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Cord Blood Stem Cell Transplantation Facts

No. 2 in a series providing the latest information for patients, caregivers and healthcare professionals

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Highlights

- Stem cell transplants may use the patient's own stem cells (autologous transplants) or use donor stem cells (allogeneic transplants). Donor cells may come from either a related or an unrelated matched donor.
- Umbilical cord blood, like bone marrow and peripheral blood, is a rich source of stem cells that can be used for transplantation. There may be advantages for certain patients to have cord blood stem cell transplants instead of transplants that use bone marrow or peripheral blood stem cells (PBSCs).
- Cord blood for transplantation is collected from the umbilical cord and placenta after a baby is delivered. Donated cord blood is tested, frozen and stored at a blood bank for future use.
- Cord blood stem cell transplantation, including transplants with two or more cord blood units, is an established practice.
- Research studies are testing ways in which more cord blood cells can be grown in the laboratory. Researchers are also studying ways to make the cord blood stem cells travel and grow better in the bone marrow.

Stem Cell Transplantation

A stem cell transplant is a procedure that replaces damaged or diseased stem cells with healthy stem cells. Stem cells are found in the bone marrow. Without healthy bone marrow, the spongy material inside the center of the bones, a patient is unable to produce the blood-forming or "hematopoietic" stem cells (HSCs) that develop into red blood cells, white blood cells or platelets. These blood cells are essential for life. These are the cells that carry oxygen throughout the body, fight infections, and prevent bleeding. The transplantation of these blood-forming cells is an accepted treatment to restore the body's ability to make its own blood and immune cells. After the stem cells are transplanted into the patient's bloodstream, the stem cells travel to the bone marrow where they begin to produce new healthy blood cells in a process known as "engraftment."

Patients with leukemia, lymphoma, myeloma, myelodysplastic syndromes (MDSs) or other blood cancers may receive high-dose chemotherapy or radiation therapy to treat their cancer. While these treatments kill cancer cells, they may also result in severe injury to blood-forming stem cells in the bone marrow. Damaged or diseased stem cells can result in the body not having enough red blood cells, white blood cells or platelets. Stem cell transplants are used to reestablish stem cell production in a patient's body when the bone marrow has been destroyed.

Sources of Stem Cells for Transplantation

The cells used in transplants can come from three sources: peripheral blood; bone marrow; and cord blood, the blood that is retrieved from the umbilical cord and placenta after a baby's birth.

- Currently, peripheral blood is the most common source of stem cells for transplant. Peripheral blood stem cells (PBSCs) are blood-forming stem cells released from the bone marrow into the bloodstream. Peripheral blood is also called "circulating blood." Normally, the bone marrow releases only a small number of stem cells into the blood. To obtain enough stem cells from the peripheral blood to use for a transplant, a donor is given medication that encourages more blood-forming stem cells to move from the bone marrow to the blood. These cells are collected from the blood using a process called "apheresis." For apheresis, a needle is placed in the donor's vein, usually in the arm. The donor's blood passes through a machine that removes the stem cells and then returns the rest of the blood to the donor. The donor's body replaces the cells in two to three weeks.

- Bone marrow stem cells that can be used for transplant come from the liquid center of the bone, called the "marrow." To obtain the cells, a doctor removes the marrow from the donor's hip bone in a surgical procedure. The liquid marrow is pulled out through a needle. The donor's body replaces the donated bone marrow in four to six weeks.
- Cord blood stem cells are collected from the umbilical cord and placenta after a baby is born. Cord and placental blood contain large numbers of blood-forming stem cells. The donated cord blood is checked to make sure it has enough blood-forming cells for a transplant and if it meets established criteria it is frozen and stored at a cord blood bank for future use. The stored cord blood collected from the umbilical cord and placenta after a baby has been born is called a "cord blood unit."

