



Bone Marrow or Blood Stem Cell Transplants in Children With Certain Rare Inherited Metabolic Diseases*

A Review of the Research for Parents and Caregivers

* Wolman Disease, Farber Disease, Niemann-Pick Disease, Gaucher Disease, Early Infantile Neuronal Ceroid Lipofuscinosis, Hunter Syndrome, or Sanfilippo Syndrome



Is This Information Right for Me?

This information is for you if:

- Your child's doctor has said your child has one of these rare "inherited metabolic diseases":
 - Wolman disease
 - Farber disease type 2 or 3
 - Niemann-Pick (pronounced NEE-mon-pick) disease type A
 - Gaucher (pronounced go-SHAY) disease type 3
 - Early infantile neuronal ceroid lipofuscinosis (NCL)
 - Hunter syndrome (mucopolysaccharidosis type 2)
 - Sanfilippo syndrome (mucopolysaccharidosis type 3)
- Your child's doctor has talked with you about a **hematopoietic** (pronounced he-MAH-tuh-poy-ET-ic) **stem cell transplant (HSCT)** using stem cells from a donor. It may also be called a blood stem cell transplant or a bone marrow transplant.
- Your child is under the age of 21. The information in this summary is from research on children younger than 21.

What will this summary cover?

This summary will cover:

- Information about each rare inherited metabolic disease
- Possible benefits of an HSCT
- What researchers have found about treating children who have one of these diseases with an HSCT using stem cells from a donor
- What an HSCT is and how it is done
- Possible risks of an HSCT

This summary can help you talk with your child's doctor about whether an HSCT might help your child.

Note: An HSCT may not be helpful for all children with one of these diseases. Go to page 8 to see what researchers found about treating each disease with an HSCT using stem cells from a donor.

Where did the information come from?

Researchers reviewed studies on HSCTs in children with different diseases. These studies were published between January 1995 and August 2011. The researchers were funded by the Agency for Healthcare Research and Quality (AHRQ), a Federal Government research agency.

The researchers wrote a report on what they found, and this summary is based on that report. The report was reviewed by doctors, researchers, other experts, and the public. You can read the report at www.effectivehealthcare.ahrq.gov/stem-cell-children.cfm.



Understanding Your Child's Condition

What are rare inherited metabolic diseases and how might an HSCT help?

Wolman disease, Farber disease, Niemann-Pick disease, Gaucher disease, early infantile NCL, Hunter syndrome, and Sanfilippo syndrome are all “inherited metabolic diseases.” They are rare diseases caused by a certain gene that does not work correctly. These diseases are not caused by anything the mother did while pregnant.

Inherited metabolic diseases can be passed down in families even when both parents are healthy. A child gets two copies of the gene from his or her parents. A child only needs one copy of the gene to work right in order to be healthy. But when a child receives two genes that do not work (one from the mother and one from the father), the child can develop a metabolic disease.

Rarely, a child may receive one gene that works and one that does not, and the working gene may become damaged on its own. This can cause the child to develop a metabolic disease.

In children with Wolman disease, Farber disease, Niemann-Pick disease, Gaucher disease, or early infantile NCL:

- The body does not make enough of a certain chemical (called an enzyme) needed to break down or process fat molecules.
- Because the body cannot break down fat molecules correctly, a harmful amount of these molecules builds up in the body and damages organs.

In children with Hunter syndrome or Sanfilippo syndrome:

- The body does not make enough of a certain chemical (called an enzyme) needed to break down or process sugar molecules.
- Because the body cannot break down sugar molecules correctly, a harmful amount of these molecules builds up in the body and damages organs.

In an HSCT to treat rare inherited metabolic diseases, healthy stem cells from a donor (a person who donates stem cells) are put into your child's body. Healthy blood cells develop from the stem cells. The hope is that these new blood cells may provide the missing enzyme your child's body needs.

In children with rare inherited metabolic diseases that can damage the brain and spinal cord, the hope is the HSCT may prevent this damage if it is done early enough. An HSCT cannot undo damage that has already been done.

