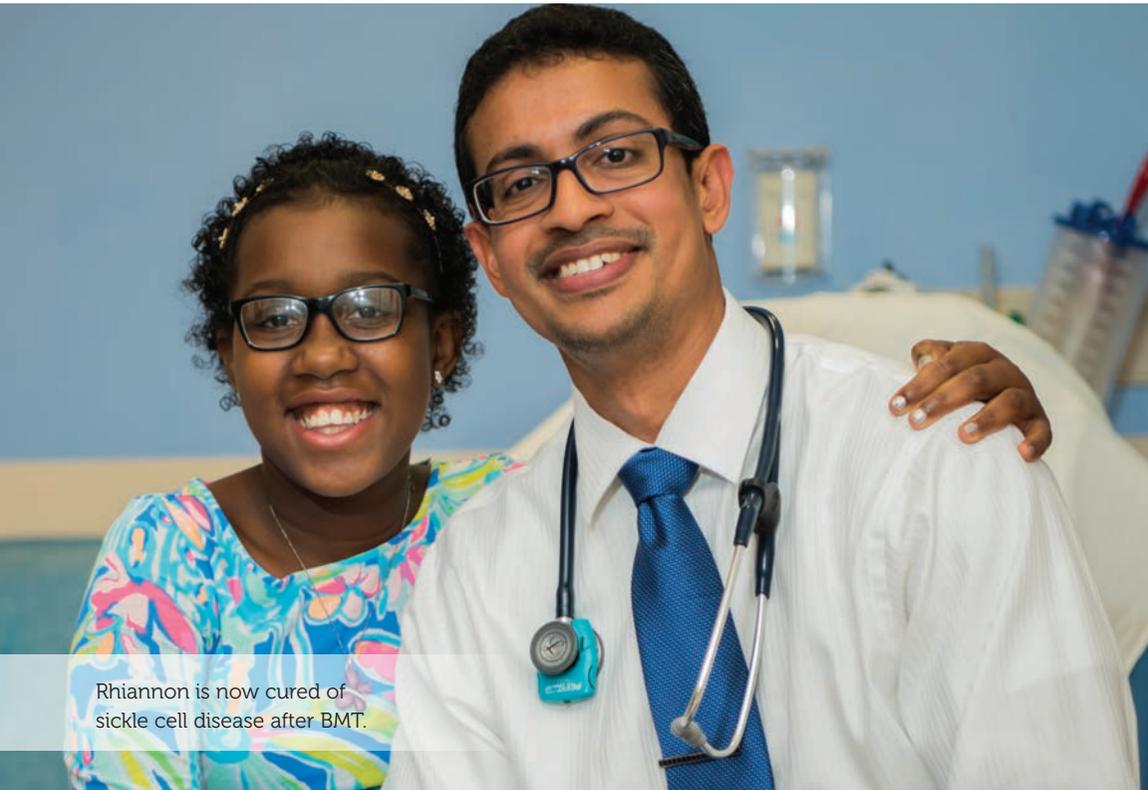


Blood and Marrow Transplant (BMT) for Sickle Cell Disease



Rhiannon is now cured of sickle cell disease after BMT.

Blood and marrow transplant (BMT) is a proven cure for sickle cell disease.

This handbook was created to help answer common questions about BMT. If you have questions after reading the handbook, please share them with your health care team.