Cord Blood Stem Cell Transplants

The first successful cord blood stem cell transplant was performed in 1988 in Paris, France. The patient was a boy with Fanconi anemia, a genetic and potentially life-threatening type of anemia. Cord blood stem cell transplants have now been given successfully to children and adult patients with malignant and nonmalignant diseases, including acute lymphoblastic leukemia (ALL); acute myeloid leukemia (AML); myelodysplastic syndromes (MDSs); chronic myeloid leukemia (CML); juvenile myelomonocytic leukemia (JMML); chronic lymphocytic leukemia (CLL); Hodgkin lymphoma (HL); non-Hodgkin lymphoma (NHL); neuroblastoma; thalassemia; severe combined immunodeficiency (SCID); Wiskott-Aldrich syndrome; metabolic diseases, such as adrenoleukodystrophy and Hurler syndrome; and severe aplastic anemia. To date, more than 35,000 cord blood stem cell transplants from unrelated donors have been performed worldwide.

Cord blood stem cell transplants can have complications similar to those of allogeneic stem cell transplants from bone marrow or peripheral blood and should be done only at centers experienced in the transplantation of allogeneic sources of stem cells.

Potential Advantages for Patients

For certain patients, there may be advantages to using donor cord blood stem cells instead of donor peripheral blood or donor bone marrow stem cells. Some potential advantages are

- **Availability.** Cord blood stored in a public cord blood bank has been prescreened, tested and frozen and is ready to use; whereas, it can take weeks to months to find and confirm a bone marrow or peripheral blood donor.
- **Human Leukocyte Antigens (HLA) Matching.** Cord blood stem cell transplants do not have to be as closely matched as bone marrow or peripheral blood transplants. The outcome of a stem cell transplant is strongly affected by the degree of HLA matching between the transplant recipient and the donor. People have different sets of proteins called HLAs, on the surface of their cells. In most cases, the success of allogeneic stem cell transplants depends, in part, on how well the HLA antigens of the donor's stem cells match the HLA antigens of the recipient's stem cells. The higher the number of matching HLA antigens, the greater the chance that the patient's body will accept the donor's stem cells. If the tissue match between the donor and the recipient is not close, the patient's immune system may perceive the donor's cells as foreign and attack them. In general, patients are less likely to develop a complication known as graft-versus-host disease (GVHD) if the stem cells of the donor and patient are closely matched. Even though a cord blood unit that is a close HLA match between the donor and the recipient is preferred, clinical studies suggest that the HLA match may not have to be as close of a match as is necessary for a bone marrow or peripheral stem cell transplant. Consequently, cord blood transplants can be performed in cases where the donor and the recipient are partially matched, increasing the patient's chances of finding a suitable donor.
- **Graft-Versus-Host Disease.** Studies have found that after a cord blood stem cell transplant, fewer patients got GVHD and, among those patients who did develop GVHD, the complication tended to be less severe than it was in patients who had bone marrow or peripheral blood stem cell transplants. GVHD is a serious and sometimes fatal complication of allogeneic stem cell transplantation. With GVHD, the donor's immune cells (the graft) attack the patient's healthy tissue (the host).
- **Diversity.** As a result of extending collection efforts to hospitals where births from diverse ethnic backgrounds are well represented, donated cord blood units have the potential to provide a source of stem cells that reflects racial diversity. In addition, since there may be less stringent HLA-matching requirements for cord blood transplants, it is easier to find donors for members of minority groups.
- **Infectious Disease Transmission.** Cord blood stem cell transplants carry less risk of transmission of blood-borne infectious diseases compared with the risks associated with stem cells obtained from the peripheral blood or bone marrow of related or unrelated donors.

Potential Disadvantages for Patients

Some potential disadvantages are

- **Engraftment.** The number of stem cells per unit of cord blood is much smaller than the number of stem cells per unit of bone marrow or peripheral blood. Since there are fewer stem cells per unit of cord blood, cord blood stem cells take longer to engraft—to establish themselves in the recipient's body and to begin producing blood cells. The longer it takes for the cells to become engrafted, the longer the body is not producing the white blood cells that fight

against infections. Until engraftment occurs, patients are at risk of developing life-threatening infections. Thus, cord blood transplant recipients may be vulnerable to infections for an average of up to one to two months longer than bone marrow and peripheral blood stem cell recipients. The number of cells required to give a transplant patient the best chance for engraftment and for surviving the transplant is based on the patient's weight, age and disease status. A unit of cord blood may contain too few stem cells for adults, so this source of stem cells is often limited to small adults and children. For more information, see *Treatments Undergoing Investigation* on page 4.

