HISTIOCYTOSIS UK
No-one should die of Histiocytosis

LANGERHANS CELL HISTIOCYTOSIS

LCH-CHILDREN

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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.

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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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Langerhans Cell Histiocytosis, LCH for short.

Histiocytes called Langerhans cells, which are normally found in the skin, may spread to many organs and damage them, so that symptoms vary depending on which organs are affected, but skin rashes, destruction of bone, breathing problems and damage to the brain are common.

LCH occurs in children, often during infancy but also in adults. It is usually a chronic disease and may cause severe disabilities due to brain damage. The diagnosis is made by microscopic examination of a tissue specimen obtained by biopsy. The prognosis depends very much on the extent of disease and organs affected, which can be assessed by imaging studies. LCH is thought to be caused by alterations in the DNA of Langerhans cells.

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.

About 50 children in the UK develop LCH each year. It can affect children of any age and is more common in boys than in girls.

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 are therefore usually treated by children’s cancer specialists (paediatric oncologists/ haematologists).

The vast majority of children 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.

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

1. What causes LCH?
In more than half of LCH patients, the LCH cells have amutation called V600E in a gene called BRAF. This mutation is found in tumours such as melanoma and thyroid cancer. In some other LCH patients, related mutations are found. These findings indicate that LCH is related to, but probably not a fully developed, cancer.

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. What is considered to be remission?
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. 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.

5. 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.

6. What are the different therapies/treatments commonly used to treat LCH?
Treatment is based upon the organ(s) involved, extent of disease and 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.

7. Can an infant be tested at birth for LCH?
A biopsy of the affected tissue, rather than a blood test, is required for diagnosis and would therefore not be appropriate as a routine test unless this disease is suspected.

8. 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.

9. Signs, Symptoms & 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 child 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 such as cradle cap or nappy rash may occur if the skin is affected. A discharge from the ear or hearing problems can occur if the ear is affected. The child 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 child 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, causing poor growth or delayed puberty, which can also be treated. The exact mechanism that causes lesions to appear in other locations in the body is not yet known. However, some researchers believe that abnormal LCH cells travel through the blood like tumor cells and “seed” in different locations, creating new lesions.

10. Is there a blood test to diagnose LCH?
LCH is diagnosed with 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.

11. 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 but because it is considered a childhood disease it is under diagnosed in adults.

12. With the diagnosis and treatment of LCH, is my child 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.

13. 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 behaviour 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

14. What are the chances my child will develop permanent consequences?
One or more permanent consequences are reported in an estimated 50% of all LCH patients, making long-term follow-up a necessity. Severity and type depends on the affected organs, number of lesions, and the treatment administered. Read more about permanent consequences of LCH.

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

16. 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.

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. What kind of doctor should we use?
A paediatric oncologist most often provides primary treatment and coordinates a team of health professionals, which may include, but are not limited to, the primary care physician, paediatric surgeon, radiologist, paediatric nurses, and social workers.

19. What should I look for in a doctor?
LCH is most often followed and treated by an oncologist, who specializes in cancer-type illnesses. The level of experience with LCH can vary widely among physicians. If he/she is not knowledgeable about this disease, a willingness to learn more and consult with the experts can go a long way. Other qualities to look for are accessibility and good communication skills with you, as well as other physicians.

20. Will my child grow normally?
Most children with LCH do grow normally; it is believed that growth hormone deficiency affects approximately 10% of children with this disease.

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What are the side effects?

What are the side effects of vinblastine?

Side effects include:
a. Low blood counts (with higher risk of infection). Mild nausea/vomiting/constipation
b. Easily sunburned
c. Skin irritation at site of injection
d. Thin or brittle hair
e. Fatigue
f. Bone pain
g. Hoarseness
h. Seizures
i. Shortness of breath
j. Nerve damage (especially in adults) with tingling, numbness and/or pain of the hands and feet

What are the side effects of prednisone?

