CONDITION

Systemic aleukemic reticuloendotheliosis

An outdated name for severe multisystem Langerhans cell histiocytosis, in which abnormal immune cells build up in several organs.

WHAT IT IS
A historical form of multisystem Langerhans cell histiocytosis

BODY SYSTEM
Immune system and multiple organs

MAIN SYMPTOMS
Skin rash, bone pain, fever, enlarged liver or spleen

WHAT CAUSES IT
Acquired changes in the MAPK cell-growth pathway

HOW IT IS DIAGNOSED
Tissue biopsy with CD1a and langerin testing

MAIN TREATMENT
Systemic medicines, including chemotherapy or targeted therapy

CAN IT BE CURED?
Sometimes - treatment can bring lasting remission

IS IT AN EMERGENCY?
Sometimes - breathing trouble or extreme drowsiness

LONG-TERM OUTLOOK
Often treatable, but organ damage and relapse can persist

Overview

Systemic aleukemic reticuloendotheliosis is an outdated name. It was used for a severe, widespread form of what is now called Langerhans cell histiocytosis , or LCH. Older publications may also connect it with acute disseminated LCH or Letterer-Siwe disease.

LCH happens when abnormal immune cells related to dendritic cells collect in tissues. Dendritic cells normally help the immune system recognize threats. In LCH, the affected cells multiply and trigger inflammation, which can damage nearby tissue.

"Systemic" means that several body systems are involved. "Aleukemic" means abnormal cells may not be prominent in the bloodstream. It does not mean that the condition is mild. "Reticuloendotheliosis" is an older term for conditions involving immune cells in tissues.

Doctors no longer use this historical label as a precise diagnosis. Modern diagnosis describes which organs are affected and whether important organs such as the liver, spleen, or bone marrow are involved. This gives more useful information about treatment and outlook.

LCH is sometimes described as both an inflammatory condition and a blood-cell cancer. It is not a typical leukemia, and it is not contagious.

Symptoms

Symptoms depend on where abnormal LCH cells collect. They may develop over weeks or months. Some people have symptoms in one area, while the historical systemic form affects several organs.

Possible symptoms include:

Excessive thirst and urination can result from diabetes insipidus , a hormone problem caused by LCH affecting the pituitary gland near the brain. Despite its name, this is not the same as diabetes mellitus, which affects blood sugar.

Symptoms such as rash, fever, and bone pain have many more common causes. Testing is needed to tell LCH apart from infection, eczema, other blood conditions, and bone or skin tumors.

- A persistent, scaly, crusted, or bruise-like skin rash, often on the scalp or in skin folds
- Bone pain, swelling, a lump, loose teeth, or a bone fracture
- Fever, tiredness, poor appetite, or difficulty gaining weight
- A swollen abdomen from an enlarged liver or spleen
- Easy bruising, unusual bleeding, pale skin, or repeated infections
- Swollen lymph nodes
- Ear discharge, hearing changes, or swelling around the ear
- Cough, chest discomfort, or shortness of breath
- Excessive thirst and frequent urination
- Headaches, balance problems, behavior changes, or other nervous system symptoms

Causes and risk factors

LCH is linked to acquired changes in a cell-growth signaling system called the MAPK pathway .

This pathway tells cells when to grow and survive. Changes in genes such as BRAF or MAP2K1 can leave the pathway switched on.

These genetic changes arise in affected cells during a person's lifetime. They are not usually present throughout the body, and LCH is not generally considered an inherited condition. Having LCH does not usually mean that a person's children will develop it.

Why these changes happen is often unknown. Nothing a parent did during pregnancy is known to cause childhood multisystem LCH.

Smoking has a strong connection with LCH limited mainly to the lungs in adults. That form is different from the severe childhood multisystem presentation historically described by this article's title. Smoking can still worsen lung health in anyone with LCH.

Diagnosis

Diagnosis requires a biopsy , in which a small sample is taken from an affected area such as the skin, bone, or lymph node. A pathologist examines the cells under a microscope.

