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# *Facts & Statistics*



**Blood cancers such as leukemia, Hodgkin lymphoma, non-Hodgkin lymphoma, myeloma and myelodysplastic syndromes are cancers that originate in the bone marrow or lymphatic tissues. They are considered to be related cancers because they involve the uncontrolled growth of cells with similar functions and origins. The diseases result from an acquired genetic injury to the DNA of a single cell, which becomes abnormal (malignant) and multiplies continuously. The accumulation of malignant cells interferes with the body's production of healthy blood cells.**

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## 1.1..1 New Cases, Incidence and Deaths

**Every 4 minutes one person is diagnosed with a blood cancer.**
**An estimated 139,860 people in the United States will be diagnosed with leukemia, lymphoma or myeloma in 2009. New cases of leukemia, Hodgkin and non-Hodgkin lymphoma and myeloma account for 9.5 percent of the 1,479,350 new cancer cases diagnosed in the United States this year*.**
**Overall incidence rates per 100,000 population for leukemia, lymphoma and myeloma are almost identical for data reported in 2008 and 2009 [(leukemia 12.2, 2009 vs.12.3, 2008); (NHL, 19.5, each year); (Hodgkin lymphoma, 2.8, each year); (myeloma, 5.6, each year)].**
**Leukemia, lymphoma and myeloma will cause the deaths of an estimated 53,240 people in the United States this year. These blood cancers will account for nearly 9.5 percent of the deaths from cancer in 2009 based on the 562,340 total cancer-related deaths.**
**Every ten minutes, someone dies from a blood cancer. This statistic represents nearly 146 people each day, or more than six people every hour.**
**Leukemia causes more deaths than any other cancer among children and young adults under the age of 20. In general, the likelihood of dying from most types of leukemia, lymphoma or myeloma decreased from 1996 to 2005 (the most recent data available).**
***Facts and statistics from *Leukemia, Lymphoma, Myeloma Facts 2009-2010*, June 2009.**

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## 1.1..2 Drug and Radiation Therapy

**The dramatic improvement in managing blood cancers is mainly the result of chemotherapy (anticancer drugs), usually in combinations of two or more drugs. More than 50 different drugs are now used to treat people with blood cancers and a number of potential new therapies are under study in clinical trials. People living with some types and stages of blood cancer can benefit from treatment with radiation. When radiation therapy (RT) is used, it is usually part of a treatment plan that includes drug therapy.**

**The type of radiation (called "ionizing radiation") that is used for RT is the same type that is used for diagnostic x-rays, but it is given in higher doses. External beam radiation is the kind of ionizing radiation used most often for therapy. Current methods of delivering RT are improved so that there is less "scatter" of radiation to nearby healthy tissues.**

**During the past decade, several important new drugs (and new uses for established drugs) have greatly improved blood cancer cure and remission rates for many people. Today, there are several new classes of drugs with different mechanisms of action. These drugs may be used alone for certain types and stages of disease; however, they are often combined with chemotherapy. This is important because it may mean that cancer cells—which often elude the damaging effects of chemotherapy—are less likely to be resistant (or develop resistance) to the effects of novel agents and chemotherapy given in combination.**

**Some of the newer classes of drugs are BCR-ABL tyrosine kinase inhibitors [such as imatinib mesylate (Gleevec®), dasatinib (Sprycel®) and nilotinib (Tasigna®)], histone deacetylase inhibitors (HDACs) [such as vorinostat (Zolinza®)], hypomethylating or demethylating agents [such as azacitidine (Vidaza®) and decitabine (Dacogen®)], immunomodulators [such as lenalidomide (Revlimid®) and thalidomide (Thalomid®)], monoclonal antibodies, and proteasome inhibitors [such as bortezomib (Velcade®)]. Many of the drugs are used to treat several types of blood cancer and are often given in various combinations of two or more drugs.**

**Some of the US Food and Drug Administration (FDA) approved drug therapies are:**

***Alemtuzumab* (Campath®) is indicated as a single agent for chronic lymphocytic leukemia (CLL) treatment. It is especially active against the lymphocytes in CLL.**

***All-trans-retinoic acid* or ATRA (Tretinoin®) in combination with chemotherapy (anthracycline antibiotic) has significantly improved the remission rate and duration of remission for people with acute promyelocytic leukemia [a type of acute myelogenous leukemia (AML)]. Arsenic trioxide (Trisenox®) also adds to the drugs available to treat this type of AML. Trisenox is indicated for people who have relapsed disease or are resistant to treatment with chemotherapy and ATRA.**