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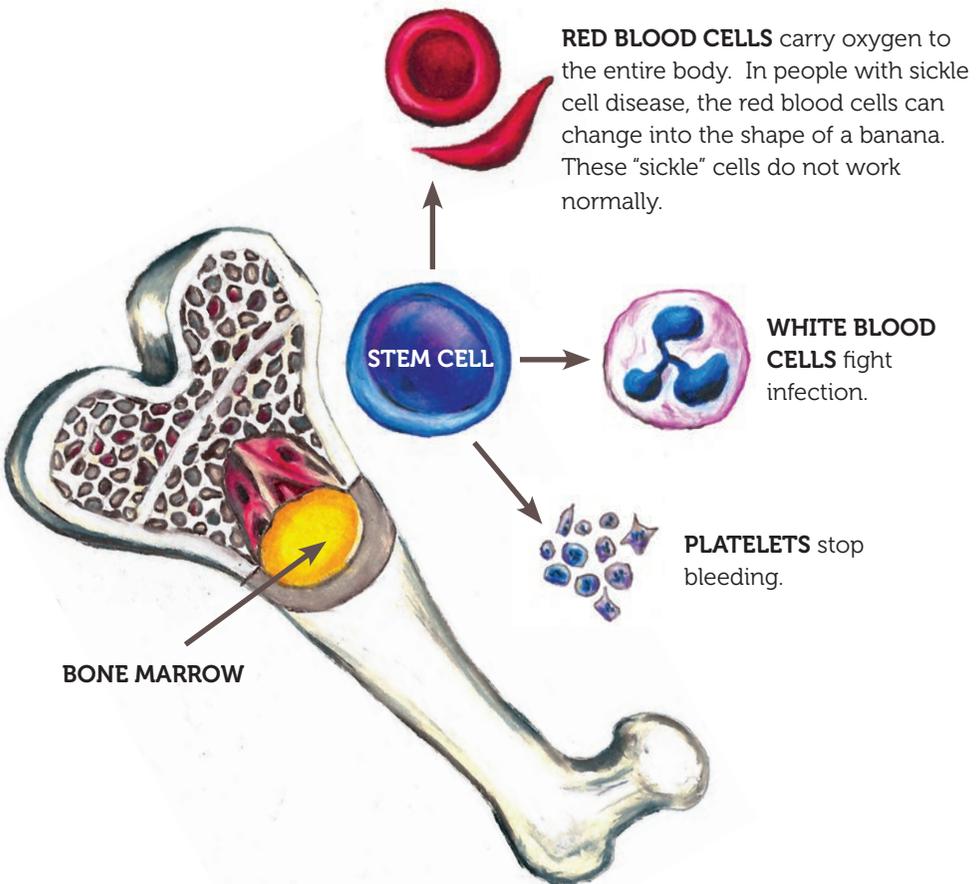
BMT Basics

BMT is not a surgery.

Blood and marrow transplant (BMT) is not like other transplants. BMT is a process to replace a patient's bone marrow with a donor's bone marrow.

Bone marrow is the factory that makes blood cells.

Bone marrow is located in the center space inside bones. The bone marrow contains blood stem cells, which are special cells that grow to become red blood cells, white blood cells, or platelets.



Finding a Donor: HLA Typing

The first step for a patient thinking about BMT is looking for a donor. In general, the best donor is a full sibling. A full sibling is a brother or sister who shares the same mother and father.

What is HLA?

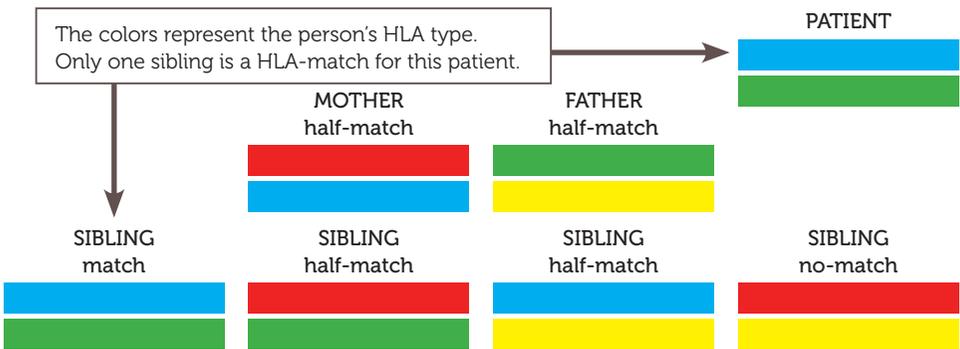
HLA stands for Human Leukocyte Antigen. An HLA type is like a blood type for your immune system. A BMT works best if a donor is an HLA-match.

How is HLA typing done?

A tube of blood or mouth swab is sent for testing. We recommend testing all healthy full siblings and parents. It usually takes a few weeks to get the results of this test.

Will a sibling be an HLA-match?

Each full sibling has a 25%, or one in four, chance of being an HLA-match. This means that some siblings will be a match, but many siblings will not be a match. If a sibling is a blood type match, he or she may or may not be an HLA-match. **Parents usually are not a match for their children.**



What if there is no matched sibling?