Special laboratory stains are used to confirm that the abnormal cells produce characteristic proteins. LCH cells usually test positive for CD1a and langerin , also called CD207 . Testing for S100 may support the diagnosis but is not specific enough by itself.

Molecular testing may look for BRAF, MAP2K1, or other MAPK pathway changes. These results can help confirm the biology of the condition and may guide targeted treatment.

Further tests show how much of the body is affected. They may include:

The care team will identify whether LCH involves one system or several. They will also check for liver, spleen, or bone marrow involvement because problems in these organs can make the condition more serious.

A second pathology review at a center experienced in histiocytic conditions may be helpful, especially when the biopsy findings or historical diagnosis are uncertain.

- Blood counts and tests of liver, kidney, and clotting function
- Imaging of the bones, chest, abdomen, or brain
- Urine tests and hormone testing
- Hearing, dental, lung, or neurological assessments
- Bone marrow sampling when blood counts suggest marrow involvement

Treatment and management

Treatment is based on age, affected organs, symptoms, and whether organ function is at risk. Because systemic aleukemic reticuloendotheliosis is an old term, treatment should be planned using the current LCH diagnosis rather than the historical label.

Some limited forms of LCH can be observed or treated locally. Multisystem LCH usually needs medicine that reaches the whole body.

Treatment may include:

Chemotherapy plans are not the same for every age group. Children and adults may receive different medicines, and the choice can also change when the liver, lungs, brain, or bone marrow is involved. Targeted therapy may be considered for severe, persistent, or relapsed LCH with a suitable MAPK pathway change.

Supportive care is also important. It can include treatment for infections, transfusions for very low blood counts, skin care, pain relief, nutritional support, and dental or hearing care.

Hormone problems may need long-term replacement treatment even after LCH is no longer active. For example, diabetes insipidus often requires ongoing medicine to control thirst and urination.

People with lung involvement are strongly encouraged to stop smoking. Stopping does not replace specialist treatment when several organs are involved.

- Chemotherapy-based treatment to control abnormal cells and inflammation
- Corticosteroids like prednisone or hydrocortisone as part of some treatment plans
- Targeted medicines that block altered BRAF or MEK proteins
- Additional treatment if LCH does not respond or becomes active again
- Rarely, surgery or radiation for selected local problems

Complications

Complications can result from active LCH, lasting tissue damage, or treatment. The risk is greatest when vital organs are affected.

Possible complications include:

LCH can become active again after treatment. A recurrence may affect the same organ or a different one. New symptoms therefore deserve assessment even after a long remission.

Some complications, particularly hormone deficiencies or established organ scarring, may remain after the abnormal cells have been controlled.

- Low blood counts, leading to infection, anemia, bruising, or bleeding
- Liver inflammation, scarring, or damage to the bile ducts
- Breathing problems, lung cysts, or a collapsed lung
- Permanent pituitary hormone deficiencies
- Hearing loss, dental problems, or changes in facial bones
- Growth, puberty, or fertility problems
- Problems with balance, coordination, memory, or behavior
- Treatment-related infections or effects on healthy organs

Prevention

Multisystem LCH generally cannot be prevented. The cell changes associated with it are usually acquired for reasons that are not understood. There is no routine screening test for people without symptoms.

Not smoking can reduce the risk of adult pulmonary LCH and protects the lungs from further damage. It is not known to prevent childhood multisystem LCH.

Early assessment of persistent symptoms cannot prevent the condition, but it may allow treatment before more organ damage develops.

Living with it and what to expect

The course of LCH differs according to the organs involved and how well the condition responds to treatment. Some people complete one course of therapy and remain in remission, meaning there is no evidence of active LCH. Others need further treatment because the condition persists or returns.

Doctors usually check the response during treatment with examinations, blood tests, and selected imaging. Follow-up often continues for years. The exact schedule is based on previous organ involvement and treatment.