***Azacitidine* (Vidaza) and *decitabine* (Dacogen) are two drugs that are**

**indicated for all types of MDS. These drugs may help the marrow function more normally and may reduce the need for blood transfusions in some individuals with MDS.**
***Bendamustine*** **(Treanda®) is a chemotherapeutic agent that is approved to treat CLL and indolent (slow-growing) B-cell NHL that has progressed during or within six months of treatment with rituximab (Rituxan®) or a Rituxan-containing regimen.**
***Bortezomib*** **(Velcade) is indicated to treat people with myeloma and people with mantle-cell lymphoma who have had at least one prior therapy. Velcade in combination with pegylated doxorubicin (Doxil®) offers an important option for treating relapsed or refractory myeloma.**
***Cladribine*** **(Leustatin®) induces long-term remissions in nearly 90 percent of individuals with hairy cell leukemia (HCL) who are treated at diagnosis for only one week.**
***Pentostatin*** **(Nipent®) is another effective drug that can be used in people with HCL who do not respond to cladribine. There are other novel agents being studied for people with HCL who are resistant to both cladribine and pentostatin.**
***Clofarabine*** **(Clolar®) is approved to treat children with relapsed or refractory acute lymphocytic leukemia (ALL) who have received at least two prior therapies. Clolar is being studied in clinical trials for adults with acute leukemia or MDS.**
***Dasatinib*** **(Sprycel) is an approved "second-generation" oral drug for chronic myelogenous leukemia (CML) treatment. This oral therapy produces an excellent response in people who do not respond to Gleevec, develop resistance to it or cannot tolerate its side effects (see Imatinib mesylate).**
***Denileukin diftitox*** **(Ontak®) is approved for the treatment of persistent or recurrent cutaneous T-cell lymphoma in patients whose malignant cells express the CD25 component of the interleukin-2 receptor (CD24+).**
***Gemtuzumab*** **(Mylotarg®) is a monoclonal antibody that is indicated for people 60 years or older with CD33 positive acute myelogenous leukemia (AML) in first relapse. This agent is also being studied in clinical trials in combination with other drugs to treat children with relapsed AML.**
***Ibritumomab*** **(Zevalin®) and** ***tositumomab*** **and** ***iodine I 131 tositumomab*** **(Bexxar®) are two conjugated monoclonal antibodies that are approved to treat individuals with relapsed B-cell NHL.**
***Imatinib mesylate*** **(Gleevec) is now the standard of care for newly diagnosed individuals with CML. Gleevec is an oral drug that blocks the oncogene-encoded protein product that allows for the development of the CML cell. The effectiveness of the drug, its tolerance by older persons and the data from the eight-plus years of study in clinical trials clearly indicate that Gleevec prolongs remission when compared to former therapies for CML. A minority of people with CML either do not respond to Gleevec, develop resistance to it or cannot tolerate its side effects. For these individuals, there are second-generation oral therapies (see Dasatinib and Nilotinib). Gleevec,**

**Sprycel and Tasigna may also be important in the treatment of Philadelphia-positive ALL, chronic eosinophilic leukemia, certain forms of myeloproliferative diseases and systemic mastocytosis. Clinical trials are under way to determine if these second-generation drugs should be used for initial therapy for some, or all, people with CML, and if the combined use of two drugs would be better than one. A number of third-generation drugs are in early development. Some of these drugs are targeting a specific mutation in the BCR-ABL gene called "T315I." This mutation is one of the more common ones observed when a response to one of the three approved oral CML drugs is lacking or lost.**

***Lenalidomide*** **(Revlimid) is approved in combination with dexamethasone to treat people with myeloma who have received at least one prior therapy. Revlimid is also indicated for the treatment of people with a specific subtype of MDS that results from a partial deletion of chromosome 5. (In addition, Revlimid appears to benefit about 20 percent of people with MDS without this specific chromosome 5 abnormality).**

***Nilotinib*** **(Tasigna) is an approved second-generation oral drug for CML treatment. This oral therapy produces an excellent response in people who do not respond to Gleevec, develop resistance to it or cannot tolerate its side effects (see Imatinib mesylate).**

