PID UK
www.piduk.org

Patient information sheet
ADA-SCID

# Adenosine deaminase-deficient severe combined immunodeficiency (ADA-SCID)

This information should be read in conjunction with the general overview leaflet on SCID available at **www.piduk.org/static/media/up/SCID.pdf**

ADA-SCID is a specific form of severe combined immunodeficiency (SCID). It is inherited as an autosomal recessive condition. This means that a child has to inherit the faulty gene from both parents to have the condition. There may be a family history of previously affected children, particularly if there are first or second cousin marriages or partnerships in the family. More information about autosomal recessive inheritance can be found in our leaflet *Genetic aspects of immunodeficiency*, available on our website at **www.piduk.org/whatarepids/geneticaspectsofpid**

## Causes of ADA-SCID

ADA-SCID is caused by mistakes (mutations) in the *ADA* gene, which result in absent or very low levels of the enzyme ADA. Enzymes are protein substances that help speed up chemical reactions in the body. Lack of the ADA enzyme causes a build-up of a toxic substance called deoxyadenosine. This prevents cells from dividing effectively.

White blood cells (especially lymphocytes, and more specifically T cells, B cells and natural killer (NK) cells) that are important for a healthy immune system are very sensitive to these toxic effects and fail to develop normally, leading to SCID. However, the *ADA* gene is important in all cells of the body, and therefore patients with ADA-SCID often also have symptoms and signs outside the immune system. In some cases there may be a low level of working ADA enzyme, leading to a less severe 'delayed' onset of combined immune deficiency (CID) – please refer to our separate CID information leaflet **www.piduk.org/static/media/up/cidinchildren.pdf**

## Signs and symptoms of ADA-SCID

The signs and symptoms of the immunodeficiency in ADA-SCID are the same as in all other forms of SCID. However, patients with ADA-SCID can also have some or all of the following problems:

- Bones: unusual rib ends may be seen on a chest X-ray, and other changes of bone development sometimes occur but do not usually cause symptoms.
- Central nervous system: development may be slower than in healthy children and there may be behavioural and psychological problems, such as hyperactivity and poor social behaviour.
- Hearing: deafness is sometimes a problem.

There may also be problems with other body systems, including the kidneys, liver and lungs.

## Diagnosis of ADA-SCID

Infants with typical early onset ADA-SCID have poor growth and frequent, severe and unusual infections, such as pneumonia with an organism called *Pneumocystis jirovecii* (a yeast-like fungus) that does not usually cause illness in healthy individuals. Breathing difficulties can also occur in infants with ADA-SCID without any detectable infection.

Blood count testing shows a very low lymphocyte count, and basic immunology tests show very low or absent levels of T, B and NK lymphocytes. Doctors refer to this pattern of SCID as 'T -, B -, NK - SCID', and this is highly suggestive of a diagnosis of ADA-SCID. The level of ADA enzyme activity in the blood can be measured and is usually less than one per cent of the normal levels seen in healthy children. Additionally, the levels of adenosine can be measured and will be much higher than normal.

### Other (non-immunology) investigations

If ADA deficiency is confirmed, it is important to assess hearing as early as possible because of the high risk of deafness. A psychologist will also carry out a developmental assessment. The need for other investigations will depend on whether other systems of the body are involved.

## Treatment of ADA-SCID

The first stages of treatment and precautions are the same as in all forms of SCID.

However, in contrast to other forms of SCID, it is possible to replace the missing enzyme using a medication known as PEG-ADA. This is often referred to as enzyme replacement therapy. It is given as a weekly injection into a muscle, for instance, the thigh muscle.

PEG-ADA treatment corrects the ADA and adenosine levels in the blood, and usually leads to gradual improvement and partial correction of immune function. It can be used until a more definitive therapy is available, such as haematopoietic stem cell transplant (HSCT) or gene therapy.

Clinical trials of gene therapy for ADA deficiency are ongoing in Europe and the USA, with Great Ormond Street Hospital being one of the centres where this treatment is available. A related, commercial gene therapy treatment called Strimvelis has been recently approved by NICE and is available to families as an alternative treatment in Milan. The differences between these different gene therapy options will be discussed with the families in detail. The choice between HSCT or gene therapy will depend on whether there are well-matched donors available for transplant and will be discussed at length between the parents and the transplant and gene therapy teams.

It can be helpful to meet another family who has a child with SCID and who has undergone HSCT or gene therapy. Speak to your immunology team, who may be able to arrange a meeting with a suitable family.

## What does this mean for the future?

Long-term follow-up will be important even after successful treatment of ADA-SCID. The non-immune signs and symptoms of ADA-SCID, particularly developmental, behavioural and psychological effects, will need to be carefully monitored and managed.

Genetic counselling is important for future family planning as both parents will usually carry a copy of the faulty gene and any subsequent children born will have a 1 in 4 chance of being affected. This risk is the same with every pregnancy. Carrier testing for at-risk family members and prenatal testing for future pregnancies are available once the genetic mutation has been identified in the family. Please refer to PID UK's booklet *Genetic aspects of PID* for furtherinformation: **www.piduk.org/static/media/up/geneticaspectsofpid.pdf**

*The information 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 ADA-SCID and endorsed by the PID UK Medical Panel but should not replace advice from a clinical immunologist or a geneticist. (February 2018).*

## About Primary Immunodeficiency UK

Primary Immunodeficiency UK (PID UK) is a national organisation supporting individuals and families affected by primary immunodeficiencies (PIDs). Our website 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. Visit www.piduk.org for further information.

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

## Other sources of support

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