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Registered Charity No 1111075

This leaflet has been prepared in good faith to provide patients with a guide to current services and information. Neither GIG nor The XLP Research Trust can be held responsible for the accuracy of the information it contains. Links to other organisations are included for information purposes only and are not recommendations from GIG or The XLP Research Trust.

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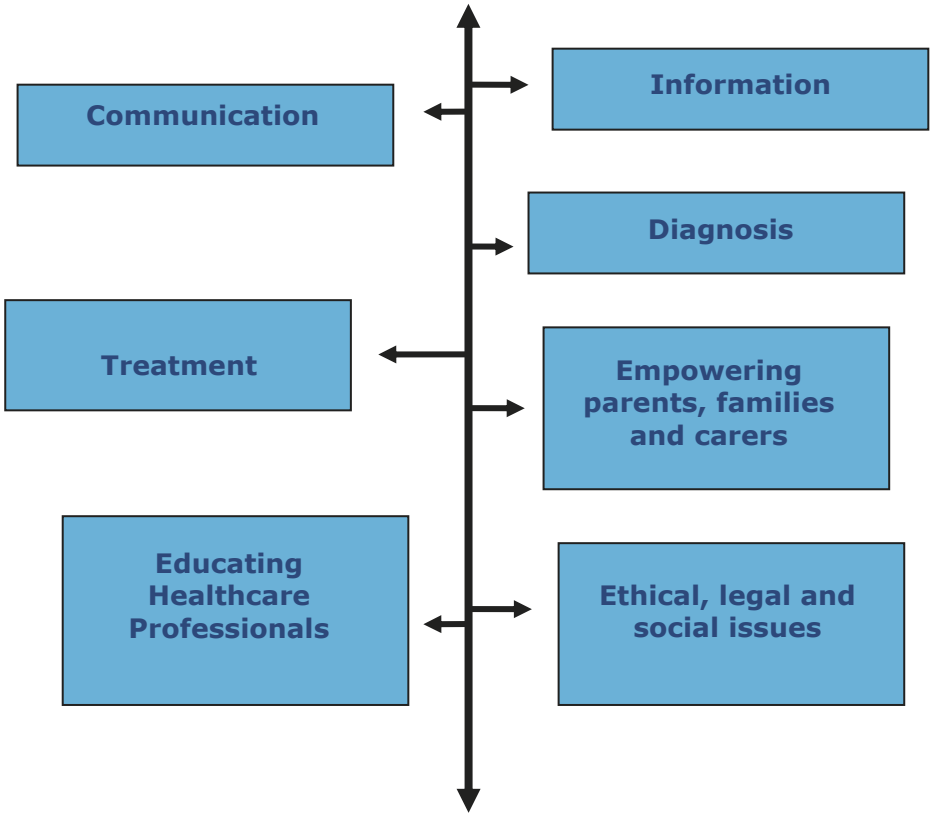
Version 2.0

X-Linked Lymphoproliferative Syndrome

Family Route Map

This Family Route Map is a guide to current UK services and information.



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INTRODUCTION

This leaflet is designed to provide signposts to sources of current information and appropriate services for patients, their families and carers, together with healthcare professionals. The issues and concerns raised during a series of patient focus groups in 2006 organised by the Genetic Interest Group (GIG) identified seven themes (see front cover) which have been used as the basis for developing this resource. This guide will help you find the information you need about X-linked Lymphoproliferative syndrome (XLP) quickly and easily.

The XLP Research Trust was founded in the UK by David and Allison Hartley who have four sons with XLP. Official charity status was granted in September 2005.

The main aims and objectives are to:-

- Promote and fund research into the cause, management, symptoms and cure for XLP
- Provide a point of contact and support for those families affected by XLP
- Raise the awareness of XLP amongst the medical profession and the general public

Contact details*:*

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Links to other useful organisations:

British Society for Gene Therapy (BSGT): **www.bsgt.org**

Contact-A-Family: **www.cafamily.org.uk** Tel: 020 7608 8700

Department of Health have produced a set of 'Questions to ask' to take with you to your appointment with a specialist. Available in several different languages; use the Search option on their website. **www.dh.gov.uk**

Directgov **www.direct.gov.uk** A website with help on benefits and entitlements

Disability Benefits Office Tel: 08457 123456

Disablement Income Group Scotland **www.digscotland.org.uk**
Tel: 0131 555 2811

GIG (Genetic Interest Group) have a range of patient leaflets on their website **www.gig.org.uk/eurogentest_patientleaflets.htm** Tel: 020 7704 3141

Primary Immunodeficiency Association (PiA) is a UK umbrella organisation supporting people with and promoting awareness of primary immunodeficiencies and disorders of the immune system. **www.pia.org.uk**

Bone Marrow Registries

Because bone marrow transplant is the definitive treatment of choice today it is worth finding more information on this option from the following organisations.

Anthony Nolan Trust: **www.anthonynolan.org.uk**

National Blood Service for England and North Wales: **www.blood.co.uk**

Scottish Blood Transfusion Service: **www.scotblood.co.uk**

The Welsh Blood Service: **www.welsh-blood.org.uk**

UK Hospitals specialising in bone marrow transplant for XLP

The following hospitals are the usual centres for undergoing a bone marrow transplant for XLP.