***Rituximab*** **(Rituxan) was initially indicated for the treatment of people with indolent types of lymphoma, such as follicular lymphoma. Rituxan is now also approved to treat aggressive lymphomas, such as diffuse large B-cell lymphoma, in combination with chemotherapy. Rituxan is also used in combination with chemotherapy to treat some individuals with myeloma or CLL. Rituxan in combination with fludarabine (Fludara®) and high-dose cyclophosphamide (Cytoxan®) appears to produce high-quality responses in previously untreated individuals with CLL.**

***Thalidomide*** **(Thalomid), in combination with dexamethasone, is approved for newly diagnosed myeloma.**

***Vorinostat*** **(Zolinza), an agent that is approved to treat cutaneous lymphoma, is also being studied to treat people who have MDS.**

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**Immunotherapy. This treatment approach uses immune cells or antibodies to fight blood cancer. Immunotherapies enhance the specificity of treatment and reduce the toxic effects on healthy tissues. Monoclonal antibody therapy, cancer vaccines and donor lymphocyte infusion (DLI) are types of immunotherapy being used or being explored as treatments for people with blood cancer.**

***Monoclonal Antibody Therapies.*** **Monoclonal antibody therapies are laboratory-produced proteins that can be infused, when indicated, to treat individuals with certain blood cancers. These agents target specific antigens on the surface of cancer cells. The antigens are named by "cluster designation" (CD) and number. For example, the monoclonal antibody (mAb) Rituxan targets the CD20 antigen on B lymphocytes. The mAb Campath is directed against the antigen CD52 found on T and B**

**lymphocytes. The mAb Mylotarg, which is linked to a calicheamicin (a chemical toxin) is targeted to CD33 on leukemia blast cells. An mAb can also be linked to a radioactive isotope to deliver radiation directly to the cancer cells. The conjugated mAbs ibritumomab (Zevalin) and tositumomab and iodine I 131 tositumomab (Bexxar) are examples of this treatment. A number of potentially effective new monoclonal antibody therapies are being studied in clinical trials for several types of blood cancer.**

***Experimental vaccines*** **are being studied to treat certain types of blood cancer. The goal is to extend the duration of remission achieved by various other types of therapy. Cancer vaccines would be used in people who have small amounts of residual blood cancer after chemotherapy or stem cell transplantation. Some cancer treatment vaccines under study are intended to induce an immune response against the cancer cells present in the individual.**

***Donor lymphocyte infusion*** **is used for people who have relapsed disease after stem cell transplantation for certain blood cancers, such as CML or myeloma. The infusion of the original stem cell donor's lymphocytes may induce another remission. This type of treatment is being studied intensively to learn more about the basis for this immune cell effect and to expand it for use in other types of blood cancer.**

**Gene Therapy. One approach to gene therapy (treatment that alters a gene's DNA or RNA) is to use agents that disable oncogenes and prevent the formation of corresponding oncoproteins. Oncoproteins cause the transformation to various types of cancer cells. For example, in CML treatment studies, researchers are trying to modify the BCR-ABL oncogene, which produces an oncoprotein that stimulates CML cell growth. (Note that the approved CML oral drug therapies, Gleevec, Sprycel and Tasigna do not alter the oncogene. These drugs work by interfering with BCR-ABL tyrosine kinase (the CML oncoprotein) and blocking its effect on the cell.)**

**Two other potentially important gene therapy approaches include the application of "RNA interference (RNAi)," a modality that uses molecules of RNA to silence disease-promoting genes, and "aptamer treatment," a technique that prepares small molecules in the laboratory that have the ability to inactivate disease-causing proteins. New forms of cancer therapy may be developed if RNAi can be applied to oncogenes and/or aptamer treatment can be applied to oncoproteins.**

**Risk-Adapted Therapy. Research is under way to identify biomarkers that may give doctors information about the type and amount of therapy needed by different patients who have the same broad diagnosis. Risk-adapted therapy may be viewed as "personalized medicine" that can be applied if there is enough information about the individual and/or the specific disease to tailor the treatment. Biomarkers may also be able to indicate which patients have a higher-than-normal risk of developing specific long-term or late effects.**

**Biomarkers can be high levels of certain substances in the body such as antibodies or hormones, or genetic factors that can increase susceptibility to**

**certain effects.**

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## 1.1..3 Stem Cell Transplantation

**Stem cell transplantation was introduced approximately 50 years ago and is an important therapy for many children and adults who are being treated for blood cancer. The purpose of stem cell transplantation is to restore the function of the marrow (the blood-forming organ in the body). The marrow may be impaired due to the blood cancer and/or treatment.**