It is possible to use an "alternative donor." Alternative donors include:

- unrelated (non-family) HLA-matched volunteer
- donated umbilical cord blood
- half-match (haploidentical) family member

Transplant using alternative donors for sickle cell disease is currently only done on research studies. These studies are trying to make transplant using alternative donors as successful as transplant using an HLA-matched sibling.

Transplant Timeline

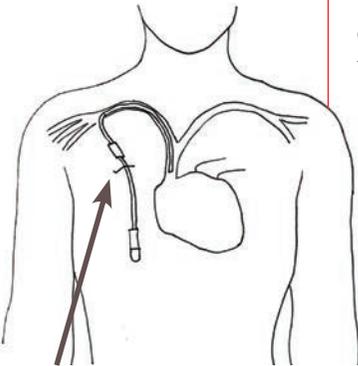
BMT IS A LONG PROCESS THAT INVOLVES SIX STAGES:

1

WORK-UP >>

1 to 3 months before BMT

A patient has tests to check how different organs are working to make sure a patient is healthy for transplant. During this time a patient also has a minor surgery to get a central line. A central line is a more permanent IV.



CENTRAL LINE: A central line is inserted in a large vein near the heart. Medicines and blood transfusions can be given through it.

2

PREP >>

1 to 3 weeks before BMT

A patient is admitted to the hospital and receives “conditioning” medicines. These medicines make room in the bone marrow and turn down the immune system to prevent rejection of the new donor cells. Conditioning usually involves chemotherapy, but it may be possible to decrease or not use chemotherapy for some transplants.

3

TRANSPLANT >>

Day 0

Day 0 is transplant day. On this day a patient receives the donor’s stem cells through their central line. This is like a blood transfusion. This is not a surgery.



4

ENGRAFTMENT >>

2 to 6 weeks after BMT

After transplant, a patient waits for the stem cells from the donor to start making new blood cells. During this time the immune system is very weak and the patient is more likely to get an infection. A patient also needs to receive red blood cell and platelet transfusions. When the bone marrow starts making new blood cells, a patient is “engrafted.” A patient usually remains in the hospital for a month after the transplant if there are no major problems.

5

EARLY AFTER BMT >>

1 to 6 months after BMT

During this time a patient is usually out of the hospital but needs to come to the BMT clinic often for visits. Initially there will be many visits and later less visits are needed. A patient must continue to take medicines to make sure the transplant works. The immune system is still weak so a patient should not go to school and should avoid large crowds.



6

LATE AFTER BMT

6 months to years after BMT

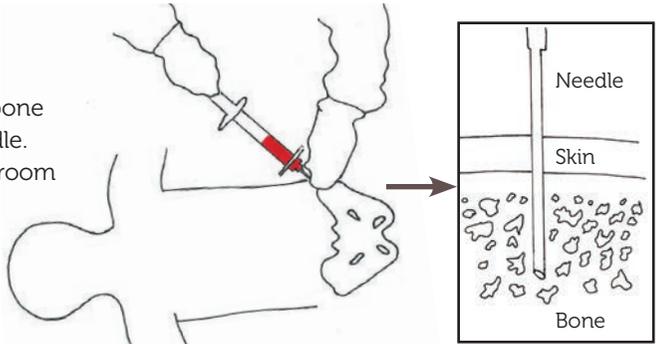
Most patients are able to decrease or stop some medicines 6 months after BMT. Some patients need them for a longer time. A patient has a brand new immune system after BMT; therefore, all childhood vaccines must be repeated. Even years after BMT, a patient continues to be followed in BMT clinic to monitor for long-term effects.

Being a Donor

There are **three ways** to give blood stem cells for transplant:

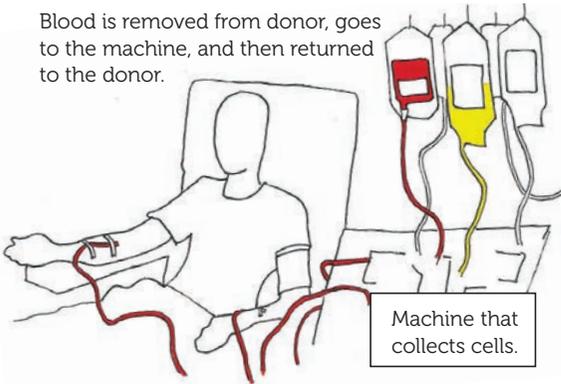
1. BONE MARROW

Bone marrow inside the hip bone can be collected using a needle. This is done in the operating room with anesthesia (medicine to make the donor sleep and not feel pain during the procedure). Most children who donate bone marrow can go back to school the next day.