Even when treatment controls the active condition, some effects may be permanent. Hormone deficiencies, hearing loss, dental damage, liver scarring, or neurological problems may need separate long-term care. Rehabilitation, school support, workplace adjustments, or mental health support can help when these effects interfere with daily life.

Children may need monitoring of growth, puberty, learning, and bone health. Adults may need

ongoing review of lung function, hormone levels, cardiovascular health, and treatment-related effects.

Many people return to school, work, family activities, and exercise, although this may happen gradually. Energy levels can take time to recover. The care plan may need to change if symptoms return or late effects become apparent.

When to get medical help

Arrange a routine medical appointment for a persistent unexplained rash, ongoing bone pain or swelling, repeated ear discharge, unusual thirst and urination, or an unexplained swollen abdomen. These symptoms are not specific to LCH, but they should be assessed if they continue.

If you already have LCH, contact your care team promptly about new symptoms, increasing pain, worsening rash, changes in thirst or urination, jaundice, unusual bruising, or a return of previous symptoms.

Seek urgent same-day advice for a fever during chemotherapy or other treatment that weakens the immune system. Infection can become serious when white blood cell levels are low. Follow the fever instructions provided by your treatment center.

Go to an emergency department or call emergency services for:

- Severe or rapidly worsening breathing difficulty
- Blue or grey lips
- A seizure, new confusion, or difficulty waking
- Uncontrolled bleeding
- Sudden severe chest pain, especially with shortness of breath
- Signs of severe dehydration, such as very little urine and marked drowsiness

Common questions

Is systemic aleukemic reticuloendotheliosis a type of leukemia?

It is an old name for severe multisystem LCH, not a typical leukemia. LCH begins in blood-forming immune cells and can affect the bone marrow, but it usually forms inflammatory collections in tissues rather than behaving like common leukemias.

Why does my old medical record use this name?

Medical understanding and classification have changed. Older records may use systemic aleukemic reticuloendotheliosis or another historical term for a presentation now classified as LCH. A specialist can review old biopsy material and records if the exact diagnosis still matters.

Is Langerhans cell histiocytosis cancer?

LCH involves a clone of abnormal cells with acquired growth-pathway mutations, so many specialists classify it as a myeloid neoplasm, which is a type of blood-cell growth disorder. It also causes strong inflammation. This mixed biology is why descriptions may differ between sources.

Can it go away completely?

Treatment can bring lasting remission, and some people have no further active LCH. Others experience reactivation or have permanent effects from earlier organ damage. Remission does not always mean that hormone, hearing, liver, or neurological problems will disappear.

Can I pass it to my children?

LCH is not contagious and is not usually inherited. The genetic changes are generally found only in the abnormal cells and are acquired during life, rather than passed from parent to child.

Will I need follow-up after treatment ends?

Usually, yes. Follow-up looks for reactivation, monitors previously affected organs, and checks for late effects of LCH or its treatment. The type and duration of follow-up are tailored to the organs involved.

Sources

- National Cancer Institute. Childhood Langerhans Cell Histiocytosis Treatment (PDQ®)-Health Professional Version
- Goyal G, Tazi A, Go RS, and colleagues. International expert consensus recommendations for the diagnosis and treatment of Langerhans cell histiocytosis in adults. Blood . 2022;139(17):2601-2621
- Allen CE, Merad M, McClain KL. Langerhans-Cell Histiocytosis. New England Journal of Medicine . 2018;379:856-868
- Haupt R, Minkov M, Astigarraga I, and colleagues. Langerhans cell histiocytosis guidelines for patients up to 18 years of age. Pediatric Blood & Cancer . 2013;60(2):175-184



- Girschikofsky M, Arico M, Castillo D, and colleagues. Management of adult patients with Langerhans cell histiocytosis: recommendations from the Euro-Histio-Net expert group. Orphanet Journal of Rare Diseases . 2013;8:72