ALPS

Autoimmune lymphoproliferative syndrome (ALPS)

Information for families

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NHS Foundation Trust

THE great north CHILDREN'S HOSPITAL

PID UK
Supporting families affected by primary immunodeficiencies

About this leaflet

This leaflet is designed to help answer the questions families may have about the condition called autoimmune lymphoproliferative syndrome (ALPS).

It has been produced jointly by PID UK and the paediatric immunodeficiency centres at Great Ormond Street Hospital (GOSH) and the Great North Children's Hospital. The information has been reviewed by the PID UK Patient Representative Panel and families affected by ALPS and endorsed by the PID UK Medical Panel but should not replace advice from a clinical immunologist or a geneticist.

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Autoimmune lymphoproliferative syndrome (ALPS) First edition April 2018

What is ALPS?

Autoimmune lymphoproliferative syndrome (ALPS) is a rare genetic disorder associated with an excessive number of lymphocytes (lymphoproliferation), leading to enlargement of the lymph nodes (lymphadenopathy) and the spleen (splenomegaly). These lymphocytes can attack other parts of the body, particularly other blood cells, leading to autoimmune disease. This often shows up as anaemia or bruising.

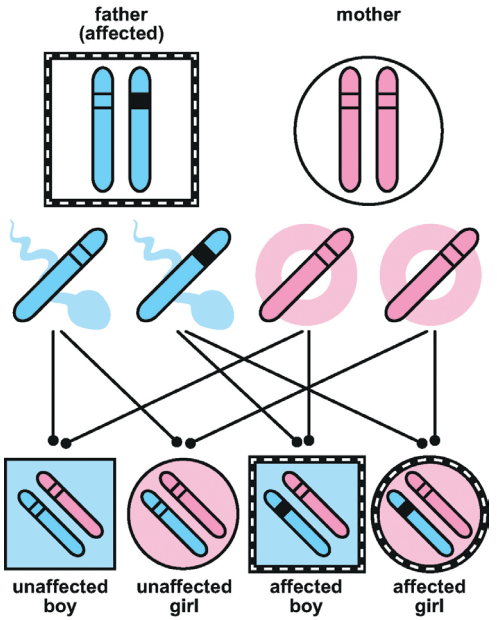
What causes ALPS?

ALPS results from mistakes (mutations) in one of a number of genes controlling how lymphocytes work. The most common gene affected is called *FAS*. These mutations cause the immune system to remain active even when no infection is present.

Inheritance and ALPS

In most people with ALPS, a single copy of the faulty gene is passed on from one parent and a normal copy from the other parent. This is called autosomal dominant inheritance. Not all people with a faulty copy of the gene get ALPS. 40 per cent will not show any symptoms, so parents may not realise they carry the gene.

Sometimes new gene defects can occur 'out of the blue' in people with no history of the disorder in their family. If the genetic change occurs at the time of conception (in the eggs or sperm) it is called 'sporadic' and could be passed on to the next generation. If it occurs later in the development of the embryo, the gene mutation only affects blood cells and is called a 'somatic' variant, which cannot be passed on to future generations.



Mechanism of autosomal dominant inheritance

Rarely ALPS is inherited in an autosomal recessive pattern, which means that each parent passes on the altered gene but does not show any symptoms themselves.

More information about the different patterns of inheritance and their implications for family planning can be found in our leaflet *Genetic aspects of primary immunodeficiency*: **www.piduk.org/whatarepids/geneticaspectsofpid**

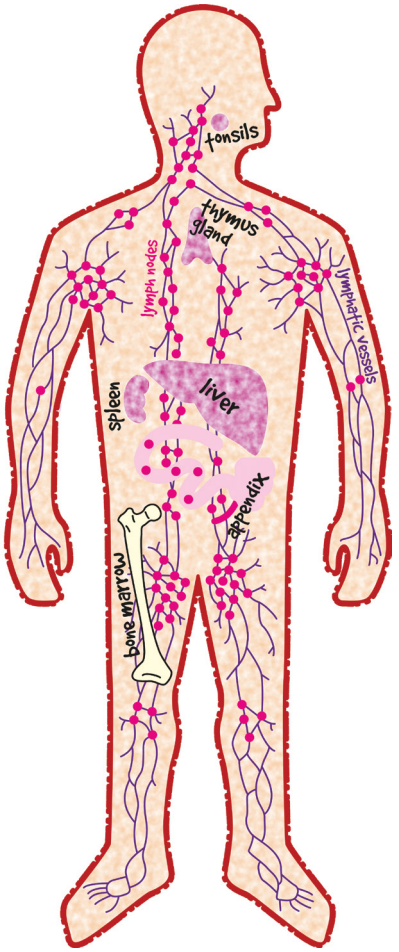
What are the signs and symptoms?

ALPS shows up in various ways at different stages of life.

Lymphoproliferation affecting the spleen and lymph nodes generally appears during childhood. Parents may notice persistently enlarged glands in the child's neck, armpits and groin. Often there are no other symptoms at this stage.

Patients with ALPS are at increased risk of autoimmune disease, which occurs when the immune system malfunctions and attacks the body's own tissues. A classic form of ALPS-related autoimmunity occurs when antibodies are formed that attack red blood cells (haemolytic anaemia) and platelets (thrombocytopenia), leading to tiredness and pallor, easy bruising and bleeding. This combination is called Evans syndrome. Other autoimmune diseases are much less common.

