

About Primary Immunodeficiency UK

Primary Immunodeficiency UK (PID UK) is a national organisation supporting individuals and families affected by primary immunodeficiencies (PIDs).

We are the UK national member of the International Patient Organisation for Primary Immunodeficiencies (IPOPI), an association of national patient organisations dedicated to improving awareness, access to early diagnosis and optimal treatments for PID patients worldwide.

Our website at www.piduk.org provides useful information on a range of conditions and topics, and explains the work we do to ensure the voice of PID patients is heard.

If we can be of any help, please contact us at hello@piduk.org or on **0800 987 8986**, where you can leave a message.

Support us by becoming a member of PID UK. It's free and easy to do via our website at www.piduk.org/register or just get in touch with us. Members get monthly newsletters.

PID UK is reliant on voluntary donations. To make a donation, please go to www.piduk.org/donate



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HLH

Haemophagocytic lymphohistiocytosis (HLH)

Information for families

hello@piduk.org
0800 987 8986
www.piduk.org



About this leaflet

This booklet has been produced jointly between PID UK, Great Ormond Street Hospital (GOSH) and the Great North Children's Hospital and in association with Histo UK. The information has been reviewed by the PID UK Patient Representative Panel and endorsed by the PID UK Medical Panel but should not replace advice from a clinical immunologist or a geneticist. It is designed to help answer questions families may have about the condition called haemophagocytic lymphohistiocytosis (HLH).

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What is HLH?

Haemophagocytic lymphohistiocytosis (HLH) is a rare immune disorder where the body reacts inappropriately to a 'trigger', usually an infection. Specialised white blood cells (known as T-cells and macrophages) become over-activated, causing severe inflammation and damage to tissues such as the liver, spleen and bone marrow.

HLH is a rare disease and it can be difficult to diagnose because many of the symptoms can mimic severe infection or other conditions.

What causes HLH?

There are two main types of HLH: primary ('familial') and secondary. Primary HLH is caused by a genetic mistake (mutation) that can be passed on from parent to child. In primary HLH, mutations usually affect the ability of white blood cells to clear infections.

It can be inherited either in an autosomal recessive manner, which means that a child has to inherit the faulty gene from both parents to develop the condition (Figure 1), or in an X-linked manner, which means that the faulty gene is carried on the X chromosome and only affects boys (Figure 2).

Sometimes mutations can just happen, by chance, and are not inherited from parents. More information about genetics is available in our separate leaflet: www.piduk.org/static/media/up/geneticaspectsofpid.pdf

Secondary HLH is not inherited but rather develops as a result of another illness, usually a widespread infection or immune disorder.

Primary HLH usually shows up within the first year of life, while secondary HLH typically develops later in childhood, although it can appear at any age. Both types can present in the same serious and life-threatening way.

What are the signs and symptoms of HLH?

The symptoms of HLH can be confused with common childhood illnesses but are more severe. They include a skin rash, raised temperature and swollen liver, spleen and lymph glands. There may be anaemia, infection or bruising and bleeding. If the brain is affected, a child may show symptoms such as seizures, ataxia (wobbliness) or drowsiness.

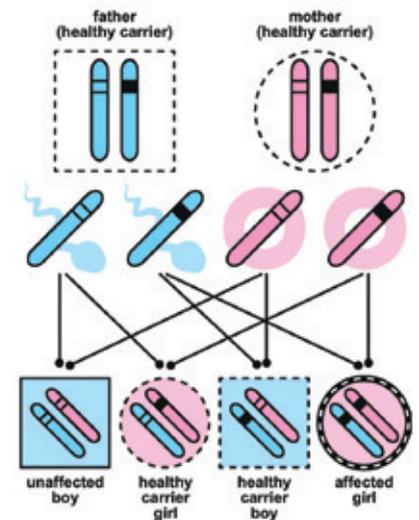


Figure 1:
Mechanism of autosomal recessive inheritance
Diagram: © UCL Health Creatives 2015

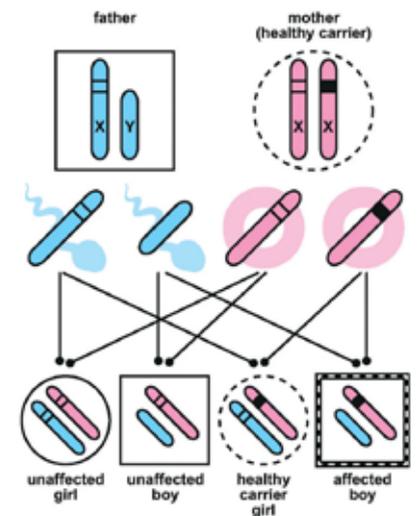


Figure 2:
Mechanism of X-linked inheritance
Diagram: © UCL Health Creatives 2015



How is HLH diagnosed?

