CONDITION

Histiocytosis

Histiocytosis is a group of conditions in which certain immune cells build up and may damage tissues or organs.

WHAT IT IS
Group of conditions involving abnormal immune-cell accumulation

BODY SYSTEM
Bones, skin, lungs, glands, blood, and other organs

MAIN SYMPTOMS
Bone pain, skin rash, swollen nodes, excessive thirst

WHAT CAUSES IT
Acquired cell mutations, immune dysregulation, sometimes inherited defects

HOW IT IS DIAGNOSED
Tissue biopsy, blood tests, imaging, and genetic testing

MAIN TREATMENT
Observation, local treatment, medicines, or targeted therapy

CAN IT BE CURED?
Sometimes - localized forms may resolve or be removed

IS IT AN EMERGENCY?
Sometimes - severe breathing difficulty, seizures, or confusion

LONG-TERM OUTLOOK
Often good when localized; multisystem forms can be serious

Overview

Histiocytosis is the name for a group of rare conditions involving histiocytes. Histiocytes are immune cells that normally help fight infection, remove damaged material, and control inflammation.

In histiocytosis, these cells collect in tissues where they are not normally present in large numbers. The cells may form a lump or cause inflammation and tissue damage. One area may be affected, or the condition may involve several organs.

The main types include Langerhans cell histiocytosis, Erdheim-Chester disease, and Rosai-Dorfman-Destombes disease. Hemophagocytic lymphohistiocytosis, usually called HLH, is a related condition involving severe immune-system overactivity. These conditions have different causes, treatments, and likely courses.

Some forms are driven by acquired changes in genes that control cell growth. "Acquired" means the change developed in certain cells during life and is not usually passed from parent to child. Because of these changes, some types are classified as blood-cell growth disorders or cancers, although they may behave very differently from common cancers.

Histiocytosis matters because it can affect important structures, including the bones, lungs, brain, pituitary gland, liver, spleen, and blood-forming bone marrow. At the same time, some localized forms remain mild, resolve without treatment, or are removed successfully.

Symptoms

Symptoms depend on the type of histiocytosis and which tissues are involved. They can develop gradually or, less often, appear quickly.

Bone involvement may cause ongoing pain, tenderness, swelling, or a lump. A weakened bone can occasionally fracture. The skull, jaw, ribs, spine, pelvis, and long bones of the arms or legs may be affected.

Skin changes may include red, brown, yellow, or scaly patches. In babies, the rash can resemble cradle cap or severe nappy rash. Adults may notice persistent patches on the scalp, body folds, or genital area.

Other possible symptoms include:

Histiocytosis affecting the pituitary gland can reduce production of arginine vasopressin, a hormone that helps the body conserve water. This may cause extreme thirst and frequent urination, including during the night. Other pituitary hormones can also be affected, potentially changing growth, puberty, menstrual periods, sexual function, or energy levels.

HLH often causes a different pattern, with persistent fever, an enlarged liver or spleen, low blood-cell counts, and marked inflammation. It can become serious quickly and needs prompt specialist assessment.

These symptoms have many more common causes. Having one of them does not mean that you have histiocytosis.

- Swollen lymph nodes or painless lumps
- Fever, night sweats, tiredness, or unintended weight loss
- Persistent cough, chest discomfort, or shortness of breath
- Abdominal swelling, yellow skin or eyes, or easy bruising
- Ear discharge, hearing problems, or swelling around the eyes

- Poor balance, weakness, headaches, or changes in thinking

Causes and risk factors

There is no single cause of histiocytosis.

Many cases of Langerhans cell histiocytosis and Erdheim-Chester disease contain acquired changes in the MAPK pathway. This is a set of signals that tells cells when to grow and survive. Changes involving the BRAF gene are one example. These findings help explain why the abnormal histiocytes continue to collect and can help guide treatment.

These acquired changes are usually found only in affected cells. They are not caused by something a parent did, and they are generally not inherited by children.

Some forms of HLH are caused by inherited gene changes that prevent immune cells from switching off normally. Other cases of HLH are triggered by an infection, cancer, autoimmune condition, or certain medicines.

The clearest avoidable risk factor relates to pulmonary Langerhans cell histiocytosis, which affects the lungs and occurs mainly in adults who smoke cigarettes. Smoking does not explain most other forms of histiocytosis.

In many people, it is not possible to identify why the condition developed.