Although the majority of people with ALPS do not get lymphoma, ALPS is associated with an increased risk of this cancer of the white blood cells in adulthood. Lymphoma causes symptoms such as fever, fatigue, loss of appetite, weight loss or more marked enlargement of one or more lymph nodes. Doctors and patients will look out for these features so that appropriate tests and treatment can be arranged.



The lymphatic system and lymph nodes
Lymph nodes are located in groups in the body. They are small glands that filter lymph, the fluid that circulates through the lymphatic system.

How is it diagnosed?

The diagnosis of ALPS depends on recognition of suggestive clinical features, along with blood tests looking at the different types of lymphocytes, particularly some called double-negative T lymphocytes. There are many conditions that can cause similar symptoms and it is important that careful evaluation is performed to exclude any of these. Special tests, including genetic tests, are available if ALPS is strongly suspected.

Complications of ALPS may need to be evaluated in their own right; for example, by scans or further blood tests. If lymphoma needs to be ruled out, a small biopsy of one of the lymph glands might be performed.

How is it treated?

Most patients do not require any treatment but just need to have the size of their glands and the number of blood cells present in a blood sample monitored regularly. Some patients might require medication to control the overgrowth of lymphocytes or autoimmune complications. This immunosuppressive treatment will be individualised for each patient's problems and needs. For very severe disease, replacement of the abnormal lymphocytes by haematopoietic stem cell transplantation might be considered, but this is rare.

The patient's spleen can be quite big, but generally this should be treated with medicines rather than splenectomy (surgical removal of the spleen). This is because the spleen does an important job in protecting us from serious infection.

What does this mean for the future?

Most people with ALPS have a good outlook. Symptoms often improve after puberty. The increased risk of lymphoma means patients should be followed up by a specialist. Genetic counselling, both for affected people and for family members, is important if the genetic cause is known.

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**

PID UK is affiliated to the International Patient Organisation for Primary Immunodeficiency (IPOPI) (**www.ipopi.org**)

Glossary of terms

anaemia a condition of abnormally low haemoglobin in oxygen-carrying cells, causing pallor and tiredness. Can be caused by poor diet, autoimmunity and other medical conditions.

autoimmunity immune reaction against the body's own tissues.

autosomal dominant a type of inheritance. If a faulty gene is dominant, it will show an effect even though there is a working copy of the gene on the other chromosome. A person only needs to inherit one faulty gene from one parent to develop a disease in a dominantly inherited condition.

autosomal recessive a type of inheritance where the presence of one copy of a faulty gene does not affect the individual him or herself. However, when two carriers of the same faulty gene have children there is a 25 per cent (or 1 in 4) chance of a child inheriting two copies of the faulty gene (one from each parent) for each pregnancy. If this happens, the child is affected by the disorder.

biopsy for diagnostic purposes, surgical removal of a small sample of tissue for examination under a microscope.

double-negative T cells a subgroup of T cells, normally present in very low numbers, that are increased in number in patients with ALPS.

Evans syndrome the combination of autoimmune haemolytic anaemia, neutropenia and/or thrombocytopenia.

FAS a highly specialised protein involved in controlling the number of cells. Defects in this type of protein are one of the causes of ALPS.

gene section of DNA on a chromosome that codes for a functional RNA molecule and thus a protein. Put another way, a word, rather than a letter, in the genetic code. Genes are the fundamental units of inheritance that carry the instructions for how the body grows and develops.

genetic counselling advice from a specialist geneticist regarding the implications of carrying or being affected by a genetic disorder.

haematopoietic stem cell transplant (HSCT) transfer of stem cells from a donor – either related or unrelated – to a recipient. Stem cells may be obtained from bone marrow (from the hip bones – this is also known as bone marrow transplantation), peripheral blood (PBSCs), or from stored umbilical cord blood. Haematopoietic means 'blood-forming'. The donor cells are given by intravenous infusion and make their way to the recipient bone marrow to provide a new immune system and cure the immunodeficiency.

haemolytic anaemia anaemia caused by destruction of the red blood cells.

immunosuppressives medications that suppress or 'damp down' the immune system; used to suppress inflammation and autoimmunity.

lymphadenopathy enlargement of the lymph nodes.

lymphocytes small white blood cells, normally present in the blood and in lymphoid tissue, that carry out the functions of the immune system. There are two major forms of lymphocytes, B cells and T cells, which have distinct but related functions in generating an immune response.

lymphoma a cancerous growth of lymphocytes.

lymphoproliferation excessive numbers of lymphocytes, causing enlarged lymph nodes, liver and spleen, and sometimes affecting other organs.

mutation a change in the structure of a gene or group of genes. When mutations occur in the germline (eggs/sperm), such changes can be passed on to the next generation. Many mutations cause no harm, but others can cause genetic disorders, such as primary immune deficiencies.

neutropenia abnormally low numbers of neutrophils in the blood.

platelets tiny cell fragments that circulate in the bloodstream and which are important for preventing bleeding by forming blood clots.

splenectomy surgical removal of the spleen.

splenomegaly enlargement of the spleen.

T cells (or T lymphocytes) lymphocytes that are processed in the thymus, an organ in the chest. They are important players in the immune response.

thrombocytopenia abnormally low numbers of platelets in the blood.

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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Part of Genetic Disorders UK