The next few pages give a brief description of the rare inherited metabolic diseases covered in this summary.



Wolman Disease

Wolman disease appears in the first few weeks after birth. It causes harmful amounts of fat molecules to build up in the liver, spleen, bone marrow, small intestine, and on the glands that lay on top of the kidneys. Children with Wolman disease are not able to absorb nutrients, which causes severe malnutrition. Children with this disease often do not live past 6 months to 1 year.

Symptoms can include:

- Not growing, not gaining weight, or not developing normally
- Jaundice (yellowed skin and yellowed whites of the eyes)
- A low number of red blood cells (the cells that carry oxygen throughout the body)
- Severe vomiting
- Diarrhea
- Swelling of the belly
- Swelling of the liver and spleen

Farber Disease Types 2 and 3

Farber disease types 2 and 3 appear in the first few weeks after birth. This disease causes harmful amounts of fat molecules to build up in the body, especially in the joints. Fat molecules can also build up in the brain and spinal cord. Types 2 and 3 are the milder forms of Farber disease. Children with one of these forms may live into their teenage years.

Symptoms can include:

- Small lumps of fat (nodules) under the skin, in the lungs, or in other parts of the body
- Swollen and painful joints
- Difficulty breathing and/or swallowing
- Vomiting
- A weak cry
- Hoarseness
- Swelling of the liver and spleen
- Mental disability

Niemann-Pick Disease Type A

Niemann-Pick disease type A appears in the first months after birth. It causes harmful amounts of fat molecules to build up in the liver, spleen, lungs, bone marrow, and brain. Type A is the most severe form of Niemann-Pick disease, and children with this disease often do not live past 3 years.

Symptoms can include:

- Weak muscles
- Sensitivity to touch
- Trouble swallowing
- Slurred speech
- Trouble learning
- Inability to move the eyes up and down
- Mental disability
- Swelling of the liver and spleen

Gaucher Disease Type 3

Gaucher disease type 3 can appear anytime during childhood or the teenage years. It causes harmful amounts of fat molecules to build up in the liver, spleen, lungs, bone marrow, and brain. Children with Gaucher disease type 3 may live into adulthood.

Symptoms can include:

- Bone pain and broken bones
- Easy bruising
- A low number of red blood cells (the cells that carry oxygen throughout the body)
- Swelling of the liver and spleen
- Eye problems
- Seizures
- Mental disability
- Lung problems

Early Infantile Neuronal Ceroid Lipofuscinosis

Early infantile NCL appears in the first year of life. It causes harmful amounts of fat molecules to build up in cells usually in the child's brain or eyes and sometimes in the child's skin, muscles, and other tissues. Children with this disease often do not live past 6 to 13 years.

Symptoms can include:

- Vision loss that leads to blindness
- Seizures
- Trouble sleeping
- Trouble speaking
- Behavior problems
- Movement problems and trouble walking
- Mental disability



Hunter Syndrome

Hunter syndrome appears in children as young as 18 months and affects mostly boys. It causes harmful amounts of sugar molecules to build up in the child's cells, blood, and tissues between the organs and bones. There are severe and mild forms of Hunter syndrome. The severe form usually starts in early childhood (as early as 18 months) and causes mental disability. Children with severe Hunter syndrome often live 10 to 20 years. The mild form usually starts later in childhood or in the teenage years. Children with mild Hunter syndrome often live 20 to 60 years.

Symptoms can include:

- A large head
- Problems with hearing, vision, or both
- Stiff joints
- Stiff muscles
- Aggressive behavior
- Thick facial features, especially the lips and nose
- Carpal tunnel syndrome (numbness or weakness in the hands and fingers)
- Enlarged organs
- Trouble breathing because of thickened nasal passages and windpipe
- Delayed development and growth

Sanfilippo Syndrome

Sanfilippo syndrome appears after the first year of a child's life. It causes harmful amounts of sugar molecules to build up in the cells mainly in the child's brain and spinal cord. Children with this disease often only live into their teenage years.