Bone marrow is collected with a needle inserted into the hip bone.

Blood is removed from donor, goes to the machine, and then returned to the donor.



2. PERIPHERAL BLOOD

A donor can be given a shot that contains a medicine called G-CSF. This medicine makes the stem cells leave the bone marrow and go out into the blood. This shot is usually given daily for 5 days. The stem cells are then collected with a special machine through a type of IV line.

3. UMBILICAL CORD

After a baby is born, blood can be collected from the leftover blood in the umbilical cord and placenta (the organ that feeds the baby and comes out with the baby). A special program can store the cord blood of a full sibling for a patient with sickle cell disease.

IS IT SAFE TO BE A DONOR?

YES. But before someone can donate, a doctor first needs to check to make sure the donor is healthy. **People with sickle cell trait can be BMT donors.** There are some minor risks with donating bone marrow or peripheral blood stem cells. Donors may feel some pain, but usually this pain is mild and only lasts for a short time.

History of BMT for Sickle Cell

1980s: First patient cured of sickle cell disease through BMT. This child also had leukemia and BMT cured both her leukemia and sickle cell disease.

1990s: First international clinical trial of BMT for sickle cell disease.

BMT for sickle cell disease has been done for over **30** years. During this time we have learned how to better support patients during transplant.

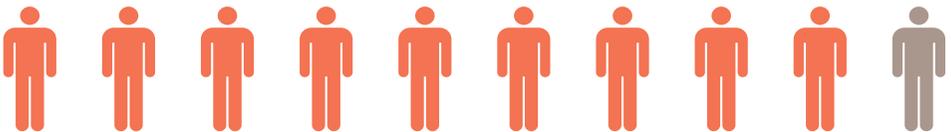
A recent study reported the outcomes of **1000** patients who had BMT with a matched sibling donor for sickle cell disease.

Overall
survival:
92.9%

Cured of sickle
cell disease:
91.4%

Younger patients (**less than age 16 years**) and patients transplanted more recently (**after 2006**) **had better outcomes.**

Gluckman, E et al. Sickle cell disease: an international survey of results of HLA-identical sibling hematopoietic stem cell transplantation. Blood 2017;129(111):1548-56.



On average when 10 children underwent matched sibling BMT, **9** of these children were cured.

Today the cure rate for children with sickle cell disease undergoing BMT using a matched sibling donor is **about 95%.**

Risks of BMT

Short-term Side Effects

Chemotherapy given during prep can cause **nausea, vomiting, diarrhea, mouth sores, and hair loss**. Blood cell counts also become low. If less chemotherapy is given, then less side effects should occur.

Infection

After BMT the **immune system is weak** so a patient can get serious infections. A patient needs to take medicines and follow special instructions to lower the chances of getting an infection.

Graft-Versus-Host Disease (GVHD)

GVHD occurs after BMT when the new donor immune system sees the patient's body as different and attacks it. GVHD can be **mild but sometimes it can be severe**. It can **involve the skin, the gut, the liver, and other parts of the body**. It can usually be treated, but sometimes it does not go away with treatment.

This image was originally published in ASH Image Bank. Cowen, E. Acute GVHD. ASH Image Bank. 2014; 00028142. © the American Society of Hematology.



Severe skin GVHD

Rejection

The patient can reject the new donor cells. When this happens **sickle cell disease usually returns**.

Long-term Side Effects

Chemotherapy given during prep can cause infertility (inability to have children). If less chemotherapy is given, then this side effect may not occur. **We are still learning about the long-term side effects of BMT for sickle cell disease.**

Death

Patients have died from problems after BMT, usually due to infection or GVHD. This risk depends on the type of transplant, the patient, and the donor.

These are some of the risks of BMT. Other problems can also occur. Your health care team can give you more information about your risks.

Benefits of BMT

Cure

If the BMT works, a patient is cured of sickle cell disease. This means that the patient will no longer have sickle cell pain episodes or acute chest syndrome.

Stop Sickle Cell Organ Damage

Unfortunately beginning in early childhood, sickle cell disease can cause serious damage to many organs and this worsens over time. After BMT, this organ damage slows or organs gain some more normal function. For example, the spleen is better able to filter the blood after BMT in most children. Permanent damage to organs like the brain (stroke) is not reversed after BMT, but BMT can help prevent more damage.