**Autologous and Allogeneic Transplantation. The main types of stem cell transplantation are autologous transplantation (the transplant patient has his or her own cells collected and infused back) and allogeneic transplantation (matched cells from a donor are collected and transplanted to the patient). For both types, stem cells are usually collected from the circulating blood, but may be collected from the marrow or, in some cases, from umbilical cord blood.**

**Compared to an autologous transplant, an allogeneic transplant is associated with a higher risk for serious side effects of the procedure, or death. In general, with autologous transplant there is a higher risk of disease recurrence than with a successful allogeneic transplant. The decision to do a transplant, and whether the transplant should be autologous or allogeneic, depends on the type of blood cancer, the age of the individual, the choice(s) of other effective treatment options and the availability of a stem cell donor.**

**To donate his or her own cells for autologous transplantation, an individual needs to have a sufficient number of healthy stem cells in his or her marrow or blood. Drugs such as plerixafor (Mozobil®), given with a white cell growth factor may be given to move stem cells from the marrow to the blood for collection and subsequent autologous transplantation.**

**The donor for an allogeneic transplant may be a sibling with the same tissue type as the transplant candidate (a "match"). The chance of having a full match with a sibling is about 25 percent. When a matched sibling donor is not available, a matched unrelated donor is sought through a search of the National Marrow Donor Program registry. The efforts of the National Marrow Donor Program and other donor registries have created a bank of more than 7.4 million potential stem cell donors.**

***Reduced-Intensity Transplantation.*** **A modified form of allogeneic transplantation called "nonmyeloablative" or "reduced-intensity" allogeneic stem cell transplantation may be an option for people with certain types of blood cancer. If the results of ongoing clinical trials prove effective, this therapy will extend the upper age range of persons who can benefit from an allogeneic transplant.**

***Umbilical Cord Blood Stem Cell Transplantation.*** **Umbilical cord blood is another source of stem cells for allogeneic transplantation, especially for children and smaller adults. To date, there have been about 6,000 cord blood stem cell transplants from unrelated donors and several hundred from**

**sibling donors, worldwide. The National Marrow Donor Program registry includes nearly 90,000 cord blood units. The numbers of stem cells in cord blood are often insufficient for the needs of larger adolescent and adult patients. Clinical trials of transplantation with two cord blood units (double cord blood transplant) have shown promising results with more rapid engraftment than that seen with single-unit transplants, and improved survival. Researchers are also studying methods to increase the number of stem cells so that cord blood transplants will engraft faster. Expanding the number of stem cells by growing them in a test tube would especially benefit full-grown adolescents and adults.**

# 2. Bone Marrow/Stem Cell Transplants (BMT)

Some children diagnosed with cancer undergo a "bone marrow" or a "stem cell" transplant, often referred to in the shorthand "BMT". The goal of a BMT is to replace nonfunctioning or defective bone marrow with healthy stem cells. Healthy stem cells can be obtained from bone marrow, peripheral blood, or umbilical cord blood, which in turn can be either from the child who is undergoing the transplant or a related or unrelated "donor".

Bone marrow transplants are intensive and potentially life-threatening. But, the goal of a bmt is a *cure*. From Oncolink (1999): "The goal of BMT is a cure. Cure rates are still low, but are steadily increasing. Even if there is no cure, most transplants result in a period of remission. But you should be aware that there are no guarantees. BMT is an intensive procedure with many risks, and some patients will die despite BMT, from complications of transplant or from relapse of the original disease. The success of BMT will be influenced by a number of factors, including a child's age, general physical condition, diagnosis, and disease stage. Different children respond in different ways."

Scroll down this page for an on-site overview of BMTs. Many external Internet sites provide excellent information on bone marrow and stem cell transplants, so if you need more detail, follow the link below to these sites.

- bone marrow transplant links annotated

The ped-onc page "BMT Parents' Comments" is a collection of writings pages by parents who have ushered their child through a bone marrow transplant. These parents have a wealth of knowledge to share: layman-style explanations, how to keep young children entertained during a BMT, recounts of personal experiences, donor drives, finding a BMT center, what the donor experiences.