Side effects include:
a. Increase in blood sugar
b. Increase in appetite
c. Heartburn
d. Bloating/fluid retention/weight gain
e. Difficulty sleeping
f. Mood/behavior/personality changes
g. Higher risk of infection
h. Slow wound healing
i. Muscle weakness
j. Loss of bone calcium
k. Increased hair growth

More unusual side effects may include:
a. Problems with vision/eye pain
b. Seizures
c. Confusion

What are the side effects of methotrexate?

Side effects include:
a. Mouth sores/swollen, tender gums
b. Nausea/vomiting/diarrhoea/decreased appetite
c. Low blood counts
d. Dizziness/drowsiness
e. Headache

More unusual side effects may include:
a. Blurred vision or loss of vision
b. Seizures
c. Confusion
d. Weakness/difficulty moving one or both sides of the body
e. Loss of consciousness
f. Lung damage
g. Allergic reactions

What are the possible side effects of 6-MP (mercaptopurine)?
More common signs/symptoms include:
a. Low blood counts (red cells, white cells, and clotting cells)
b. Nausea/vomiting/decreased appetite
c. Headache
d. Weakness/fatigue/achiness
e. Rash/darkening of the skin

What are the possible side effects of 2-CdA (cladribine/leustatin)?
More common signs/symptoms include:
a. Flu-like symptoms (Fever, chills, headache, fatigue, nausea/vomiting)
b. Decreased appetite
c. Constipation
d. Low blood counts (red cells, white cells, and clotting cells)
e. Skin rash/redness/itching

How is it Diagnosed

How is LCH diagnosed?
The diagnosis of LCH is usually made by performing a biopsy of an affected part of the body. A biopsy is the removal of a small piece of tissue while a patient is under an anaesthetic. This piece of tissue is then examined under a microscope.

Doctors will be carrying out a number of further tests. These tests are done to see how LCH affects that part of the body and if any other systems are involved (multi-system disease). This information helps the medical team to decide on the best treatment for your child.

Some of the following tests may be carried out on your child:
• Blood tests these are done to check how many of the of different types of blood cells there are and to assess how well the liver and kidneys are working

• Urine test to evaluate how concentrated/dilute the urine is

• X-ray pictures of the chest and of the bones (also known as a skeletal survey).

• Ultrasound Scan – sound waves are used to build up a picture of the inside of the body. A clear gel is spread over the skin and a microphone is passed over the body. The sound waves bounce off the organs inside the body and are picked up by the microphone. A computer turns the sound waves into pictures.

• CT Scan – A CT (Computerised Tomography) scan takes a number of x-ray pictures of the body from different angles and uses a computer to convert them into cross-sectional x-ray pictures or ‘slices’ of the body. Depending on how big a part of the body is being scanned this can take between a few seconds and a few minutes. CT scans are painless, but small children may need to be sedated or anaesthetised (‘put to sleep as for an operation’) to ensure they remain still while the scan takes place.

• MRI Scan – Magnetic Resonance Imaging (MRI) Scan uses magnetic and radio waves to take pictures of the body. It is painless, but usually takes longer than a CT scan and is quite

noisy. As it is important to keep very still, small children are normally sedated or given an anesthetic.

• Biopsy – the removal of a small piece of tissue from an organ or part of the body for microscopic examination. Most often the biopsy is done of affected bone or skin but biopsies may also need to be carried out on the liver, lung or bone marrow.

• Water Deprivation Test – if doctors suspect there is a hormone problem known as diabetes insipidus, your child may need to undergo a water deprivation test. This is a test to measure how much urine is made and how concentrated it becomes when no water is given to a patient for a certain amount of time (also called fluid privation test) to complete all of these tests can take between a few days and a couple of weeks and may involve a stay in hospital.

Diagnosis

LCH is divided into two main groups – single system and multi-system

Single system disease
When LCH is described as a 'single system' disease, it means that it is only affecting one system in the body – for example, skin, bone or an organ. The majority (>70%) of patients have single system disease. If the LCH is only present in one place in that particular system, it is called single site and if in more than one place, it is called multi-site or multi-focal disease. Therefore, a child with several affected bones, but no disease elsewhere, is considered to have 'single system, multi-focal' disease.