Symptoms can include:

- A large head
- Thick facial features, especially the lips and eyebrows
- Stiff joints
- Trouble walking
- Diarrhea
- Behavior problems
- Delayed development
- Severe mental disability

What have researchers found about treating children who have a rare inherited metabolic disease with an HSCT?

The chart below shows what researchers found about using an HSCT to treat children with a rare inherited metabolic disease.

Note: It is important to note that the research findings for each disease are based on only a very small number of studies with very few children. Talk with your child's doctor about whether these research findings apply to your child and whether an HSCT may help your child.

Rare Inherited Metabolic Disease	Researchers found that an HSCT:	Number of Patients Studied in the Research
Wolman disease	<ul style="list-style-type: none"> Increased the chance of surviving when compared with only treating symptoms to help make the child more comfortable 	7 patients
Farber disease type 2 or 3	<ul style="list-style-type: none"> Reduced the number of nodules under the skin more than usual treatment Reduced the number of swollen joints more than usual treatment* 	5 patients
Niemann-Pick disease type A	<ul style="list-style-type: none"> Did not appear to increase the chance of surviving when compared with only treating symptoms to make the child more comfortable 	3 patients
Gaucher disease type 3	<ul style="list-style-type: none"> Did not appear to improve mental** development more than enzyme replacement therapy‡, but more research is needed to know for sure 	18 patients
Early infantile NCL	<ul style="list-style-type: none"> Did not appear to improve mental** development when compared with only treating symptoms to make the child more comfortable 	3 patients
Mild Hunter syndrome	<ul style="list-style-type: none"> May improve mental** and physical† development more than enzyme replacement therapy‡, but more research is needed to know for sure 	6 patients
Severe Hunter syndrome	<ul style="list-style-type: none"> May improve physical† development more than enzyme replacement therapy‡, but more research is needed to know for sure Did not appear to improve mental** development more than enzyme replacement therapy‡, but more research is needed to know for sure 	8 patients
Sanfilippo syndrome	<ul style="list-style-type: none"> Did not appear to improve mental** or physical† development more than usual treatment*, but more research is needed to know for sure 	9 patients

* Usual treatment is different for each disease. Talk with your child's doctor to see what usual treatment is for your child's disease.

** Mental development includes IQ, social skills, speech and language skills, ability to concentrate, and school performance.

† Physical development includes the ability to grow normally, the ability to move and walk, flexibility of the joints, and bone development.

‡ Enzyme replacement therapy is a treatment in which a man-made version of your child's missing enzyme is given through an intravenous (IV) tube in the arm.

Understanding Hematopoietic Stem Cell Transplants

What are hematopoietic stem cells?

Hematopoietic stem cells are young cells that develop into blood cells. There are three types of blood cells:

- **Red blood cells** carry oxygen throughout your body.
- **White blood cells** are an important part of the immune system, which protects your body from germs.
- **Platelets** help your blood to clot.

Stem cells are found mostly in your bone marrow (the spongy tissue inside your bones). In the bone marrow, stem cells multiply and develop into blood cells. When the blood cells are fully developed, they go into your bloodstream. Some stem cells can also be found in your bloodstream.

Note: Hematopoietic stem cells are not stem cells taken from an embryo (a human egg that has been fertilized by sperm) and are not the same as stem cells used in cloning.





What is the process of getting an HSCT?

For an HSCT to treat rare inherited metabolic diseases, healthy stem cells from a donor (a person who donates stem cells) are put into your child's body. For an HSCT to work, the stem cells must come from a donor whose "tissue type" closely matches your child's. Tissue type is not the same as blood type. There are thousands of different tissue types. The first step in getting an HSCT is finding a stem cell donor match.

Finding a stem cell donor match

Usually the closest tissue-type match is a brother or sister from the same parents. If your child does not have any brothers or sisters or if the tissue type of the child's siblings is not a good match, your child's doctor can help you look for an unrelated donor in stem cell donation registries. These registries help match patients who need a stem cell transplant with people who volunteer to donate their stem cells. The registries have millions of possible donors.