- parents' comments on bone marrow transplants

## 2.1 Free Sibling Cord Blood Donor Program

The Children's Hospital of Oakland offers a free sibling cord blood donor program. This means that they will store a new sibling's cord blood. This program is sponsored by NCI and is available to families anywhere in the US who have a child with a medical condition that may at some point require a transplant. Labs, typing, collection costs, shipping, and storage are all FREE. There's no need for cancer affected families to pay for this service that they can all use if having another baby. The program can be reached at 510- 450-7605, or www.chori.org/Services/Sibling_Donor_Cord_Blood_Program/indexcord.html.

Viacord will bank cord blood for free, especially that of a sibling of a child wiht cancer.

## 2.2 Overview of a bone marrow/stem cell transplant

The main reference for the following outline is the section on the BMT InfoNet site: The Nuts and Bolts of Bone Marrow Transplants. It is one of the best sources which your editor found on the Internet for the nitty-gritty on BMTs.

**Quick links to some terms:**

- HLA
- allogeneic
- syngeneic
- autologous
- peripheral blood stem cell transplant
- cord blood transplant
- aspergillus
- GVHD

**Preparation**

Before the transplant begins, your child will undergo a battery of tests to determine whether or not he/she is healthy enough to endure the rigors of transplant. A healthcare team and BMT coordinator will be arranged for your child. These professionals will help you find a donor (if necessary), set up the hospital stay, help you find housing near the hospital, and advise you on insurance and financial issues. The healthcare team should also offer emotional and psychological support for both the child and parents. If it is to be an autologous transplant, stem cells will be harvested during this preparation stage.

*The total time in hospital for a bone marrow transplant is about 4-8 weeks, depending on complications.*

**Conditioning, or preparative regimen** (several days to a week or more)

The child first undergoes several days of chemotherapy and/or radiation which destroys bone marrow and cancerous cells and makes room for the new bone marrow. The exact regimen of chemotherapy and/or radiation varies according to the disease being treated and the preferred treatment plan of the facility where the BMT is being performed. The BMT chemotherapy/radiation regimen is much stronger than chemo/radiation regimens for children who do not undergo a BMT.

**Transplant** (less than an hour)

The transplant itself is given as an IV (usually through the Hickman or mediport) and takes place in the child's room.

**Engraftment** (two to four weeks)

This is the critical time. The patient is placed in protective isolation since he/she has essentially no immune system at this point, while the new cells are finding homes and beginning to grow. The child is also susceptible to infection from normally harmless pathogens which live in our bodies. They will have few red blood cells or platelets. The BMT team will monitor your child carefully and administer antibiotics and blood products as necessary. If the transplant is from a donor, medications will be given to suppress and control GVHD.

From the BMT news site: "The bone marrow transplant is a debilitating experience. Imagine the symptoms of a severe case of the flu - nausea, vomiting, fever, diarrhea, extreme weakness. Now imagine what it's like to cope with the symptoms not just for several days, but for several weeks. That approximates what a BMT patient experiences during hospitalization."

**Recovery**

Recovery continues at home. Your child will continue to be immune suppressed for a varying period of time and will remain closely monitored by the BMT team. The "100 day mark", which is 100 days post-transplant, is generally considered a milestone - by this time, the child is

considered past the worst of the procedure and on the path to recovery. Full recovery is slow, with it taking up to two years for the patient to return to full health.

## 2.3 Complications of bone marrow/stem cell transplants

Complications of BMTs include side effects of heavy chemotherapy and radiation, as well as problems that occur when the donated bone marrow is "engrafting".

**Chemo/radiation side effects**

Side effects of chemotherapy treatments are discussed in general on the ped-onc Treatment side effects page. Since the conditioning therapy for BMTs is very intense, side effects are to be expected. Your child will be immune-suppressed, with an ANC of 0. Blood counts will be low, requiring transfusions of whole blood and platelets (to prevent bleeding). Mucousitis (inflammation of the mucous membranes, both in the mouth and intestine) is common (see the ped-onc Mouth Care page).

Opportunistic infections sometimes invade the patient's body in a BMT procedure. Aspergillus infections are particularly hard to eliminate. The following link takes you to more information on this serious infection:

- Aspergillus links from this site

**Graft Versus Host Disease - GVHD**

In an allogenic transplant, the newly transplanted stem cells/immune system does not exactly match the patient's own system. What happens is the transplanted cells do not recognize the patient as "self" and they proceed to attack their new host, especially the skin, liver, stomach, and intestines. This is called *graft versus host disease*, or GVHD. GVHD can be mild or severe (even life-threatening), and occurs less frequently in children than in adults. In leukemias, a small amount of GVHD is felt to be beneficial, as it searches and destroys any residual leukemia cells which are in the patient's body after the preparative regimen.

