HISTIOCYTOSIS UK
No-one should die of Histiocytosis

Langerhans Cell Histiocytosis – Adult

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Introduction

Despite the misery it causes, Histiocytosis is too rare a disease to have generated substantial research in medical circles. Unfortunately, for every child or adult fighting for his or her life, the pain and suffering are just as severe for children and adults afflicted with other better-known disorders receiving funding.

For the children and adults battling these illnesses, there is now reason to hope. To ensure the research continues, we ask for your help, to complete the funding puzzle.

Our awareness and research programmes provide a beacon of hope for the many children and adults battling Histiocytosis, to ensure this research continues we ask you to pledge your support.

Table of Contents

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What is Histiocytosis?

Histiocytosis is an umbrella term applied to a group of rare diseases, characterised by increased numbers of white blood cells called histiocytes in the blood and tissues. In all forms of histiocytosis, these cells, which are part of the protective immune system, begin to attack the body, targeting many organs of the body including the bone marrow, liver, spleen, lungs, skin, bone and brain.

The prognosis for patients varies greatly depending on the form of histiocytosis.

Please be advised that all the information you read in this document is not a replacement for the advice you will get from your consultant and their team.

Who we are?

Histiocytosis UK is a registered charity dedicated to promoting and funding scientific research into uncovering not only the causes of all histiocytic diseases, which include Langerhans Cell Histiocytosis and Haemophagocytic Lymphohistiocytosis, but also ensuring early diagnosis, effective treatment and a cure.

The Charity aims to support patients and their families by means of information and awareness as well as raise public and professional awareness of histiocytic disorders.

Its team of Trustees include the UK's leading paediatric and adult LCH and HLH specialists.

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LCH Adult

What is Langerhans Cell Histiocytosis (LCH)

Langerhans Cell Histiocytosis (LCH) is the most common of the histiocytic disorders and occurs when the body accumulates too many immature Langerhans cells, a subset of the larger family of cells known as histiocytes. Langerhans cells are a type of white blood cell that normally help the body fight infection. In LCH, too many Langerhans cells are produced and build up in certain parts of the body where they can form tumours or damage organs. Most data support the concept that LCH is a diverse disease characterized by a clonal growth of immature Langerhans cells, that in more than half the cases have a mutation called V600E of the BRAF gene and related mutations in some other cases. V600E is found in tumours such as melanoma and thyroid cancer.

There has been some controversy about whether LCH is a cancer, but it is classified as such, and sometimes requires treatment with chemotherapy is not a fully developed malignant cancer. It is not contagious, nor is it believed to be inherited.

LCH is an unusual condition. It has some characteristics of cancer but, unlike almost every other cancer, it may spontaneously resolve in some patients while being life-threatening in others. LCH is classified as a cancer and sometimes requires treatment with chemotherapy. LCH patients can therefore be treated by cancer specialists (oncologists/ haematologists).

The vast majority of patients will recover completely from LCH.

Histiocytosis was first described in the medical literature in the mid to late 1800s. Through the years, it has been known by various names, such as histiocytosis-X, eosinophilic granuloma, Abt-Letterer-Siwe disease, Hashimoto-Pritzger disease, and Hand-Schüller-Christian syndrome. In 1973, the name Langerhans Cell Histiocytosis (LCH) was introduced This name was agreed upon to recognize the central role of the Langerhans cell.

LCH is believed to occur in 1:200,000 children, but any age group can be affected, from infancy through adulthood. In new born and very young infants, it occurs in 1-2 per million. It is, however, believed to be under-diagnosed, since some patients may have no symptoms, while others have symptoms that are mistaken for injury or other conditions. It occurs most often between the ages of 1-3 years and may appear as a single lesion or can affect many body systems, such as skin, bone, lymph glands, liver, lung, spleen, brain, pituitary gland and bone marrow.

Information has been collected in various studies which show that bone involvement occurs in approximately 78% of patients with LCH and often includes the skull (49%), hip/pelvic bone (23%), upper leg bone (17%) and ribs (8%). Skin LCH is seen in as many as 50% of patients. Lung lesions are seen in 20% to 40% of patients, while 30% of patients have lymph node involvement.

LCH is divided into two main groups

Symptoms depend on the location and severity of involvement. It is usually diagnosed with a tissue biopsy, in addition to other testing, such as x-rays and blood studies. A biopsy of an involved site is necessary to make a definitive diagnosis.
While some limited cases of histiocytosis may not require treatment, for patients with more extensive disease, chemotherapy may be necessary. Haematologists and oncologists, who treat cancer, also treat children with Langerhans cell histiocytosis.
Most patients with LCH will survive this disease. LCH in the skin, bones, lymph nodes or pituitary gland usually gets better with treatment and is called “low-risk.” Some patients have involvement in the spleen, liver, bone marrow, lung and skeleton. This is called “high-risk disease” and may be more difficult to treat. Some patients may develop long-term side effects such as diabetes insipidus, stunted growth, loss of teeth, bone defects, hearing loss, or neurologic problems; while other patients remain without side effects. In a minority of cases, the disease can be life-threatening.