Multi-system disease
When LCH is found in more than one 'system', for example, in both the skin and bone, it is described as 'multi-system' disease. Children with 'multisystem' disease affecting the liver, spleen or bone marrow, are considered to have a more serious form of LCH. This is then described as multi-system disease with 'risk organ' involvement and may require more intensive treatment.

This classification helps doctors to decide what treatment is required and for how long it should be given.

How is it Treated

LCH is different to almost all cancers because in some cases it may 'burn itself out' without any treatment. We don't know how or why this happens.

In other cases, treatment is needed to get the disease under control and prevent too much damage. Treatment may involve an operation (surgery) and/or medication. The treatment will be tailored to your child and will depend on the extent and sites of their disease.

What are the main treatment options?

• Surgery

The diagnosis of LCH is made by taking a small sample of tissue from an affected part of the body (biopsy). If there is only a single bony lesion, the biopsy is sometimes combined with curettage (scraping out of the abnormal tissue in the lesion). These procedures may initiate a process of healing in the LCH lesion and sometimes this is all that is required.

• Medication

Steroids – corticosteroids are medicines used to reduce inflammation and stop the body's immune system acting in the wrong way. Your child may be given prednisolone (a type of steroid) which is usually taken by mouth. Steroids can also be injected into an LCH lesion.

Chemotherapy – this is used to destroy LCH cells and is generally given intravenously. This means that the chemotherapy medicine is diluted in fluid and given straight into a vein (into the bloodstream). Some chemotherapy medicines may be taken by mouth.

Your oncologist or haematologist will decide on a treatment plan for your child once all the relevant tests are completed. A protocol is a special plan that will detail your child's treatment if medication is required. There are international treatment protocols, developed over many years through large clinical trials.

The protocol will describe the frequency, timing and length of the different elements of treatment. Your child's treatment plan may change since it is dependent on how he or she responds to the treatment. You will be given a copy of your child's flow sheet so that you can follow progress throughout the treatment.

If your child needs chemotherapy, he or she will probably need a central line. This is a tube that is inserted into a large blood vessel and tunnelled under the skin to where it can be easily accessed. It allows blood samples to be taken and treatment, including chemotherapy, to be given easily and painlessly. The central line is put in under general anaesthesia and can stay in place until the end of your child's treatment. Your hospital will provide more information about the types of central lines they offer.

If your child is unwell or requires very intensive treatment he or she will need to be in hospital. Most children however, receive all their intravenous treatment by visiting their hospital's out-patient or day-care facility. This may only be available at your treating oncologist/haematologist's hospital or it may be available at your local hospital under a shared care arrangement with a local doctor. Some treatment, like that taken by mouth, can be given at home.

While on chemotherapy and for up to 6 months afterwards, your child will be susceptible to infections. This is known as being immunocompromised. If he or she develops a fever or becomes unwell you need to contact your treating team immediately for advice. Your child may need immediate hospital admission and treatment with antibiotics.

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What are the side-effects of the medication?

The main drugs used to treat LCH and their common side effects are described below. Different drugs cause different side effects. Everyone is different and will react to treatment in a different way. Some children may have very few side effects while others will have a lot. Almost all side effects are only short-term and will gradually disappear once the treatment has stopped.

• Steroids – Prednisolone/Prednisone - this is a type of corticosteroid (steroid) that can reduce inflammation and suppress the immune system. It is usually given by mouth, in the form of pills to swallow, pills that dissolve in water, or as a liquid medicine. Possible side-effects include: irritation of the stomach lining (indigestion/ discomfort/pain), increased appetite, weight gain, changes in behaviour (mood swings/difficulty in sleeping/anxiety/irritability), increase in blood sugar level (like someone with diabetes), high blood pressure, increased risk of infection due to suppression of the immune system, impaired wound healing, irregular or absent periods, and inflammation of the pancreas.