To combat GVHD, allogeneic transplants are given drug therapy (cyclosporine, prednisone, and/or methotrexate) before and after transplant. If GVHD continues for more than three months, it is considered chronic. Because GVHD may involve the skin, mouth, eyes, liver, muscles, joints and other body parts, these will be examined frequently. In a few children, the damage will be permanent. The most significant effect of chronic GVHD is infection, as the immune system does not return to normal.

Article: Chronic graft-versus-host disease: where is promise for the future? Leukemia (2005) 19, 1532?1535. doi: 10.1038/sj.leu.2403856; published online 30 June 2005.

**Graft Rejection**

Sometimes the patient's own immune system attacks and destroys the donor's cells; this is called "graft rejection". If this happens, a new transplant is usually done immediately.

## 2.4 FAQs: Frequently asked questions about bone marrow/stem cell transplants

**What is a bone marrow or stem cell transplant?**

The bone marrow of the patient is first destroyed and then replaced with healthy stem cells. Hence the name, "transplant". In an allogeneic transplant, post-transplant the recipient has the bone marrow system of the donor; this means that they have the blood type and immune system of the donor.

**What's the difference between a bone marrow and a stem cell transplant?**

The stem cells can be collected in one of several ways. One source is bone marrow, used because it is rich in "stem cells". Stem cells can also be obtained from umbilical cord blood, which is rich in stem cells. Although circulating (peripheral) blood is not very rich in stem cells, filtration techniques can be used to concentrate the stem cells for a transplant.

Note that the two terms "bone marrow" and "stem cell" transplants are sometimes used interchangeably by nonprofessionals, however, all bone marrow transplants are stem cell transplants but not all stem cell transplants are bone marrow transplants.

**What types of childhood cancers are treated by a stem cell transplant?**

Leukemias, aplastic anemia, lymphomas, and neuroblastoma have been successfully treated with BMTs. In cancers of the blood (leukemias), very aggressive chemotherapy is used to kill off the abnormal cells, a process which also kills normal blood and bone marrow. Solid tumors (lymphomas, neuroblastoma) are treated with intensive chemotherapy which kills the bone marrow cells as a side effect; a BMT restores the bone marrow with healthy cells.

### Who is the donor of the bone marrow or stem cells?

The stem cells can come from either the patient or from someone else: a "donor". If they come from a donor, preferably he/she is related to the patient.

### How can a patient receive their own stem cells, wouldn't these stem cells be damaged or defective?

True, a patient with a blood cancer like leukemia cannot receive their own stem cells because the bone marrow and peripheral blood are contaminated with cancer cells (although, new techniques are becoming available to "filter out" cancer cells). In other types of cancers, the bone marrow cells are normal, but are destroyed by intense chemo and radiation used to treat the cancer. Thus, they are harvested *before* the intense chemo/radiation, frozen, and reinfused after treatment to rescue the bone marrow which has been damaged by the treatment.

### I've heard that donors have to "match" - what's that about?

In allogeneic transplants, the donor and recipient must be "compatible": their HLA types must be close. HLA (Human Leukocyte Antigen) type is determined by a blood test (or sometimes DNA testing).

HLA are antigens on the surface of a person's cells and are easily found on the leukocytes. These mark the cells as being "of self". If the antigens do not match, the donated stem cells will attack all cells of the recipient, because they see the recipient as "foreign". If the antigens match (or nearly match), the donated marrow will peacefully take up residence in the recipient's body and work to supply healthy blood cells.

The antigens named HLA-A, HLA-B, and HLA-DR are known to be important for successful stem cell transplants. There are two of each of these HLA antigens that are important, making a total of 6. (Some centers, especially the military, test for 8 antigens.) A 6/6 match is ideal, although new procedures are developing which allow transplants with 5/6, 4/6, or even 3/6 matches (especially from a relative). Since these antigen types are inherited, it is more likely that a relative (especially a sibling) is a 6/6 match than that a non-relative is a match. People of the same race and ethnic group are more likely to match each other. The genes for HLA antigens are linked together in strands of three: you get three antigens from your mother, and three from your father.

When donors are added to the NMDP Registry, they are usually HLA typed for the A and B antigens only. An initial search of the NMDP registry will designate potential donors, who then are asked to come in for further compatibility testing.