Certain factors affect the chance of recovery and options for treatment. These factors include the extent of the disease, whether “risk organs” (liver, spleen, lung, bone marrow) are involved, and how quickly the disease responds to initial treatment.

Patients with LCH should usually have long term follow-up care to detect late complications of the disease or treatment. These may include problems of skeletal deformity or function, liver or lung problems, endocrine abnormalities, dental issues or neurological and neurocognitive dysfunction

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FAQ

LCH in Adults

The questions specifically relate to LCH in Adults.

1. What causes LCH?

The cause of LCH is unknown. In recent years, it has become apparent that LCH cells carry one of a range of mutations (e.g. BRAF V600E, MAP2K) that causes these dendritic cells to act in an abnormal way, causing LCH. It is not yet clear why and how this mutation occurs, but this discovery provides us with potential targets for new experimental therapies. These mutations are not present in the cells of the rest of the body and are therefore not passed on in families.

2. Is there a cure for LCH?

While some patients go into remission and may live normal lives with or without treatment, we usually don't use the term "cure" with this disease. No specific amount of time without active disease has yet been established for adults to determine when a patient is considered to be cured.

3. Follow-up care and What is considered to be remission?

It is important to know that the vast majority of patients will recover completely from LCH. Some however, are left with persistent/recurring problems and for a very small number of patients with multi-system LCH, it can be a life-threatening condition. After successfully completing treatment, patients will have follow-up clinic appointments. LCH sometimes comes back ('reactivates') and may need treatment again. If this happens, treatments for LCH that have worked for them before may be effective again. The same or different treatment may then be required. Patients are also monitored for possible permanent consequences of the disease (e.g. a low production of certain hormones, hearing problems) and may need treatment for these conditions.

If you have specific concerns about your condition and treatment, it's best to discuss them with your specialist medical team who know the situation in detail.

Complete remission means that there is no evidence of disease, whereas partial remission means that most of the signs and symptoms of LCH are gone, but some still remain. Doctors use the term response and "non-active" to describe patients who are free of symptoms and signs of LCH. Usually a cure is linked to being in remission for a certain period of time.

There is no established period of "non-active" disease before LCH is considered cured, but the chance for recurrence is low after five years from end of treatment.

4. Is LCH fatal?

It can be. A small percentage of patients, most often those with multisystem risk-organ involvement that is unresponsive to treatment, may not survive.

5. Signs, Symptoms and Can LCH spread?

The symptoms of LCH will depend on which part of the body is affected and whether the disease is affecting more than one part of the body. The lymph glands may be enlarged, and the patient may be irritable and have a poor appetite.

Pain in the bone and/or swelling and lumps on the skull can occur if LCH is affecting the bone. A skin rash may occur if the skin is affected. A discharge from the ear or hearing problems can occur if the ear is affected. The patient may have breathing difficulties if LCH affects the lungs or chest. Tummy problems such as diarrhoea and liver problems including jaundice can occur if LCH affects the gut or liver.

In 10–20% of patients with multi-system disease, the pituitary gland at the base of the brain is affected, causing hormonal problems. This can lead to the patient passing larger amounts of urine and being very thirsty. This is called diabetes insipidus, which is different from sugar diabetes and can be well-controlled with specific medicines. Occasionally, other pituitary hormones may be affected.

6. Is LCH hereditary?

Although there are rare families (less than 2% of all cases) documented with more than one member diagnosed with LCH, at this point, there is no clear evidence that this disease is inherited.

7. Where did LCH get its name?

In 1868, the German pathologist Paul Langerhans discovered a type of white blood cell which eventually came to bear his name. The various manifestations of LCH were previously known by a number of different names (histiocytosis-X, eosinophilic granuloma, Letterer-Siwe disease, Hand-Schüller-Christian syndrome, etc.). In 1983, it was suggested that this disorder be named “Langerhans Cell Histiocytosis,” to recognize the key role of the Langerhans cell in all of the different manifestations.

8. What are the different therapies/treatments commonly used to treat LCH?

Treatment is based upon the organ(s) involved, extension of disease, and in some cases, age of the patient. In some cases, no treatment is necessary. Others may respond to surgical removal, steroids, or anti-inflammatory drugs (NSAIDs). Low-dose radiation is helpful in some situations but should be carefully used in children. There are patients who require chemotherapy such as vinblastine, vincristine, etoposide (VP-16), methotrexate,

cytosine-arabinoside (Ara-C), and/or 6-MP. In patients with severe disease that does not respond to initial treatment, stronger chemotherapy combinations may be used. Ultraviolet light (PUVA) may be helpful for limited skin disease. In very rare instances, a transplant of the liver, lung, or bone marrow may be necessary.

9. How is LCH diagnosed?

LCH is diagnosed by a biopsy of the affected tissue. Blood tests may be done to help determine the extent and/or severity of involvement, but blood tests are not diagnostic of the disease.