• Chemotherapy – Drugs used to treat cancer. These drugs work by killing cells that are in the process of multiplying (by dividing and forming new cells). The main areas of the body that may be affected by chemotherapy are those where cells rapidly divide and grow. Examples include the lining of the mouth causing a sore mouth, the digestive system causing diarrhoea, skin and hair, causing hair loss, and the bone marrow (spongy material that fills the bones and produces new blood cells), causing low blood counts.

There are three main types of blood cells:
• Red blood cells which carry oxygen around the body
• White blood cells which fight infections
• Platelets which help the blood to clot to prevent bleeding and bruising

Chemotherapy reduces the production, and therefore, the number of blood cells in the body. Too few red blood cells cause anemia, and the person becomes tired and pale. If there are too few white blood cells, particularly ones called neutrophils (neutropenia), the person is at increased risk of infection. Too few platelets means the person is at increased risk of excessive bleeding when injured, having nose-bleeds or bruising easily. If the counts get really low, your child may need a red cell transfusion or platelet transfusion. Only a small number of LCH patients require transfusions, but in some more severe cases, transfusions play an important part in supporting patients. Transfusions are also needed to support those patients who undergo intensive chemotherapy.

As the chemotherapy affects your child’s immune system, he or she may need antibiotics to help fight infections. This means, if your child has a temperature of 38°C or more or becomes unwell (even with a normal temperature), you should immediately contact your medical team. Your child may need tests, antibiotics and admission to hospital for a few days. You may also be asked to avoid using paracetamol and ibuprofen since these drugs lower high temperatures and may mask an infection. In addition, if your child is in contact with someone who has chickenpox, shingles or measles, then you should let your hospital know as these are potentially dangerous infections for a child with a low (suppressed) immune system. Both your child and the rest of your family should ideally have the annual flu jab during the autumn/winter.

Chemotherapy can cause nausea and vomiting. Anti-sickness medicines, known as anti-emetic drugs, are given to control this side effect.
Hair loss can occur, but this does not always happen with the chemotherapy used to treat LCH. Young children often get used to hair loss fairly quickly but for parents it is far more traumatic, reminding them that their child is ill. Fortunately, all hair loss from chemotherapy is temporary and hair growth returns once treatment has stopped.

The chemotherapy normally used to treat LCH does not affect fertility, but you should discuss your child's particular treatment with your oncologist/haematologist for more information.
Chemotherapy can cause increased skin sensitivity to sunlight, therefore avoid intense sunlight and use sun block during treatment.

The two most commonly used chemotherapy drugs for LCH are Vinblastine and 6-Mercaptopurine.
Vinblastine
– is a chemotherapy drug that is injected into your child's blood stream through the central line. This drug is administered by a 'push' rather than a slow drip through. The process only takes about 10 minutes, but your child will be in hospital for longer since a number of checks need to be carried out before the drug is given.
Once completed, your child will be able to go home.

In addition to the side-effects previously described, Vinblastine can sometimes, though rarely, cause tingling sensations in the hands and feet, hoarseness, constipation, muscle weakness and bone pain. It may also cause damage to the skin if it is injected directly into a vein (rather than through a central line) and then leaks into the skin.

6-Mercaptopurine – is a chemotherapy drug taken either as tablets or in a liquid form. It is usually taken at home.

In addition to the other side effects already mentioned, 6-mercaptopurine may affect the liver and this will be monitored by your doctor.

Sometimes other drugs are used to treat LCH, for instance when the above mentioned drugs are not successful or when the disease returns. Should this become necessary, your doctor will discuss the different options with you.

Late Effects and Clinical Trials

What happens to patients after they had LCH?

It is important to know that the vast majority of children will recover completely from LCH. Some children 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, most 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) and may need treatment for these late effects.

What Are Clinical Trials?

Clinical trials are an essential step in the development of treatment for various diseases and are necessary for improving the outcome for patients. Clinical trials are the only way to find out if a new treatment approach to a disease is better than the standard treatments currently used. Patients volunteering to take part in a trial are randomly assigned to either receiving the standard treatment or a different or experimental treatment. This is known as a randomised trial and is the most common way in which treatments are compared. This process (randomisation) ensures that the groups are similar in every way other than the fact that they receive different treatments. Any difference in outcome between the groups is then likely to be caused by the difference in the treatment and not by other differences between the groups. If an experimental treatment proves to be better than the standard treatment and does not cause unacceptable side-effects, it is recommended as the new standard treatment for future patients. This is how new treatments or approaches to treatment are introduced to patients.