Initially, blood samples are taken for testing in the laboratory. A wide range of tests will be carried out, including full blood count to look for low numbers of each type of blood cell. More specialised tests will check liver function and look for signs and causes of infection. Some of these blood tests have to be sent to a specialist laboratory and it takes several days for the results to come through.

Other samples, such as bone marrow or lymph node tissue, may give extra clues. If there are neurological (brain) symptoms, a sample of cerebrospinal fluid may be taken by lumbar puncture.

If HLH is strongly suspected, genetic tests will be done which can identify the faulty genes in the primary forms of HLH.

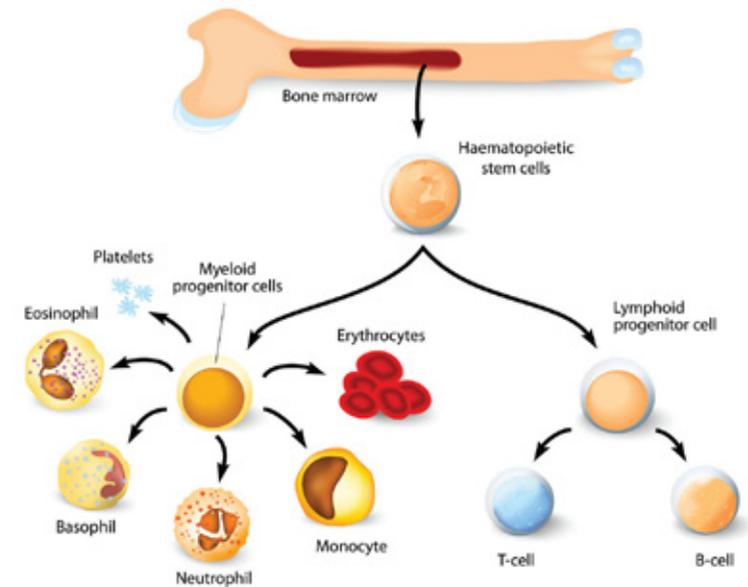
How is HLH treated?

As HLH is uncommon and serious, treatment is usually coordinated by a specialist centre experienced in treating rare immune disorders.

The priority of treatment is to damp down (suppress) the immune system to reduce the over-reaction and lessen the risk of tissue damage. This will often involve courses of corticosteroids and chemotherapy medicines, usually given into a vein (intravenously) in hospital. Some of the medicines used are listed in the table below but new treatments are being developed all the time.

Treatment will be individualised to minimise side effects, which your medical team will discuss with you. If an infectious trigger is suspected, anti-infection treatment may be given, such as antibiotics or other medication. In the case of primary HLH, this treatment usually puts the condition into remission but the risk of relapse remains.

Type of drug	Example	How it is given
Steroids	Dexamethasone, prednisolone	Daily injection into a vein or by mouth
Calcineurin inhibitor	Cyclosporin	Twice daily, into a vein or by mouth
Cytotoxic chemotherapy	Etoposide	Into a vein, twice weekly at first then less often over time
	Methotrexate	By injection into the fluid around the spinal cord, up to four doses weekly if the brain is affected
Biologics	Alemtuzumab	Into a vein, daily for a few days



Corrective treatment of HLH

In many cases, haematopoietic stem cell transplant (HSCT, including bone marrow transplant, or BMT) offers the potential for long-term cure of primary HLH. HSCT aims to replace the faulty immune system with an immune system from a healthy donor. Stem cells, from which all the cells of the immune system develop, can be obtained from healthy bone marrow, or in some cases from umbilical cord blood or donor blood. The healthy stem cells can be given by transfusion into a vein to a child with HLH. More information on HSCT can be found at www.piduk.org/whatarepids/treatment/bonemarrowtransplantation

What happens next?

The outlook for children with HLH has improved, owing to better recognition of the condition and better diagnostic tests so that treatment can start as quickly as possible. New types of medicine are also being developed to treat HLH. Treatment is intensive and has side effects but many of these can be managed. HSCT remains the only cure for primary HLH but in many cases means that children can lead a normal life afterwards.

In the inherited forms of HLH, genetic counselling for the family is important. Prenatal diagnosis is available for future pregnancies, provided that the faulty gene can be identified.

Is there a support group?

PID UK is the main support organisation in the UK for anyone affected by a primary immunodeficiency disease. Call our helpline on 0800 987 8986 or visit our website at www.piduk.org

Histio UK offers support and advice to families affected by all types of histiocytosis. Call them on 07850 740241 or visit their website at www.histiouk.org

The leaflet How to become a bone marrow donor can be obtained from Anthony Nolan by ringing 0303 3030303 or visiting their website at www.anthonynolan.org