### How are donors found for allogeneic transplants?

Close family members are typed first. Then, the bone marrow registries throughout the world are searched. These registries store the HLA data on thousands of people.

- see links under registries and HLA typing

Becoming registered in the bone marrow registry is an entirely volunteer process. Often people register because they are close to someone who has needed or may need a bone marrow transplant. Sometimes concerned volunteer organizations organize a donor drive in their area. Media stories raise awareness about the need for bone marrow donors and encourage people to sign up.

### Does it hurt the donor?

The marrow is removed with a hollow needle and syringe from the back of the pelvic bone. All donors are given either a general anesthesia (which makes you unconscious) or a regional anesthesia. The marrow is removed through a surgical needle which is inserted multiple times into a few small punctures made in the hip bone. Typically, the donation procedure itself lasts between 45 to 90 minutes. Marrow is constantly regenerating itself so the donor's system completely replaces the donated marrow within several weeks.

More information at:

- NMDP site donor information

**Where are BMTs done, and how do we choose a center at which to have the BMT done?**

Please see these links:

- JLS Foundation page
- BMT InfoNet site
- ped-onc BMT Links page
- ped-onc Parents' Comments page

**How much does a bone marrow transplant cost? Who pays for it?**

About $100,000 - $250,000

Most insurance companies cover most of the cost of a bone marrow transplant. If not, or if help is needed for covering what the insurance company does not pay, see financial help for a bmt.

**How do the stem cells become healthy bone marrow?**

First, the patient's own bone marrow is destroyed by an intensive regimen of chemotherapy and radiation. Then, the donor cells are infused into the bloodstream through the right atrial catheter or mediport (central venous catheter). They travel through the bloodstream and find their way to the marrow, engraft, and (hopefully) begin producing healthy, normal blood cells.

**What's the difference between "allogeneic, syngeneic, and autologous" transplants?**

The names for the different types of bone marrow transplants pertain to the source of the stem cells: whether they are from the recipient or from a relative or stranger, and whether they are from bone marrow or blood.

## 2.5 Definitions

**Allogeneic** - The donor in an allogeneic transplant is either a relative or someone who is a close genetic match to the patient. The transplant team always looks first to family members, since there is about a 1 in 3 or 4 possibility that a sibling is a close enough genetic match to be a donor. If a brother or sister is used as the donor, it is called a "Matched Sibling BMT". (These were the earliest and are still the safest type of non-autologous marrow transplants.)

If none of a patient's family members is a close genetic match, the bone marrow registries are searched in hopes of finding an unrelated donor. Transplants using unrelated donors as the source of stem cells are called "Matched Unrelated Donor Bone Marrow Transplants" or MUD transplants for short.

**Syngeneic** - The donor is not only a close family member, but an identical twin.

**Autologous** - In an autologous transplant, the patient's own stem cells are used. The patient's stem cells are harvested from the bone marrow or from peripheral blood *before* the chemo/radiation regimen. These healthy stem cells are frozen and stored until needed. In an autologous transplant, there is no risk of GVHD.

Autologous transplants have limited effectiveness in the treatment of leukemias that infiltrate the marrow, although they can sometimes be used in leukemias after procedures which remove diseased cells. (This is usually only done when no HLA compatible donor can be found.)

**Peripheral blood stem cell transplant** (PBSCT) - The patient's or a donor's donates cells are collected from the circulating blood system instead of from bone marrow. In PBSCT's, a drug is used to "overstimulate" marrow production. This mobilizes a higher-than-normal number of stem cells into the blood stream. Apheresis is used to filter these excess stem cells from the donor's bloodstream. (Most cancer kids parents are familiar with apheresis, since it is used to filter platelets from donors to be used in supportive treatment for many childhood cancers.) PBSCT's can be either autologous or allogenic, with autologous being the more common of the two. (More info on the NMDP site)

**Cord blood transplants** (CBT) - The stem cells come from umbilical cord blood, a rich source of stem cells. Cord blood transplants are allogeneic and thus the cells must be matched with the patient. An advantage of cord blood is that the stem cells do not show a significant sense of "self"

or a large number of antibodies, so the chances of life-threatening GVHD is greatly reduced. One problem with cord blood use for transplants is that only a small amount of product can be harvested from one umbilical cord, thus, this type of transplant is usually limited to children or small adults.

Cord Blood Transplantation by Leonard Johnson, M.D. - an article in the Fall 1999 Candlelighters Newsletter