Guide for parents

Treatment for ADA deficiency

Newborn screening and prompt curative treatment for scid saves lives!

Prompt diagnosis of SCIDs, made possible by newborn screening, provides the best chance for successful treatment for your baby through an early intervention.

PID FOUNDATION Barcelona

Available at **www.pidfoundationbcn.org**

↑ Carla, 5 years old

The patient's voice

Living with ADA deficiency

What did your daughter's diagnosis of ADA deficiency mean to you?

It's a radical change in all aspects of life. The uncertainty of waiting for a donor and transplantation can be distressing.

How did you cope with stem cell transplantation (SCT)?

Our basic feeling during all stages of the process, even today four years after SCT, has been fear. However, our daughter is healthy now and we are a happy family; transplantation cured her.

What would you consider the ideal treatment for ADA deficiency?

Specific treatments to manage the disease without the need for transplantation with its associated risks.

↑ Abel, 3 years old

A patient's personal experience ...

As parents, the diagnosis meant special attention during each infection our son might have. Initially, we were concerned about the possibility of transplantation, and we were very happy when **Gene Therapy** was proposed.

This treatment is less aggressive than transplantation because the baby's own bone marrow is used, so there are no problems of compatibility and there is less need to suppress his immune system when infusing the genetically modified cells. In addition, the possibility of post-transplant rejection is much lower.

We would like the treatment to restore his immune system to levels that allow him to have a normal life.

What is ADA deficiency?

Adenosine deaminase (ADA) deficiency is one of the most prevalent forms of severe combined immune deficiency (SCID). It leads to the accumulation of toxic products that prevent proper cell turnover in the bone marrow, thymus, and lymph nodes. It has an autosomal recessive inheritance and an overall incidence of 1 case in every 200,000 newborns. The initial presentation includes recurrent fungal, viral, and bacterial infections, low levels of lymphocytes in blood, failure to thrive, and neurological disorders. The diagnosis is based on an absence or decrease of ADA levels in red blood cells.

Gene analysis by sequencing can detect most of the pathogenic variants of this disease.

Without treatment, ADA deficiency has a fatal course. Most infants with this condition will die within one year after birth, usually due to severe, recurrent infections, although later forms of presentation have been described with less severe clinical manifestations.

Dr. Olaf Neth
Virgen del Rocío Hospital (Sevilla)

Bone marrow transplantation

Hematopoietic stem cell transplantation (HSCT) remains the mainstay of treatment. However, unlike the situation in other types of SCID, 2 additional treatment options are available for ADA deficiency: enzyme replacement therapy with PEG-ADA and gene therapy. HSCT, if successful, offers permanent correction of the disease and long-term immune recovery. Overall survival is better when transplanted cells are from matched related donors than when cells are from matched unrelated and haploidentical donors.

Enzyme replacement therapy

Pegylated ADA is well tolerated and leads to improvements in the disease-onset signs and symptoms. Adverse effects are rare. The treatment is provided by weekly intramuscular infusions and should be started immediately after the diagnosis. However, it is only a bridge therapy, as the effect disappears at long-term and organ damage may occur.

Dr. Luis Ignacio González-Granado
12 de Octubre Hospital (Madrid)

What about gene therapy?

Gene therapy is a feasible and safe curative therapeutic option for these patients. With this approach, a normal copy of the defective gene is inserted into the patient's own hematopoietic stem cells using a virus as a vector (as in the tale of the Trojan horse). It is an excellent option when a family donor is not available.

Over 30 patients have now been treated with gene therapy and the preliminary data indicate excellent effectiveness and safety. One of the first-generation retroviral vectors has now been successfully developed into a commercial product (Strimvelis®). Studies with optimized vectors (lentivirus) are currently ongoing.

Dr. Pere Soler
Vall d'Hebron Hospital (Barcelona)

Ask for help!

It's normal to be anxious and distressed when you know that your baby has a serious medical problem such as SCID. There will be repeated medical visits, tests, and procedures. Maintaining your own physical and emotional health is very important, especially while your child is going through treatment.

It's important to contact a specialized medical team to answer your questions during the diagnosis and treatment of your baby. Psychological support can help you get through this difficult stage.

Don't hesitate to ask for information and help at your center.

Other Resources

Additional information and resources are available at:

- **www.adagen.com**
- **www.primaryimmune.org**
- **www.info4pi.org**
- **www.ghr.nlm.nih.gov/condition/adenosine-deaminase-deficiency**