A variety of tests and investigations may be needed to diagnose LCH. Tests are likely to include the removal of a sample of cells from an affected part of the body (a biopsy). This is usually done in an operation under a general anaesthetic. The cells are then examined under a microscope. X-rays are taken of the bones, the skull and the lungs. Blood and urine tests will also be done. Additional scans and tests may be required depending on which parts of the body is affected. These tests help the doctors decide whether the disease is a single-system or multi system type.

When you are having the tests, you may need to stay in hospital. Any tests and investigations that you need will be explained to you.

It is important to know that the vast majority of patients will recover completely from LCH.

Some however, are left with persistent/recurring problems and for a very small number of patients with multi-system LCH, it can be a life-threatening condition. After successfully completing treatment, patients will have follow-up clinic appointments. LCH sometimes comes back (‘reactivates’) and may need treatment again. If this happens, treatments for LCH that have worked for them before may be effective again. The same or different treatment may then be required. Patients are also monitored for possible permanent consequences of the disease (e.g. a low production of certain hormones, hearing problems) and may need treatment for these conditions.

If you have specific concerns about your condition and treatment, it’s best to discuss them with your specialist medical team who know the situation in detail.

10. With the diagnosis and treatment of LCH, am I more likely to develop cancer?
Although this occurs rarely, LCH is associated with cancer more often than would be expected by chance. This can occur before, during, or after the diagnosis of LCH. Some cancers following the LCH diagnosis might be related to the treatments given. When cancer occurs before LCH, the histiocytosis might represent a “reaction” to the cancer itself.

11. With a history of LCH, can I become pregnant?

Drugs used as part of the usual LCH treatment are not associated with infertility. These include vinblastine, vincristine, 2-CdA, methotrexate, Ara-C, and etoposide (VP-16). LCH can, however, affect the endocrine system, and complications can result in infertility. This is especially true if hormone loss is not diagnosed in time and if no hormone replacement is given. However, in some cases, hormone replacement therapy may restore fertility.

12. What are permanent consequences of LCH?

Permanent consequences are also known as late effects of LCH, although they can occur early on. They are believed to be mostly related to the disease rather than treatment and include:

a. Diabetes Insipidus
b. Stunted growth
c. Bone abnormalities
d. Hearing loss
e. Neurological problems, including poor coordination, unsteadiness, difficulty with handwriting, abnormal eye movements, problems with speech, learning disabilities/decreased school performance, memory loss, and behavior difficulties
f. Loss of teeth
g. Loss of spinal height
h. Delayed puberty
i. Bulging eyes
j. Scarring of lungs
k. Scarring of liver/cirrhosis
l. Secondary cancers

13. What causes chronic pain in adults with LCH?

Some pain and cramping can be a side effect of treatment, such as vinblastine and steroids. Pain may also be directly related to active disease. In cases of more chronic pain, some researchers suspect that cytokines, which are a type of messenger, stimulate white blood cells to release inflammatory molecules that produce pain.

14. What healthcare workers should I see to help with pain management?

The primary oncologist/physician can treat and manage chronic pain in many cases. However, if the pain does not respond to the usual therapy and/or if the pain compromises quality of life, referral to a pain clinic may be necessary. Clinics differ in their approach and what they offer, but most include a team of health care providers with a variety of ways to manage pain and restore quality of life.

15. What should I look for in a doctor?

Many adults with LCH have been seen by a number of specialists, depending on their symptoms. It will be important to find a doctor knowledgeable about adult LCH who is willing to serve as the primary “hub” and coordinate input from the specialists. Ideally, this physician would be an oncologist who specializes in cancer-like illnesses and is qualified to provide systemic treatment. Accessibility and good communication skills with you, as well as other physicians, are important.

16. Is it true that LCH is mostly a childhood disease?

Not necessarily. Although we do know the incidence of childhood LCH, there is not enough data to determine how many adults are affected by this disease.

17. What is “PLCH?”

PLCH (Pulmonary Langerhans Cell Histiocytosis) is LCH of the lung. It affects mostly adults who smoke and often occurs without other LCH involvement.

18. Why is cigarette smoking dangerous for me?

It is believed that there is a strong link between cigarette smoking and pulmonary LCH. An estimated 90-95% of pulmonary-only LCH patients currently smoke or have smoked. Although the exact mechanism is not understood, it is believed that smoking can cause an accumulation of Langerhans cells in the lungs.

19. Can adults with a history of LCH donate blood or bone marrow?

Although there is no data to prove a risk, adults with a history of LCH are advised against donating blood or platelets. They should also not be organ donors.

20. What is neuro-degeneration?

Neuro-degeneration is progressive loss of brain function. It occurs as a permanent consequence in some cases of LCH.

21. Can neuro-degeneration be prevented/reversed/treated?

It is not currently known whether neuro-degeneration can be prevented. It is believed that neuro-degeneration cannot be reversed, and there is controversy whether patients with neuro-degeneration can be successfully treated. There have been some promising results with Ara-C but more extensive scientific studies are required.

22. What is chemo brain?

Chemo brain is a term used for mild brain impairment that may occur during treatment. It can include symptoms such as difficulty concentrating, feeling disorganized, trouble with multi-tasking, memory lapses, slower thinking, word-finding difficulty, etc. For most patients, it lasts a short time.