- **Clinical Data.** Cord blood stem cell transplantation has been performed for more than 25 years, yet it is a relatively new procedure in comparison to transplantation of peripheral blood or marrow stem cells. Cord blood banks have various procedures in place to ensure safe transplantation of cord blood stem cells. For example, potential donors can provide a detailed health history that covers individual and family histories of disease and the expectant parents' ethnic background. If responses to the health history generate medical concern, the cord blood is not collected. Follow-up of the donor infant (for months or even years) is a precautionary measure that can be used to rule out any possibility of the presence of any genetic disease that could be passed on to a patient via the donor cord blood stem cells. For more detailed information see *The Collection and Storage of Blood From the Umbilical Cord and Placenta* on page 4.

- **Storage.** It is not known how long cord blood can be frozen and stored before it loses its effectiveness. Cord blood that has has been preserved for more than 10 years has still been successfully transplanted.

Options for Cord Blood Donation and Collection

The umbilical cord is routinely discarded after a baby is delivered unless the parents choose to do otherwise. Expectant parents may choose to have the blood remaining in the umbilical cord and placenta collected after delivery. Parents are encouraged to talk with their healthcare providers about the options that may be available. Healthy parents with healthy children can choose to donate their newborn's cord blood to cord blood banks if their hospital participates in a public cord blood collection program. Parents can also speak to an organization that can send a cord blood banking kit so the parents can have the hospital collect the blood and then return the cord blood unit to that organization.

Parents with a child or family member who has a blood cancer, an immune deficiency or certain genetic diseases and who may be a candidate for transplantation should discuss with their doctors the potential benefits of saving their newborn's cord blood for possible family use. It is important to note that there is a 25 percent chance that any two siblings will be fully matched for their HLA tissue type. A baby's cord blood will automatically share 50 percent of its HLAs with each parent; however, it will occasionally be a better match for a parent if both parents, by chance, have some of the same HLAs. However, there may not be enough stem cells in the cord blood unit for it to be used as a transplant for a parent. A baby's cord blood is less likely to be a good match for more distant relatives. Cord blood units from unrelated donors that are stored in public banks are a better source of matches for parents and distant relatives, as well as for siblings who do not have matching HLAs.

Both private and public cord blood banks collect and store cord blood. Public cord blood banks collect and store cord blood that is donated for use by anyone who may need it in the future. It is not saved for the donor's family. Private cord blood banks charge an annual fee to collect and store cord blood for a family's own use (sometimes called a "directed donation"), in the event it is needed for a transplant at a later time.

Umbilical cord blood can also be used for research studies by a laboratory or technology company. These studies help improve the transplantation process for future patients. This cord blood is not stored for transplantation, and the collection costs are free. Parents need to talk to their healthcare providers to determine whether this option is available.

Keep in mind the following points:

- Parents should talk with the doctor or midwife about the decision to donate umbilical cord blood about two months before the baby is due (before the 34th week of pregnancy).
- Not all hospitals collect cord blood for public banking; therefore, parents need to find out whether their hospital collects donations of cord blood for public banking.
- Be The Match® maintains a list of participating hospitals that collect cord blood units for their network of public cord blood banks. (See the list at www.bethematch.org/cord.)
- Public cord blood banks do not charge for collecting and storing donated cord blood. The public cord blood bank that works with the hospital will need to be contacted to ensure determination of eligibility. The mother is required to complete a thorough health history and to be screened, free of charge, for infectious agents such as the hepatitis viruses and HIV. The screening process may be initiated either during pregnancy, or before or immediately after the delivery, but it is completed in the hospital. If the mother is in good health and meets eligibility criteria, she will be asked to sign a consent-to-donate form.
- A family choosing to store its baby's cord blood for family use must make arrangements in advance with a private

cord blood bank. Usually the family will sign a contract with the company, pay an initial fee, obtain the company's special cord blood collection kit and get their obstetrician's agreement to do the collection. Initial and annual storage fees vary and may NOT be covered by health insurance.