How are stem cells collected from the donor?

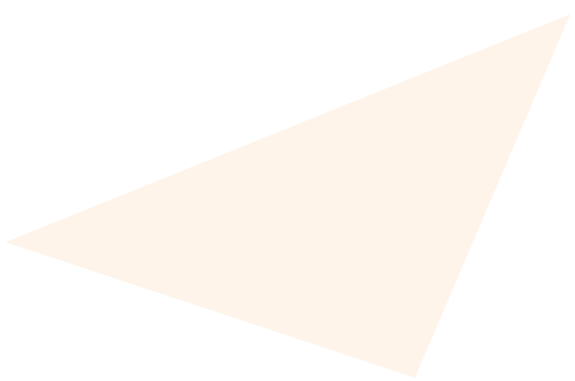
Stem cells can come from a donor's bone marrow, blood, or umbilical cord blood.

If the stem cells are taken from the bone marrow, the doctor puts a needle into the donor's hipbone to collect the stem cells. The donor is given general anesthesia so it is not painful. After the stem cells are collected, the donor may have pain for a few days in the place where the needle was stuck in.

If the stem cells are taken from the donor's blood, the donor needs to take a type of medicine that increases the number of stem cells in their blood. This medicine is usually given as a shot every day for several days. Side effects of the medicine may include aching muscles or bones and headaches. Once there are enough stem cells in the donor's blood, the doctor puts an intravenous (IV) tube into a large vein in the donor's arm or a thin tube called a central line into the donor's chest. The donor may be given general anesthesia so it is not painful. The donor's blood goes through the tube and into a machine that takes out the stem cells. The rest of the blood is then returned to the donor through the IV tube.

Stem cells can also come from donor umbilical cord blood.

Umbilical cord blood is collected from a baby's umbilical cord and the placenta after the baby is born. This does not harm the baby in any way. The umbilical cord blood is then frozen and put into a public cord blood bank.



Preparing for the HSCT

Before the HSCT, your child will need to undergo what is called “conditioning.” Conditioning lasts a few days and consists of intense chemotherapy and sometimes radiation. Conditioning is needed to severely weaken your child’s immune system so it does not attack the transplanted stem cells.

Conditioning can make your child feel sick.

Immediate side effects can include:

- Nausea and vomiting
- Diarrhea
- Loss of appetite
- Sores in the mouth
- Feeling tired
- Hair loss
- Infection

Some types of chemotherapy can also affect the heart and lungs.

There are other longer term risks from conditioning. These risks are discussed on pages 14 and 15.



Getting the HSCT

To do the transplant, the doctor will either put a thin tube called a central line into a large vein in your child's chest or an intravenous (IV) tube in your child's arm. The donor stem cells go through the tube into your child's bloodstream. This can take between 1 and 5 hours and is not painful.

Immediate side effects may include:

- A funny taste in the mouth
- Shortness of breath
- Funny smelling breath
- Tightness in the chest or chest pain
- Fever or chills
- Hives
- Low blood pressure

There are other longer term risks from an HSCT. These risks are discussed on pages 14 and 15.

The stem cells travel into your child's bone marrow, where they will start to multiply and develop into healthy blood cells over the next several weeks.

After the HSCT

After the transplant, your child may need to stay in the hospital for several weeks. It will take a few weeks for the stem cells to get to the bone marrow and start to make new blood cells. During this time, your child will only have a low number of blood cells (red blood cells, white blood cells, and platelets).

Until your child's new blood cells develop, your child may need antibiotics to prevent infection. Your child may also need to be given transfusions (red blood cells and/or platelets from donated blood are given to your child) and nutrition through an IV tube.

What are the risks of an HSCT?

An HSCT comes with many risks. Some of these risks can be life threatening.