The conduct of clinical trials is carefully regulated to ensure patients' well-being is protected. Patients will only be able to participate in a trial if there is an open trial at that time, if they meet the eligibility criteria, and if their treating hospital is taking part. Parents, and when appropriate children, must understand the implications of taking part in a clinical trial and give written consent (agreement) to allow them to be enrolled on a trial. If a trial is available to your child, your doctor will explain it in more detail and you will be given the necessary information to allow you to decide whether to take part or not. While on a clinical trial your child will be very closely monitored.

Coping

How do I cope with the diagnosis?

LCH can be difficult to diagnose and can be mistaken for other things. You may have been afraid that your child has a serious form of cancer and feel relieved that LCH is likely to be curable. You may feel angry that it wasn't picked up earlier. You will probably feel confused as you won't have heard of LCH before and worried and scared about what it means for your child.

The consultant and the rest of the medical and nursing team are there to help you through this very difficult time. They will explain the disease and the treatment your child will need.

It is very likely at this stage that you will not take in much of the information you are given. You may be in shock and find it hard to function as normal. Don't worry if you have not asked all of the questions you meant to. You will have plenty of opportunities to do so later. Quite often, parents feel overwhelmed by the enormity of what has happened and cannot deal with anything else at this time.

As parents, being able to have even a few hours alone together to get used to the news and to talk about what has happened, before starting to tell everyone else, can be very helpful. If you are a single parent dealing with this news, it is helpful if you have a close friend or family member with whom you can share your worries and fears.

Telling friends and family can be emotionally difficult, and also takes a huge amount of time. It may help to tell one family member or friend and ask them to ring round others. Some parents also set up a webpage on one of the specialised websites such as Caringbridge or Carepages . This means that the latest information can be quickly passed on to friends and family who desperately want to know what's happening, while not taking up all your time and energy having to repeat everything. It also gives people an easy way to let you know they care, through leaving messages in the guest books. Despite your best efforts, you will probably still find the telephone rings constantly. Don't feel bad about using the answerphone. Let people leave messages and call them back if and when you want to.

How do I get the information I want?
When you are worried about your child and meeting a doctor that you may not know very well, it is easy to forget what you meant to ask, and what you have been told. If you can, try to take notes when you attend the main meetings with the consultant. It might be better to take a friend or relative along with you, as they might be able to pay more attention to some of the discussion and take notes for you. It is often the case that you will remember different pieces of information and you may have different questions or concerns. Write down any questions beforehand, so that you don't forget them, and make sure you know whom to contact if you have any more questions, or urgent queries.

How do I listen to and talk to my child/their siblings about this?
A child of any age will notice a tense atmosphere and hushed conversations. It is very important that you talk to your children about what is happening. What you actually say to your child and their siblings will depend on their age. For younger children, it may be enough to say that they have some bad cells and the doctors are giving them some medicine to make the bad cells go away.

Older children and teenagers may want to know all that you know about their illness and may well have been with you when you were told the diagnosis. Being open and honest with them and talking together with the consultant about their questions will help you all to deal with the diagnosis. It may also be helpful for them to talk privately about their worries with members of the medical team, such as the doctor, social worker or psychologist. Some children may consider themselves mature enough to make their own decisions regarding their treatment and should therefore be involved.

Siblings may feel ignored and side-lined due to your child's illness. Their lives have changed a lot due to their sibling's illness and they may start to feel resentful about all the attention their sibling is receiving.

They may also be extremely worried and upset to see what their sibling is going through and it can raise difficult questions in their minds. You will need to give them opportunities to ask these questions and bear in mind that they might find it easier to talk to another adult (close friend or family) as they may not want to upset you.

