Severe Neurologic Complications after Hematopoietic (Peripheral Blood) Stem Cell Transplantation in Children

Robin L. Brey, MD

What are Hematopoietic Stem Cells?
Hematopoietic stem cells can be found in the bloodstream and have the ability to grow into any type of blood cell. These stem cells can be removed from the blood stream and then given to a patient to treat different types of cancerous and noncancerous diseases. You can learn more about stem cells and hematopoietic stem cell transplantation on the next page.

Hematopoietic Stem Cell Transplantation
Hematopoietic stem cell transplantation is the main treatment for a number of inherited and acquired diseases. In this issue of Neurology, Faraci et al. (Faraci M, Lanino E, Dini G, et al. Severe neurologic complications after hematopoietic stem cell transplantation in children. Neurology 2002;59:1895–1904.) describe severe neurologic complications in 272 children who underwent hematopoietic stem cell transplantation. Nervous system complications are a common cause of side effects of stem cell transplantation, and little has been written about them in children.

How the Study Was Performed
The authors studied the medical records of children who had hematopoietic stem cell transplantation to see what kinds of serious nervous system complications occurred. They also collected other information to see if any of the following factors were linked to serious nervous system complications:

- The disease they were being treated for
- Whether autologous (collected from patient) or allogeneic stem cells (collected from another person)
- Medications were used before and during the transplantation
- The kind of radiation treatment that was used

How Common Were Serious Nervous System Complications?
Serious nervous system complications were seen in 14% of the children in this study and a cause of death in 8.5%. These complications commonly occurred in the first year after the transplantation was performed. The main risk factors for serious nervous system complications can be found in the table.

Types of Serious Nervous System Complications
The authors found several major factors that lead to serious nervous system complications or death.

Cyclosporin A
Twenty-one children had side effects to cyclosporin A. It is only used in patients who receive stems cells from another person (allogeneic stem cells) to help prevent graft vs host disease. Although the symptoms can be severe, such as epileptic seizures or even coma, they disappear when the drug is stopped or the dose is lowered.

Radiation and Chemotherapy
Seven children developed serious nervous system complications related to total body irradiation and chemotherapy. This damage is usually permanent and can occur between 5 days and as long as 9 years after stem cell transplantation. The most common complications seen are atrophy (shrinkage) of the brain and problems with thinking and memory.

Nervous System Infections
Seven children developed serious brain infections. All received stem cells from another person (allogeneic stem cells). Patients receiving allogeneic stem cells have to take drugs like cyclosporin A that slow down the process of the blood cells growing back. Until enough of the white blood cells grow back, the patient cannot easily fight off infection. Patients who are transplanted with their own stem cells (autologous stem cells) do not have to take these drugs and usually their blood cells grow back more quickly.

Bleeding
Bleeding into the brain occurred in three children between one and eight months after the transplant. All had other complications as well, and all three died of brain hemorrhage.

Summary
Hematopoietic stem cell transplantation can cure children with particular cancers or diseases of the blood. We now know that serious nervous system complications occur in children receiving this form of treatment. The best way to lower the risk for these and other complications is to use the patient’s own stem cells for the transplantation if at all possible and to use a form of radiation therapy before the transplant that does not include the entire body.

Table Factors that Increase the Risk for Serious Nervous System Complications

- Use of stem cells from another person, especially if that person were not a blood relative (allogeneic stem cells).
- Moderate to severe “graft vs host” disease. The white blood cells from the donor (the “graft”) identifies the cells of the patient’s body (the “host”) as foreign and attacks them.
- Use of total body irradiation prior to transplantation.
What are Stem Cells?
Stem cells have the ability to grow into many different types of cells. There are two major types of stem cells. They are fetal stem cells and hematopoietic (blood) stem cells. Fetal stem cells have the ability to grow into cells of any type of organ. Hematopoietic stem cells have the ability to grow into the types of cells that are found in the blood. There are three types of blood cells: white blood cells fight infection; red blood cells carry oxygen to and remove waste products from organs and tissues; and platelets allow the blood to clot.

The most common type of stem cell used in medical treatment today is the hematopoietic stem cell. This type of stem cell can be obtained from two different places in the body: bone marrow (the soft, sponge-like material found inside bones) and peripheral blood (found in the bloodstream).