Diagnosis

Diagnosis usually begins with a medical history, physical examination, blood tests, and imaging. Imaging may include X-rays, ultrasound, CT, MRI, or PET scans, depending on the symptoms and suspected organs.

A biopsy is generally needed to confirm most forms. During a biopsy, a small sample of affected tissue is removed. A pathologist examines the cells under a microscope and uses special stains to identify their proteins. The pattern of cells and proteins helps distinguish one type of histiocytosis from another.

The tissue may also be tested for acquired gene changes, such as changes in BRAF or related genes. This can support the diagnosis and show whether targeted treatment may be useful.

Further tests assess how much of the body is involved. They may include:

HLH is diagnosed using a combination of symptoms and laboratory findings. No single biopsy result confirms every case. Testing may include blood counts, liver tests, triglycerides, fibrinogen, ferritin, immune-cell studies, bone marrow examination, and genetic testing.

Because histiocytosis can resemble infection, cancer, autoimmune conditions, or other inflammatory problems, diagnosis may take time and require review by more than one specialist.

- Blood counts and tests of liver, kidney, and inflammation markers
- Hormone tests, particularly when thirst, urination, growth, or sexual function changes
- Lung-function tests for breathing symptoms or lung findings
- Bone marrow sampling when blood-cell production may be affected
- Hearing, vision, heart, or nervous-system assessment when relevant

Treatment and management

Treatment is based on the specific type, the organs involved, the severity of tissue damage, and any gene changes found in the abnormal cells.

A small, localized area may only need monitoring. Some skin lesions disappear without treatment. A single bone lesion may be treated with a local procedure, such as a biopsy that removes much of it, limited surgery, or an injected medicine. Radiation is used only in selected situations.

When several sites or important organs are affected, treatment may involve medicines that work throughout the body. Options include chemotherapy, anti-inflammatory or immune-suppressing medicines, and targeted therapies. Targeted medicines block abnormal cell-growth signals, such as the BRAF or MEK parts of the MAPK pathway.

Treatment for lung Langerhans cell histiocytosis includes stopping smoking and monitoring lung function. Some people also need medicines, oxygen support, or evaluation for advanced lung treatment.

Severe HLH is treated by rapidly bringing the overactive immune response under control and treating any trigger. Selected people with inherited, persistent, or recurrent HLH may need a stem cell transplant.

Supportive care is also important. It can include hormone replacement for permanent pituitary problems, pain management, physical therapy, dental care, treatment for infections, and support with nutrition or fatigue.

Treatment decisions are often made by a team that may include blood, cancer, hormone, lung, skin, bone, or nervous-system specialists. Children are usually cared for by a pediatric specialist team.

Complications

Some histiocytosis lesions heal without lasting effects. Others can leave permanent tissue damage, especially when diagnosis or treatment occurs after an organ has already been injured.

Possible long-term complications include weak or deformed bones, scarring in the lungs or bile ducts, hearing loss, dental problems, and reduced kidney, heart, liver, or nervous-system function.

Pituitary damage can cause lasting hormone deficiencies. Extreme thirst and urination may continue even after other areas of histiocytosis become inactive. Hormone replacement and regular monitoring can control many of these effects.

Treatment itself can cause complications, including infection, low blood counts, fertility problems, nerve symptoms, or effects on organs. The risks are different for each treatment, so monitoring is tailored to the medicine being used.

A person who has had histiocytosis can occasionally develop new lesions after a period without active symptoms. Some types are also associated with other blood disorders or cancers. This is one reason routine long-term follow-up may continue even when treatment has finished.

Prevention

Most forms of histiocytosis cannot currently be prevented. Acquired cell changes usually happen without a known avoidable cause.

Not smoking can reduce the risk of pulmonary Langerhans cell histiocytosis. If you have this lung condition, stopping smoking may stabilize or improve it, although existing lung damage may not fully reverse. Avoiding secondhand smoke and inhaled substances may also help protect already affected lungs.

Inherited HLH cannot be prevented through lifestyle changes. When an inherited form is confirmed, genetic counselling can explain what the result may mean for biological relatives and future pregnancies. Genetic counselling provides information and choices; it does not require a particular decision.

Living with it and what to expect

The course of histiocytosis ranges from a single episode to a long-term condition requiring repeated treatment. The type and location matter more than the size of a visible skin patch or lump.