Great Ormond Street Hospital - Fox Ward: **www.ich.ucl.ac.uk**

Newcastle General Hospital - Ward 23: **www.newcastle-hospitals.org.uk**

PATIENTS, FAMILIES AND CARERS

Contacting other XLP families

The XLP Family Forum is a safe on-line environment which allows XLP affected families to communicate with other similarly affected families from around the world. This web site can be accessed through the XLP Research Trust's home web page **www.xlpresearchtrust.org**

Financial help

Living with a long-term condition requiring frequent hospital visits or admission for check-ups or treatment can put a strain on finances. The Citizens Advice Bureau (CAB) can help with advice locally about benefits and can be found through your phone directory or visit their website **www.citizensadvice.org.uk** and information on benefits, taxes and debt: **www.adviceguide.org.uk**

Psychological help

Psychological counselling is not commonly offered on diagnosis or even later on. If you feel that you need extra help in coming to terms with your condition or any other aspect of your life, don't be afraid to ask for this via your GP or immunology specialist.

Travel insurance

It is common to have difficulties finding adequate and affordable insurance policies once you have a pre-existing condition. The following company offers travel insurance for people with pre-existing conditions. There may be others available and this should not be taken as a recommendation:

The insurance group Banner - see **www.bannergroup.com** have agreed to look at and consider insuring anyone, however they cannot guarantee that they will cover everyone for all conditions. Each case is assessed on an individual basis.

TIP
Say how you feel: if you don't want medical students participating in your appointments; or clinical staff discussing your child in front of them, don't be afraid to say so.

INFORMATION

X-linked lymphoproliferative syndrome (XLP), which is also known as Duncan's syndrome, is a rare always fatal disease that affects only boys. To date only about 100 families and 400+ boys have been diagnosed worldwide. It is likely, however, that there are many more cases where the correct diagnosis has not been made.

XLP can have many symptoms including: severe glandular fever, cancer of the blood (lymphoma) and inability to fight off infections and sometimes severe anaemia. 70% of individuals with XLP die by the age of 10 years without any treatment. The cause of the condition was only found in 1998 so there is still a lot to learn.

The best 'prevention' is regular top ups of anti-viral medicines, immunoglobulin therapy or steroids, but these are not a cure. Today the only possible cure is a bone marrow transplant, in effect replacing the faulty immune system.

Genetic Testing

If XLP is suspected, then the boy should be referred to an immunology specialist. They will be able to arrange for a genetic test although currently this is only available through Great Ormond Street Hospital in London but blood can be sent there by your local immunologist. As XLP is an inheritable condition, other family members will be offered predictive gene testing if XLP is diagnosed.

There are a number of issues surrounding genetic testing particularly in relation to children and as such, many patients may wish to be seen and counselled by a consultant clinical geneticist as early on as possible. The Genetic Interest Group (GIG) website has a series of leaflets explaining more about inherited conditions and includes; a glossary of terms used in genetics, and useful questions to ask when going for an appointment.

Please see **www.gig.org.uk/eurogentest_patientleaflets.htm**

The UKGTN (UK Genetic Testing Network) has produced a patient leaflet to help understand testing. Available at their website http://www.ukgtn.nhs.uk/gtn/digitalAssets/0/211_PatientLeaflet.pdf.

DIAGNOSIS, TREATMENT AND SURVEILLANCE

The diagnosis of XLP is suspected in males who have a severe, abnormal immune system response to infection with Epstein-Barr virus (EBV). EBV is a common virus in the normal population, which causes infectious mononucleosis (glandular fever). In normal males, EBV causes no long lasting ill effects. In males with XLP, there is a either a mutation (mistake) in the XLP *SH2D1A/DSHP/SAP* gene (XLP-1) or *BIRC4* (XLP-2). These genes helps control the immune response to an EBV infection and codes for the SAP protein. As a result, males with XLP who are exposed to the EBV virus can have life-taking threatening symptoms. Patients can experience swollen lymph nodes (glands in the neck or groin), sore throat, fever, and severe hepatitis. After infection with EBV, some patients develop aplastic anaemia (low levels of all types of blood cells) and hypogammaglobulinemia (low levels of anti-bodies in the bloodstream), Severe symptoms occur because the im-mune system cannot effectively handle the EBV as in normal individuals and can include severe glandular fever and lymphoma.

Most XLP-2 affected boy develop HLH related to EBV infection (also re-ferred to as VAHS) but in some cases they show HLH without having EBV as the obvious trigger. Typical symptoms of HLH besides persistent fever are pallor (paleness), jaundice, liver and spleen enlargement, and neurological symptoms, such as irritability or even seizures.

The diagnosis will be suggested by the pattern of illness in the child and their family. In most children XLP can be confirmed using a blood test. This will check if the protein, SAP, that makes the cells work properly is present, and will also look for the mistake in the gene. In some families there may not be a mistake in these particular genes, and the diagnosis can be made on the clinical story only.

Initially treatment will be given for the symptoms that the boy presents with, this may include anti-viral medicines, immunoglobulin therapy and/or antibiotics. These will be given to keep them well in the short to medium term. Bone marrow transplant is the definitive treatment of choice at the present time, This can be a difficult procedure, requiring a prolonged hospital stay and can present its own particular risks.

INFORMATION FOR HEALTHCARE PROFESSIONALS

Information, support and articles about XLP from the XLP Research Trust at **www.xlpresearchtrust.org**

More general information can be found on the following websites:

The National Organization for Rare Diseases **www.rarediseases.org**

Orphanet (European database) **www.orpha.net**
Free-access website providing information on rare diseases. Search on 'x-linked lymphoproliferative disease'.

European Society for Immunodeficiencies **www.esid.org**

The NHS National Genetics Education and Development Centre
www.geneticseducation.nhs.uk
provide information and resources for healthcare professionals.

PubMed is a service of the U.S. National Library of Medicine and the National Institute of Health and is free to join after registration. Search for 'XLP' and a comprehensive list of worldwide medical research papers on XLP is returned. **www.pubmed.gov**

TIP
It is good to communicate with other families affected by XLP to share experiences and build friendships. The XLP Research Trust's on-line XLP Family Forum is an easy and safe way to contact other families from around the globe.