Possible Problems Right After the HSCT

- **Infection:** Your child's immune system will be very weak after the HSCT. It can take up to a year or longer for the immune system to return to normal. During this time, your child is at risk for getting a severe infection because the immune system cannot fight off germs very well. Your child's doctor may give your child antibiotics to help prevent infection. A fever is often the first sign of infection. Call the doctor right away if your child has a fever.
- **Bleeding:** After the HSCT, your child will have a low number of platelets (the blood cells that help blood clot). It can take several weeks for new platelets to form. During this time, your child can bleed or bruise easily. If your child's platelet count gets too low, your child may need a platelet transfusion (platelets from donated blood are given to your child).
- **Graft-versus-host disease (GVHD):** After an HSCT, there is a chance that your child could develop GVHD. This happens when the new white blood cells (an important part of the immune system, which protects the body from germs) mistakenly attack the child's body, which can damage the child's organs. GVHD can be mild to severe and is sometimes life threatening. It can happen right after the transplant or months later. The earliest symptom of GVHD is a rash on your child's hands or feet. Your child's doctor will watch closely for signs of this condition.
- **Transplant rejection:** Although it is rare, sometimes the body rejects the transplanted stem cells. This means that the transplanted stem cells did not travel into the bone marrow and multiply like they should have. Transplant rejection can be life threatening and is more common if the donor tissue type was not a complete match.

Possible Problems That Could Show Up Later

- **Relapse:** Symptoms of the inherited metabolic disease could come back.
- **Infertility:** The chemotherapy and/or radiation given to your child during conditioning before an HSCT can cause infertility (not being able to have children later in life). You may wish to talk with your child's doctor about egg harvesting or sperm banking before the HSCT.
- **Damage to organs:** The chemotherapy and/or radiation given to your child during conditioning before an HSCT may damage your child's organs (such as the kidneys, liver, lungs, heart, or bones). Symptoms of organ damage may not show up right away.
 - The organs that may be damaged depend on the specific type of chemotherapy and the doses of chemotherapy and radiation that your child received. Your child's doctor will discuss the possible long-term side effects to watch for in your child.
- **Growth problems:** An HSCT may stunt your child's growth.
- **Cancer:** Anyone who receives an HSCT has a higher risk of developing cancer in his or her lifetime. The cancer could develop several years after the transplant.

What are the costs of an HSCT?

An HSCT can be very expensive. The costs to you depend on your health insurance. Contact your health insurance provider to find out if your plan covers an HSCT and how much you will need to pay. Also talk with your child's doctor about whether other resources are available to help with these expenses.

Talking With Your Child's Doctor

Ask Your Child's Doctor

You may want to ask your child's doctor the following questions. Many of these questions may be best answered by a doctor who has experience with HSCTs.

- What are the possible benefits and risks of an HSCT for my child?
- What are the chances that an HSCT could help my child?
- Could an HSCT cure my child or just improve his or her symptoms?
- What are the chances that my child's disease will come back after the HSCT?
- How will we find a stem cell donor for my child?
- How should we prepare for the transplant?
- What should we expect after the transplant?
- How long will my child need to stay in the hospital?
- What serious side effects should we watch for, and when should we call you about them?
- What possible serious problems should we watch for later in my child's life?



Other questions:

Write the answers here:

Sources

The information in this summary comes from the report *Hematopoietic Stem-Cell Transplantation in the Pediatric Population*, February 2012. The report was produced by the Blue Cross and Blue Shield Association Technology Evaluation Center Evidence-based Practice Center through funding from the Agency for Healthcare Research and Quality (AHRQ).

For a copy of the report, or for more information about AHRQ and the Effective Health Care Program, go to www.effectivehealthcare.ahrq.gov/stem-cell-children.cfm.

Additional information came from the MedlinePlus® Web site, a service of the National Library of Medicine and the National Institutes of Health. This site is available at www.nlm.nih.gov/medlineplus.

This summary was prepared by the John M. Eisenberg Center for Clinical Decisions and Communications Science at Baylor College of Medicine, Houston, TX. Parents or caregivers of children who have received a bone marrow or blood stem cell transplant reviewed this summary.

