About the Association

A Rare Community

The Histiocytosis Association is a global nonprofit organization dedicated to addressing the unique needs of patients and families dealing with the effects of histiocytic disorders while leading the search for a cure. It is the only organization of its kind, connecting the patient and medical communities to:

- Grow and share knowledge of histiocytic disorders
- Provide critical emotional and educational support to patients and families
- Identify and fund key research initiatives that will lead to a world free of histiocytic disorders

Partnership for a Cure

The Histiocytosis Association works closely with the Histiocyte Society, an international organization of over 240 physicians and researchers, which is dedicated to studying the histiocytic disorders. Through this partnership, understanding of this disease has greatly increased, and survival rates and quality of life continue to improve.

Community Outreach

While the search for more effective treatments and a cure continues, the Histiocytosis Association is dedicated to supporting and empowering the patients and families who live with these diseases every day.

Funding the Association

Histiocytic disorders are considered "orphan diseases." An orphan disease is one that affects less than 200,000 individuals in the United States.* Subsequently, these disorders do not receive a high priority for government-funded research. The Association relies on contributions from corporations, foundations and individual donors to fund critical research, build awareness and conduct community outreach initiatives.

**Rare Disease Act of 2002*

You are not Alone

While the search for more effective treatments, and ultimately a cure, continues, the Histiocytosis Association is dedicated to informing and empowering those who live with histiocytic diseases every day. Outreach initiatives for patients and families include:

- Educational materials and resources
- Peer support groups and an online virtual histio community
- A directory of physicians experienced in treating histiocytic disorders

The Histiocytosis Association invites you to become a part of our rare community. We encourage you to explore our online resources by visiting our website:

www.histio.org

Making a Donation

All donations are tax deductible (Federal Tax ID # 22-2827069). Visit www.histio.org/donate to join us in the pursuit of a cure.

HISTIOCYTOSIS ASSOCIATION
A Rare Community

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What is hemophagocytic lymphohistiocytosis?

Hemophagocytic lymphohistiocytosis (HLH) is a disorder of inflammation that was first thought to affect only young infants and children but is increasingly recognized in older children and adults. According to a large, population-based study from Sweden, it was estimated to occur in 1.2 cases per million children, corresponding to 1 in 50,000 births. However, this number is probably an underestimation as physicians appear to recognize HLH more readily now than when this was published decades ago. According to a large Japanese study, around 40% of cases occur in adults.

HLH occurs when the immune system is triggered (most often by a virus) and overreacts in specific ways that make the patient severely ill. Thus, HLH is best thought of as a problem of proper immune regulation. Poor immune regulation may be caused by genetic defects (called familial HLH, or FHL) or it may occur in patients with various infections, rheumatologic diseases, or cancers, for reasons that are not entirely understood (sometimes called secondary HLH). The HLH process is like a storm of inflammatory factors, called cytokines, which involves many organs and various immune cells (macrophages/ histiocytes and lymphocytes, the cells referred to in HLH's name).

How is HLH diagnosed?

It is sometimes difficult to establish the diagnosis of hemophagocytic lymphohistiocytosis (HLH), and the combination of the physical symptoms and certain laboratory tests is required. Therefore, the Histiocyte Society recommended a set of diagnostic criteria for use in the HLH-94 research protocol, revised for the HLH-2004 protocol. The criteria include diagnosis of a specific gene defect and/or the presence of at least five of the following eight criteria: **prolonged fever, blood cell abnormalities** (low white cells, low red cells, low platelets), **enlarged spleen**,**Increased triglycerides** (a type of fat in the blood) or **decreased fibrinogen** (protein necessary for clotting) in the blood,**increased ferritin** (a protein that stores iron and reflects the activation of macrophages) in the blood, **abnormal bone marrow test evidence of hemophagocytosis**, **abnormally high sCD25** (also known as sIL2ra) in the blood indicates abnormally increased T-Cell activation, **low or absent NK** (natural killer) **cell function**.

The test for low or absent natural killer cell (NK) function has been found useful in establishing a clinical diagnosis of HLH. This abnormality is found in many patients with FHL and many cases of secondary disease but rarely in X-linked forms. A newer test, called a degranulation or CD107 mobilization assay, appears to be more consistent and is replacing NK function in many practices. However, these tests are just one piece of information and the diagnosis requires a full clinical and laboratory pattern.

What are the symptoms of HLH?

Some symptoms of the primary and secondary forms of HLH include:*

- Persistent fever, often high
- Liver and spleen dysfunction
- Coordination problems
- Sudden blindness
- Enlarged lymph nodes
- Seizures, irritability and fatigue
- Immunologic dysfunction
- Skin rash
- Abdominal swelling

Combined with evidence of immunologic dysfunction:

- Decreased NK-cell function
- Increased histiocyte activation as evidenced by increased ferritin
- Increased T-cell activation as evidenced by increased sIL2ra (soluble IL-2 receptor alpha) in the blood

How is HLH treated?

Treatment of HLH/FHL can include a combination of chemotherapy, immunotherapy and steroids. Antibiotics and antiviral drugs may also be used. These treatments may be followed by a stem-cell transplant in patients with persistent or recurring HLH or those with FHL.

FHL when NOT treated is usually rapidly fatal. Treatment is intended to achieve stability of the disease symptoms so that a patient can then receive a stem-cell transplant, which is necessary for a cure.

**It should be emphasized that not all patients have all symptoms. A more detailed list is available at www.histio.org.*

To learn more about the Association and its Scientific Initiatives, Outreach Efforts and Research Program visit www.histio.org.

The Histiocytosis Association is dedicated to raising awareness about histiocytic disorders, providing educational and emotional support, and funding research leading to better treatments and a cure.

A world free of histiocytic disorders.

www.histio.org