

X-linked Lymphoproliferative Disease (Duncan's syndrome)

X-linked lymphoproliferative syndrome (XLP) is also known as Duncan's syndrome. It is a genetic defect that causes the immune system to respond abnormally to some viral infections. This can result either in an underactive immune system (immunodeficiency) or an overactive immune system, which can cause as many problems.

How common is XLP?

XLP is extremely rare, and only about 100 families with XLP are known to exist worldwide. It is likely, however, that there are many more individuals whose disease is as yet unrecognised.

What are the features of the condition?

XLP can have many different symptoms, and we do not yet know what the full spectrum of the disease is. We think the immune system in XLP is unable to cope with some viral infections, in particular the Epstein Barr Virus (EBV). The immune system loses its normal tight regulation, and starts to malfunction.

About a third of patients have a very severe episode of glandular fever. Another third develop a cancer of their blood cells (lymphoma) and another third have low levels of immunoglobulins, the proteins in the blood that help fight infection. More rarely, patients may have a severe form of anaemia or inflammation of small blood vessels (vasculitis). It is common for one individual to have several different symptoms over the course of their illness.

What are the symptoms of the different features?

Severe glandular fever

Lymphoma - patients may be tired, anaemic and develop swollen glands.

Hypogammaglobulinaemia (low levels of immunoglobulins) - patients may get frequent infections

What causes the condition?

The cause of the condition was only found in 1999, so there is much we do not understand about it.

It is caused by a mutation (mistake) in one of the genes on the X chromosome. This means the cell does not get the right instructions it needs to work properly. In most families, the mistake is in a gene called SH2D1A. This gene normally makes a protein called SAP. Mistakes in the gene cannot be found in a number of people with the disease, and we are working hard to find out which gene is responsible in these families.

How is the condition inherited?

The X chromosome is one of the sex chromosomes: females have two X chromosomes and males have one X and one Y. Each X chromosome carries one copy of the gene. If a male has a faulty gene on his X chromosome, he will have the disease. However, because the female has two X chromosomes, the normal gene on one X can compensate for the faulty one on the other. As a result, only males get the disease, although females may carry the disease but be unaffected. This is an X-linked disease and within a family tree you may be able to pick out other affected males.

For more information about genes and genetics, please see our leaflet Genetics and inheritance: information for families.

Are all children in the family affected?

No, if a mother carries the disease, each time she has a female child, there is a 50 per cent chance the child will be a carrier. Each time she has a male child, there is a 50 per cent chance the child will be affected by the disease.

How is XLP diagnosed?

The diagnosis will be suggested by the pattern of illness in a child and his family. In most children we can confirm the diagnosis 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 this particular gene, and the diagnosis can be made on the clinical story alone.

What treatment can be given for the condition?

Initially treatment will be given for your child's symptoms, and may include anti-viral medicines, immunoglobulin therapy or steroids. Ongoing supportive treatments, such as immunoglobulin and antibiotics, will be given to keep them well in the short to medium term. Bone marrow transplantation is the definitive treatment of choice at the present time. This can be a difficult procedure, requiring a prolonged hospital stay.

What is the outlook for people with the condition?

Seventy per cent of individuals with XLP die by the age of 10 years without any treatment. However, as we are learning more about the disease we are identifying adults with milder forms of the condition.