In some cases, stem cells can be obtained from the patient who will be undergoing treatment before the transplantation is performed. These are called autologous stem cells. In other cases, the stem cells are obtained from a relative of the patient or an unrelated healthy donor. These are called allogeneic stem cells. If an identical twin is available to donate stem cells, these are called syngeneic stem cells.

What is Peripheral Blood Stem Cell Transplantation?
For the last 15 years, stem cells obtained from the blood have been used to treat patients with many different kinds of diseases. The first step in this treatment is to collect enough stem cells from the patient or donor.

The numbers of stem cells circulating in the blood is very low. They are collected using a procedure called leukopheresis. For each session, the patient or donor is hooked up to a leukopheresis machine and their blood is circulated through the machine. The blood cells are removed and the stem cells are counted, carefully prepared, and frozen for later use.

When enough stem cells have been collected, the patient is prepared to receive them. This process involves killing off the patient’s blood forming cells using radiation or chemotherapy. This is done to cleanse the patient’s system of abnormal blood cells or other cells that are making the patient ill. The stem cells are then given to the patient. It usually takes approximately 2 to 4 weeks for the stem cells to make new, healthy blood cells. This is called engraftment. Until this occurs, the patient is at risk for developing severe infections and bleeding.

What Kinds of Diseases are Treated with Peripheral Blood Stem Cell Transplantation?
Many diseases are now being treated using peripheral blood stem cell transplantation including blood diseases (certain types of anemias) and cancers of the blood (leukemias, lymphomas, and multiple myeloma). Other diseases treated with peripheral blood stem cell transplantation include bone marrow diseases such as aplastic anemia and diseases present from birth, such as sickle cell disease. During the treatment of certain cancers requiring high doses of radiation and chemotherapy, blood cells are killed off. Peripheral blood stem cell transplantation can be used to restore the patient’s blood cells. Autoimmune diseases (body’s cells attack itself) are also sometimes treated with stem cell transplantation. However, experience using stem cell transplantation for autoimmune diseases is very limited and is currently considered experimental and only used when all other treatments have failed.

What are the Side Effects of Peripheral Blood Stem Cell Transplantation?
The side effects most commonly seen at the time of the stem cell transplantation or shortly thereafter are infection, bleeding, and organ damage caused by the medications used during the transplant procedure. The risk for infection and bleeding is high until large enough numbers of all the different types of blood cells grow back. Other short-term side effects include nausea, vomiting, fatigue, loss of appetite, mouth sores, hair loss, and skin reactions.

Potential long-term risks include infertility (the inability to produce children), cataracts (clouding of the lens of the eye, which causes loss of vision), new cancers, and damage to the liver, kidney, lungs, or heart.

If the source of the stem cells is another person (allogenic stem cells), then a continued potential side effect is something called "graft vs host" disease. This can happen when the transplanted white blood cells (the "graft") recognize that the tissues of the person they have been transplanted into (the "host") are different from themselves and attack them. The damage this causes can range from mild to severe.

Occasionally, the transplanted stem cells do not grow. This is called graft failure. If this happens, another transplant is needed.

Resources
National Marrow Donor Program
Suite 500
3433 Broadway Street, NE
Minneapolis, MN 55413
http://www.marrow.org
National Cancer Institute
http://cancer.gov/clinical_trials
Severe neurologic complications after hematopoietic (peripheral blood) stem cell transplantation in children
Robin L. Brey
*Neurology* 2002;59:E13-E15

This information is current as of December 24, 2002

<table>
<thead>
<tr>
<th>Updated Information &amp; Services</th>
<th>including high resolution figures, can be found at:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><a href="http://n.neurology.org/content/59/12/E13.full">http://n.neurology.org/content/59/12/E13.full</a></td>
</tr>
<tr>
<td>Permissions &amp; Licensing</td>
<td>Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:</td>
</tr>
<tr>
<td></td>
<td><a href="http://www.neurology.org/about/about_the_journal#permissions">http://www.neurology.org/about/about_the_journal#permissions</a></td>
</tr>
<tr>
<td>Reprints</td>
<td>Information about ordering reprints can be found online:</td>
</tr>
<tr>
<td></td>
<td><a href="http://n.neurology.org/subscribers/advertise">http://n.neurology.org/subscribers/advertise</a></td>
</tr>
</tbody>
</table>