familial hemophagocytic lymphohistiocytosis

Familial hemophagocytic lymphohistiocytosis is a disorder in which the immune system produces too many activated immune cells (lymphocytes) called T cells, natural killer cells, B cells, and macrophages (histiocytes). Excessive amounts of immune system proteins called cytokines are also produced. This overactivation of the immune system causes fever and damages the liver and spleen, resulting in enlargement of these organs.

Familial hemophagocytic lymphohistiocytosis also destroys blood-producing cells in the bone marrow, a process called hemophagocytosis. As a result, affected individuals have low numbers of red blood cells (anemia) and a reduction in the number of blood cells involved in clotting (platelets). A reduction in platelets may cause easy bruising and abnormal bleeding.

The brain may also be affected in familial hemophagocytic lymphohistiocytosis. As a result, affected individuals may experience irritability, delayed closure of the bones of the skull in infants, neck stiffness, abnormal muscle tone, impaired muscle coordination, paralysis, blindness, seizures, and coma. In addition to neurological problems, familial hemophagocytic lymphohistiocytosis can cause abnormalities of the heart, kidneys, and other organs and tissues. Affected individuals also have an increased risk of developing cancers of blood-forming cells (leukemia and lymphoma).

Signs and symptoms of familial hemophagocytic lymphohistiocytosis usually become apparent during infancy, although occasionally they appear later in life. They usually occur when the immune system launches an exaggerated response to an infection, but may also occur in the absence of infection. Without treatment, most people with familial hemophagocytic lymphohistiocytosis survive only a few months.

Frequency

Familial hemophagocytic lymphohistiocytosis occurs in approximately 1 in 50,000 individuals worldwide.

Genetic Changes

Familial hemophagocytic lymphohistiocytosis may be caused by mutations in any of several genes. These genes provide instructions for making proteins that help destroy or deactivate lymphocytes that are no longer needed. By controlling the number of activated lymphocytes, these genes help regulate immune system function.

Approximately 40 to 60 percent of cases of familial hemophagocytic lymphohistiocytosis are caused by mutations in the *PRF1* or *UNC13D* genes. Smaller numbers of cases are

caused by mutations in other known genes. In some affected individuals, the genetic cause of the disorder is unknown.

The gene mutations that cause familial hemophagocytic lymphohistiocytosis impair the body's ability to regulate the immune system. These changes result in the exaggerated immune response characteristic of this condition.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- familial erythrophagocytic lymphohistiocytosis
- familial hemophagocytic histiocytosis
- familial hemophagocytic lymphocytosis
- familial hemophagocytic reticulosis
- FEL
- FHL
- FHLH
- hemophagocytic syndrome
- HPLH
- primary hemophagocytic hymphohistiocytosis

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Familial hemophagocytic lymphohistiocytosis
https://www.ncbi.nlm.nih.gov/gtr/conditions/C0272199/
- Genetic Testing Registry: Hemophagocytic lymphohistiocytosis, familial, 2
https://www.ncbi.nlm.nih.gov/gtr/conditions/C1863727/
- Genetic Testing Registry: Hemophagocytic lymphohistiocytosis, familial, 3
https://www.ncbi.nlm.nih.gov/gtr/conditions/C1837174/
- Genetic Testing Registry: Hemophagocytic lymphohistiocytosis, familial, 4
https://www.ncbi.nlm.nih.gov/gtr/conditions/C1863728/
- Genetic Testing Registry: Hemophagocytic lymphohistiocytosis, familial, 5
https://www.ncbi.nlm.nih.gov/gtr/conditions/C2751293/

Other Diagnosis and Management Resources

- GeneReview: Hemophagocytic Lymphohistiocytosis, Familial
  https://www.ncbi.nlm.nih.gov/books/NBK1444
- The Merck Manual for Healthcare Professionals
  http://www.merckmanuals.com/professional/hematology-and-oncology/histiocytic-syndromes/hemophagocytic-lymphohistiocytosis-hlh
- University of Minnesota: Pediatric Blood & Marrow Transplantation Center
  https://bmt.umn.edu/hemophagocytic-lymphohistiocytosis

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Health Topic: Immune System and Disorders
  https://medlineplus.gov/immunesystemanddisorders.html

Genetic and Rare Diseases Information Center

- Hemophagocytic lymphohistiocytosis
  https://rarediseases.info.nih.gov/diseases/6589/hemophagocytic-lymphohistiocytosis

Educational Resources

- Disease InfoSearch: Hemophagocytic Lymphohistiocytosis (HLH)
  http://www.diseaseinfosearch.org/Hemophagocytic+Lymphohistiocytosis+%28HLH%29/3306
- MalaCards: hemophagocytic syndrome associated with an infection
  http://www.malacards.org/card/hemophagocytic_syndrome_associated_with_an_infection

- Orphanet: Familial hemophagocytic lymphohistiocytosis
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=540
- The Merck Manual for Healthcare Professionals
  http://www.merckmanuals.com/professional/hematology-and-oncology/histiocytic-syndromes/hemophagocytic-lymphohistiocytosis-hlh
- University of Minnesota: Pediatric Blood & Marrow Transplantation Center
  https://bmt.umn.edu/hemophagocytic-lymphohistiocytosis

Patient Support and Advocacy Resources

- Histiocytosis Association of America
  https://www.histio.org/sslpage.aspx?pid=387

GeneReviews

- Hemophagocytic Lymphohistiocytosis, Familial
  https://www.ncbi.nlm.nih.gov/books/NBK1444

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22familial+hemophagocytic+lymphohistiocytosis%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Lymphohistiocytosis,+Hemophagocytic%5BMAJR%5D%29+AND+%28familial+hemophagocytic+lymphohistiocytosis%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS, FAMILIAL, 1
  http://omim.org/entry/267700
- HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS, FAMILIAL, 2
  http://omim.org/entry/603553
- HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS, FAMILIAL, 3
  http://omim.org/entry/608898
- HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS, FAMILIAL, 4
  http://omim.org/entry/603552
- HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS, FAMILIAL, 5
  http://omim.org/entry/613101

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