Improved Quality of Life

After BMT a patient may have more energy and feel better.

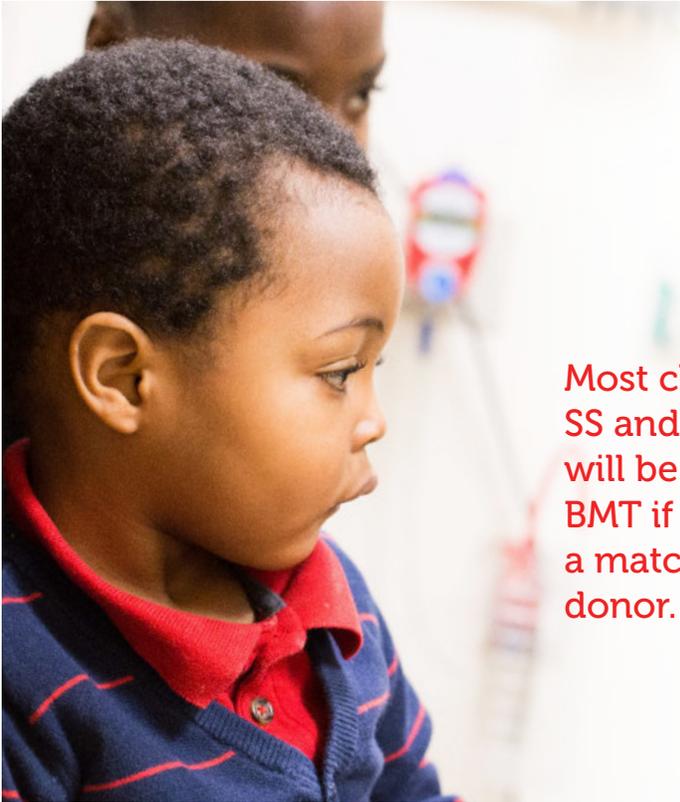
It is currently estimated that the average person with SS or S β ° sickle cell disease lives to only about 40 years.



BMT may help people with sickle cell disease have a more normal life.

Is BMT for my child?

In the past, only children who had major problems from their sickle cell disease (such as a stroke) were eligible for BMT. Since we know most children do well after BMT using a matched sibling donor, more children are undergoing BMT today.



Most children with SS and S β ⁰ disease will be eligible for BMT if they have a matched sibling donor.

What if my child does not have a matched sibling?

BMT using other donors (parents, unrelated donors) is currently only done on research studies. Research studies have rules on who can participate in the study.

It can be very difficult to decide to have or not have BMT. It is important to talk with your health care team and your family about your child's treatment options.

New Research

Researchers at the National Institutes of Health (NIH) and the University of Illinois have done **BMT with no chemotherapy in adults with sickle cell disease**. The results on 43 patients have been published.

WITH THIS RESEARCH:

- ▶ No patients have died from BMT.
- ▶ 88% of patients have been cured.
- ▶ No patients have had GVHD.

Hsieh, MM et al. Nonmyeloablative HLA-Matched Sibling Allogeneic Hematopoietic Stem Cell Transplantation for Severe Sickle Cell Phenotype. JAMA 2014;312(1):48-56.

Saraf, SL et al. Nonmyeloablative Stem Cell Transplantation with Aletuzumab/Low-Dose Irradiation to Cure and Improve the Quality of Life of Adults with Sickle Cell Disease. Biol Blood Marrow Transplant 2016;22:441-8.

The **SUN Trial** is studying **BMT with no chemotherapy in children**.



SUN stands for **S**ickle transplant **U**sing **N**onmyeloablative approach. Nonmyeloablative means that the patient's bone marrow will not be completely destroyed or wiped out.

In this study participants will:

- get low dose irradiation instead of chemotherapy
- get peripheral blood stem cells from a matched sibling
- need to take a daily medicine (sirolimus) for over 1 year to make sure the transplant works.

This study hopes to show that the side effects from BMT will be less.

For more information about the SUN Trial

Minimizing toxicity in HLA-identical sibling donor transplantation for children with sickle cell disease

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Talk to your doctor to learn more about BMT for sickle cell disease and your child's treatment options.

