with familial HLH usually develop symptoms around the same age. Several different inherited changes, or mutations, in DNA are associated with HLH.

Acquired Haemophagocytic Lymphohistiocytosis

Acquired HLH is also called secondary HLH and can occur at any age. The frequency is unknown but it is thought to be more common than the genetic type. Like the genetic types of HLH, acquired HLH is usually triggered by an infection, often a virus. HLH can also occur in children with some cancers.

Macrophage Activation Syndrome

Macrophage Activation Syndrome (MAS) is an extremely rare condition that occurs in both children and adults with auto-immune diseases, such as rheumatoid arthritis. It has the same features as HLH but some of the initial blood changes may be less severe and problems with clotting and the function of the heart may be worse.

Like other forms of HLH, viruses have been shown to trigger MAS. Those suffering from MAS have a better outcome than HLH, with a survival rate of 80-90%. Treatment is similar to HLH, but less intensive.

Please see the website for further information.

How You Can Help

LCH and HLH are rare diseases, but for the few they affect, they cause devastation, fear and sometimes, death.

Research into LCH and HLH has been very limited due to lack of funds and has been the result of donations and fundraising. In order to find a cure as well as provide practical support for both patients and their families, we need to continue raising as much money as we can.

By working together and raising money, we can achieve this.

Ways to Donate

There are several different ways in which you can make a difference. You may want to consider either organising a fundraising event, a regular gift, payroll giving, taking out a subscription, a one-off donation, a gift in celebration, a gift in memory or leaving a legacy.

How and where to contact us

For further information about the Trust, Volunteering, Fundraising or Research:

www.hrtrust.org

Head Office: +44 (0) 7850 740 241

Email: **Info@HRTrust.org**

Registered in England & Wales
Charity Number: 1004546

THE HISTIOCYTOSIS RESEARCH TRUST

Together we will find a cure

The Histiocytosis Research Trust was set up as a registered charity in 1991 and is dedicated to promoting and funding scientific research into uncovering not only the causes of all histiocytic diseases, which include Langerhan's Cell Histiocytosis and Haemophagocytic Lymphohistiocytosis, but also ensuring early diagnosis, effective treatment and a cure.

The Trust also aims to support patients and their families as well as raise public and professional awareness of histiocytic disorders. Its team of Trustees include the UK's leading paediatric LCH and HLH specialists.

The H R Trust is closely linked to the Nikolas Symposium, The Artemis Association, The Histiocyte Society, Euro Histionet and The Histiocytosis Association.

About the Two Commonest Diseases

Langerhan's Cell Histiocytosis (LCH) is a rare disease. It is estimated that 1 in 200,000 children will become ill with it each year and adults can also be affected. In the UK alone, there are 50 new cases each year. Doctors are often unable to diagnose it because it presents with many different symptoms and as a result, diagnosis and treatment is delayed.

People suffering from LCH have too many histiocytes – a type of white blood cell that normally helps to fight infection. However, in those suffering from LCH, the histiocytes gather together in large numbers causing damage to healthy parts of the body. LCH is similar to cancer because of the uncontrolled accumulation of histiocytes and more than half of patients have a specific change, or mutation, in the DNA of the histiocytes. Because LCH has similarities to cancer it is currently treated with chemotherapy, radiation and steroids.

Doctors call LCH an 'orphan' disease because it is so rare. As a result, research into why it happens, how it can be treated and even cured, has been limited. Nevertheless, although doctors and scientists do not know what causes LCH – it is not hereditary and it is not infectious.

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

When LCH is described as a 'single-system' disease, it means that it only affects one system in the body – for example skin or bone or an organ. If it is only in one place in that particular system, it is single site and if in more than one, multi-site or multi-focal. So a child with several affected areas in the bones but no disease elsewhere is considered to have 'multi-focal, single-system' disease.

When LCH is found in more than one 'system', for example in both the skin and bones, it is described as 'multi-system' disease. Children with 'multi-system' disease affecting the liver, spleen, lung or bone marrow can 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.

It is important to remember that the vast majority of children will recover completely from LCH with a 90% survival rate. Some children, however, may be left with life-long problems and in a small number of multi-system cases the disease can be life-threatening.

Sometimes the disease comes back, but unlike cancer, treatments for LCH that have worked before may be used again.

Haemophagocytic Lymphohistiocytosis (HLH) is a very rare but life-threatening disease that usually affects babies and children. In the United Kingdom, about 15 children are diagnosed each year with HLH and international studies have shown there is a survival rate of only 55%.

HLH is caused by an uncontrolled growth of activated white blood cells. It can be likened to a very severe form of inflammation that the body is not able to turn off. Unfortunately, the immune system is overwhelmed by this excessive activation and functions poorly, leaving the child susceptible to infection.

Because HLH often looks at first like a normal response to infection it can take time to realise that the child's immune system is not functioning properly.

Treatment includes chemotherapy and sometimes a bone marrow transplant.

Types of HLH

There are two types of HLH, genetic or familial, and acquired. The incidence of acquired HLH is unknown but it is thought to be more common than the genetic type.

Genetic HLH is also called primary HLH and may be inherited in one of two ways:

Autosomal recessive – this is where the child has 2 copies of the abnormal gene, one from each parent.

X-linked – this is passed only to boys by one of the mother's X chromosomes which is abnormal.

Genetic or Familial HLH may occur alone, but very rare cases can be associated with other immune deficiencies such as Chediak-Higashi Syndrome 1 (CHS-1), Griscelli Syndrome 2 (gs-2) and X-linked lympho-proliferative syndrome (XLP).

Familial HLH

Most familial cases of HLH around 70-80%, develop symptoms before the age of 1 and a few, approximately 10%, experience symptoms within the first 4 weeks of life. In the same family, children