major eosinophil-active cytokine. Alemtuzumab targets the CD52 molecule, an antigen that is found on the surface of many cells. Monoclonal antibody therapy may benefit some with HES, and is reserved for patients who do not respond to other treatments.

Improved treatment options for HES are an area of ongoing research. Recent research has identified a number of investigational drugs that block eosinophils. We are hopeful that the development of these drugs will lead to more treatment options for HES.

Dexprofospoxole is an oral drug recently shown to lower eosinophils and corticosteroid requirements in patients with HES. Further clinical studies of dexprofospoxole in HES are expected to begin in 2018.

LIVING WITH HES

Hyper eosinophilic syndrome is chronic and lifelong, but with proper ongoing care and treatment, you can lead a normal life. If you or someone you love is diagnosed with HES it is important to:

- Educate yourself. Visit apfed.org to learn more about HES, and access multimedia patient resources.
- Build a support system. Connect with others, ask for help, and learn from one another. To connect with other HES patients for peer-to-peer support, visit the HES board in APFED’s online support community.” EHS Connections” on the Inspire Network at apfed.inspire.com.
- Take care of yourself. Take some time each day to do something you really enjoy. If you feel up to it, and if your doctor agrees, start a mild exercise program, like walking or stretching.
- Focus on what you can control, not what you can’t. You may feel sad, anxious, or even angry about your disease. Acknowledging and expressing your feelings can help give you a sense of control.

WHAT IS THE PROGNOSIS?

HES can impact any organ in the body, including the stomach and intestines, the heart, lungs, skin, liver, spleen, and eyes. Some patients may have only one organ involved, while others may have more than one.

HES is debilitating and can be fatal if left untreated. The prognosis in HES depends on the organ systems affected, disease severity, and response to therapy. Your doctor can best answer questions about your specific prognosis.