

Sickle cell disease: Gene therapy



What is gene therapy?

Gene therapy is a procedure that changes specific genes to help treat diseases. Gene therapy is not a surgery. It is a medical treatment that happens over months. Most often, the first month is spent in the hospital.

Gene therapy can treat sickle cell disease by:

1. Removing your child's own cells.
2. Changing them to add or turn on non-sickle hemoglobin or to help faulty genes work properly.
3. Re-infusing them back into your child.

How does gene therapy work?

To understand gene therapy, you need to understand red blood cells and sickle cell disease.

- Red blood cells carry oxygen from your lungs to all the tissues in your body. It does this with a protein called hemoglobin. A gene called the beta globin gene controls the hemoglobin process.
- People with sickle cell disease have a flawed (broken) beta globin gene. The flawed gene causes red blood cells to be crescent moon shaped. They stick together and block blood flow in small vessels. This causes pain and other complications.
- Gene therapy adds or replaces the flawed gene with one that works properly. There are 2 types of gene therapy for sickle cell disease:
 - **Gene addition** puts new, working copies of a gene into cells using a vector, or carrier.
 - **Gene editing** is done by a scientist. They cut the DNA where it is flawed and replace the broken parts with the correct parts.

What are the risks?

The risks of gene therapy include:

- Infection.
- Low blood counts.
- Bleeding and strokes.
- A weakened immune system. This is not long term.
- Infertility (not being able to get pregnant or father a child).
- Side effects that happen months to years after treatment.
- Death (very rare).

Gene therapy is a long process. It puts a lot of stress on children and their families. Your child will need:

- Antibiotics to prevent or treat infection.

In case of an urgent concern or emergency, call 911 or go to the nearest emergency department right away.

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- Platelet transfusions to prevent or treat bleeding.
- Blood transfusions to treat anemia.

What is the process for receiving gene therapy?

1. Cell collection

- Your child's stem cells are collected.
- They are collected from the blood with a special machine. The process is called apheresis.
- A temporary line is placed while your child is asleep. This line is removed after the cells are collected.
- Your child gets a medicine called plerixafor. It forces the stem cells from the bone marrow to the blood.
- The process requires a hospital stay that lasts 4 to 5 days. The care team will watch for side effects. The process may be repeated 3 to 4 weeks later.
- The cells are sent to a lab to be modified. This can take up to 6 months.

2. Preparing for treatment

- Your child gets chemotherapy (chemo) and other medicines that make their immune system weak.
- The medicines destroy the old stem cells. This helps your child's body accept the new cells.
- The medicines have side effects like nausea, vomiting (throwing up), hair loss, mouth sores, poor appetite, diarrhea and low blood counts. These side effects are temporary.

3. Treatment

- The infusion of the gene therapy product happens in the hospital.
- Your child's cells are infused through an I.V.
- It is like a blood transfusion.
- It can take a few minutes to a few hours.

4. Recovery

- The modified blood stem cells go to your child's bone marrow.
- It may take 4 to 6 weeks for the cells to engraft, or settle and start multiplying.
- Your child could be in the hospital for up to 6 weeks.
- Your child will have follow-up visits to the BMT clinic as they recover.
- Your child may require long term follow-up to monitor the effects of treatment. Chemo can cause serious side effects for months to years.

Can my child get gene therapy?

Casgevy and Lyfgenia are the 2 gene therapy products approved for the treatment of sickle cell disease in patients 12 years and older. Gene therapy is not approved for children under 12 years old. There are current studies being done to make gene therapy available for younger children.

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What should I do if my child is sick?

- Call your child's sickle cell team anytime they have a fever of 101°F (38.3°C) or higher. Your child will need to be seen right away.
- Call the doctor on call after 5 p.m. and on weekends and holidays. The doctor will contact the emergency department (ED) to help with your child's care.
- ALWAYS tell the ED doctors and staff that your child has sickle cell disease. Tell them which sickle cell clinic your child visits.

For more details on sickle cell disease and services, visit the Children's Healthcare of Atlanta website at choa.org/sicklecell.

This teaching sheet contains general information only. Talk with your child's doctor or a member of your child's healthcare team about specific care of your child.

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