There are many things you can do to help your family get through any difficult times during treatment. Some suggestions that have helped other families are:
• You and your partner spend time individually with your other children.
• Make sure that when your ill child receives presents from visitors, you even things up by giving something to your other children.
• Try and keep discipline consistent, even if it means relaxing things a little for everyone.

How do we deal with treatment?

During the period of treatment, you will have ups and downs. Although the first shock of diagnosis will fade and you will feel that at least action is being taken to deal with the illness, worries about your child's progress and prognosis will come back from time to time, particularly if things do not go according to plan. It can be difficult to maintain the stability of your child's home environment and minimise the impact on your family. Help and support from close family and friends, online support networks or your community group can all help to keep your spirits up. Doing fun activities as a family can help distract you and give you all a break from the worry and stress.

Treatment can range from just the initial biopsy or surgery in some children, to 6 months or even 2 years chemotherapy in other cases. It is helpful when you are given some idea of what treatment is planned and how long it might carry on for, so that you can try and organise your lives to cope with this situation. Talk to your Consultant about this but keep in mind that it may need to change depending on your child's response to treatment.

What happens at the end of treatment?
Even though the treatment is stressful, many parents find the end of treatment difficult. Some parents have said they felt the disease had only been kept at bay while the drugs were being given. When treatment ends, it can feel as if the 'safety net' has been taken away, so you feel more worried about the return of symptoms. This uncertainty can be eased a little by the regular follow-up that your child will receive and by talking to your medical team about any concerns you have.

If the disease recurs, known as reactivation, most patients will again respond well to treatment. Your consultant will discuss the treatment options with you. Reactivation occurs in about one third of patients who had disease in more than one system/site, but reactivation is rare in most other patients.

Resources

What resources are there for sibling or family support?
Families should be able to gain support from the group of professionals who work with their child's consultant. They are known as a multi-disciplinary team (or MDT) and usually include nurses, social workers, play therapists and psychologists. Many centers also run patient, sibling and parent support groups.

Your GP will be kept informed by the hospital, but it is also useful to keep him or her up to date yourself. They can be a useful source of support for the whole family as he or she may be able to refer you for specialised support locally if needed.

Counselling can be useful for you and/or your children. Your GP may be able to refer you to a counsellor, or a child psychologist if required. 'Relate' provides counselling for couples, which can help to mitigate the strain that can be placed on your relationship with your partner.

There are a number of different charities, such as CLIC Sargent and Barretstown that offer holidays for families with children with serious diseases.

It is not always easy to find the help you need, and you may need to ask a few people before you find the right support for you. As well as talking to your GP, try talking to the medical

team at your hospital or shared care hospital, your community nurse, paediatric oncology outreach nurse specialist or CLIC Sargent social worker.

How do I find other parents?

One of the real difficulties for parents of children with a rare disease, such as LCH, is being able to talk to other parents, who have been through, or are going through the same experience as you. Your local medical team may be able to put you in touch with other families who have been affected by LCH

You may find helpful national or regional support and advice on our Useful Links page or you may also like to join one of our Facebook groups.

- **Facebook: "Histio Champions"**' celebrating patients, families and champions of all Histio Awareness,
- **Facebook: "Histio Champions LCH"** community
- **Facebook: "Histio Campions HLH"** community
- or **Twitter**: @histiouk.

Where can I get financial support?

In the UK the NHS covers all medical treatment and tests free of charge. Prescriptions for medications are free for children. Having a sick child, however, inevitably puts additional financial pressure on families (travel, parking, loss of income etc.).

Some children may qualify for Disability Living Allowance or Personal Independence Payment. Clic Sargent has information on their website about some benefits, parental leave and flexible working at www.clicsargent.org.uk. You can also contact the disability centre or the Citizens Advice Bureau for further information.

It is vital that you talk to your employer to explain what is going on and find out what they can provide in terms of flexibility.

A carer's allowance may also be available. This is means tested, so depends on your income. For further information, talk to your outreach nurse or social worker.

CLIC Sargent offer grants and can apply to other charities to help with the additional financial costs, such as unpaid leave from work, after school care for siblings and travel. More information on these grants can be found on their website, or through your social worker.