A localized skin or bone lesion may resolve, be removed, or remain stable. Some people never have another lesion. Others develop a recurrence in the same place or a different area and need further assessment.

Multisystem histiocytosis may become inactive after treatment, return later, or require ongoing therapy. Targeted treatments can control some mutation-driven forms for long periods, but stopping treatment may sometimes be followed by renewed activity.

Damage already caused to an organ may not improve when the active histiocytosis settles. Pituitary hormone deficiencies are often permanent. Bone pain, fatigue, breathing limits, or balance problems may also continue and need separate management.

Routine follow-up can include symptom reviews, examinations, blood tests, hormone testing, and imaging. The schedule is based on the type of histiocytosis, previous organ involvement, and treatment. New thirst, urination, bone pain, skin changes, or neurological symptoms should be reported rather than saved for a distant appointment.

Many people with localized or well-controlled histiocytosis continue work, education, exercise, and family life. Others need adjustments because of fatigue, pain, treatment visits, hormone replacement, or organ damage. The likely course cannot be predicted from the diagnosis name alone.

When to get medical help

Arrange a routine medical appointment if you have a persistent unexplained rash, lump, bone pain, cough, swollen lymph node, or marked increase in thirst and urination. These symptoms are not specific to histiocytosis, but they deserve assessment if they continue.

If you have diagnosed histiocytosis, contact your care team promptly about new or worsening symptoms. Same-day advice may be appropriate for jaundice, rapidly increasing swelling, severe bone pain, inability to bear weight, dehydration, or fever while taking treatment that weakens the immune system.

Seek emergency care for:

These signs do not always come from histiocytosis, but they require urgent assessment.

- Severe difficulty breathing or blue, grey, or unusually pale lips
- A seizure, fainting, or difficulty waking

- New weakness, loss of movement, or severe confusion
- Sudden severe headache with neurological changes
- Signs of severe dehydration, such as collapse or very little urine

Common questions

Is histiocytosis cancer?

Some forms, including Langerhans cell histiocytosis and Erdheim-Chester disease, are now considered abnormal blood-cell growth conditions because the cells often contain acquired growth-driving mutations. Other forms are more strongly inflammatory or immune-driven. The word "cancer" does not describe how every case will behave.

Is histiocytosis contagious?

No. You cannot catch histiocytosis from another person or pass it through everyday contact. Infections can trigger some cases of HLH, but HLH itself is not contagious.

Can histiocytosis go away on its own?

Some localized skin or bone forms can settle without major treatment. Multisystem disease and involvement of organs such as the liver, spleen, lungs, bone marrow, or brain are less likely to resolve safely without specialist care.

Can histiocytosis come back after treatment?

Yes. Recurrence is possible in the same tissue or elsewhere, even after a period with no active condition. The chance and timing differ by type, organ involvement, and response to treatment. Follow-up helps identify changes early.

Is histiocytosis inherited?

Most Langerhans cell histiocytosis, Erdheim-Chester disease, and Rosai-Dorfman-Destombes disease is not inherited. Some forms of HLH are caused by inherited gene changes. Genetic testing may be recommended when age, symptoms, or family history suggests this possibility.

How long can you live with histiocytosis?

There is no single life-expectancy estimate for this broad group. Many people with localized disease have a good long-term outlook. Disease affecting several organs, particularly the liver, blood-forming marrow, lungs, or nervous system, can be more serious. Response to treatment and permanent organ damage also shape the outlook.

Sources

- National Cancer Institute. Langerhans Cell Histiocytosis Treatment (PDQ®)-Health Professional Version
- Allen CE, Merad M, McClain KL. Langerhans-Cell Histiocytosis. New England Journal of Medicine . 2018;379:856-868
- Emile JF, Abla O, Fraitag S, et al. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. Blood . 2016;127:2672-2681
- Goyal G, Heaney ML, Collin M, et al. Erdheim-Chester disease: consensus recommendations for evaluation, diagnosis, and treatment in the molecular era. Blood . 2020;135:1929-1945
- Abla O, Jacobsen E, Picarsic J, et al. Consensus recommendations for diagnosis and clinical management of Rosai-Dorfman-Destombes disease. Blood . 2018;131:2877-2890
- La Rosée P, Horne A, Hines M, et al. Recommendations for the management of hemophagocytic lymphohistiocytosis in adults. Blood . 2019;133:2465-2477