American Academy of Pediatrics (AAP) Policy Statement

The AAP is currently updating its policy on cord blood banking. When available, a link to that statement will be made available.

The Collection and Storage of Blood From the Umbilical Cord and Placenta

During delivery, the focus is on the mother and baby. To minimize risk to mothers and newborn infants, normal childbirth procedures should not be altered in order to collect cord blood. After the baby is delivered

- The umbilical cord is clamped. The blood from the umbilical cord and placenta is then collected, either before or after the placenta is delivered, depending upon the procedure at the hospital.
- The blood is collected into a sterile bag, given an identification number and stored temporarily.
- The cord blood is transported to a cord blood bank for testing and potential freezing and long-term storage.
- The cord blood is tested for HLA typing to determine the level of matching of the cord blood to potential recipients, cell counts and infectious agents such as the AIDS virus, cytomegalovirus and hepatitis viruses.
- The cord blood is also checked to make sure it has enough blood-forming cells for a transplant. If there are too few cells, the cord blood unit may be used for research to improve the transplantation process for future patients or may be discarded.
- The cord blood is frozen and stored at a very low temperature, usually in liquid nitrogen, for future use. When needed for a transplant, the cord blood can be shipped, often within a few days, to the transplant center where it is thawed and infused into the patient.

Treatments Undergoing Investigation

Clinical trials test new drugs and treatments, many of which are supported by LLS research programs, before they are approved by the FDA as standard treatments. Clinical trials are carefully controlled research studies, conducted under rigorous guidelines, to help researchers determine the beneficial effects and possible adverse side effects of new treatments.

Clinical trials are designed to be accurate and very safe. Patient participation in clinical trials is important in the development of new and more effective treatments and may provide patients with additional treatment options. Patients interested in participating in clinical trials are encouraged to talk to their doctors about whether a clinical trial would be appropriate for them.

For more information about clinical trials, see the free LLS publication *Understanding Clinical Trials for Blood Cancers* at www.LLS.org/booklets or visit www.LLS.org/clinicaltrials.

In the last several years, there have been numerous retrospective and prospective studies on cord blood transplantation. These studies have helped further define criteria for cord blood unit selection for individual patients and mostly demonstrated that cord blood stem cell transplantation yields outcomes similar to that of bone marrow and peripheral blood stem cell transplantations from unrelated donors.

An important randomized study in pediatrics demonstrated similar outcomes for children who have already received a cord blood unit that met HLA-matching and cell-dose criteria, and were then given a second cord blood unit in order to increase the available cell dose. Thus, the use of two cord blood units should be reserved for those who need more stem cells than are available in a single cord blood unit (a common occurrence in adults and larger adolescents, or in the context of clinical trial).

In cord blood transplantation, receiving an adequate cell dose is critical for recovery time for blood counts (white blood cells, red blood cells and platelets) and for reducing the risk of rejection after transplantation. Several cord blood transplantation specialists have been studying methods to

- Grow more cord blood cells from a single blood cord unit in the laboratory in order to have larger cell doses available at the time of transplantation.
- Treat the cord blood prior to transplant with medication that helps the blood stem cells from cord blood to find their way to the patient's bone marrow and multiply.

Reports on these clinical studies have been promising. In some cases, larger multicenter studies are ongoing and may provide a definitive answer on the efficacy of some of these strategies.

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We're Here to Help

LLS is the world's largest voluntary health organization dedicated to funding blood cancer research, education and patient services. LLS has chapters throughout the country and in Canada. To find the chapter nearest to you, visit our Web site at www.LLS.org/chapterfind or contact:

The Leukemia & Lymphoma Society
3 International Drive, Suite 200
Rye Brook, NY 10573
Contact an Information Specialist at (800) 955-4572
Email: infocenter@LLS.org.

LLS offers free information and services for patients and families touched by blood cancers. Various resources are available to you. Use the information to learn more, to ask questions, and to make the most of your healthcare team's knowledge and skills.

Consult with an Information Specialist. Information Specialists are master's level oncology social workers, nurses and health educators. They offer up-to-date disease and treatment information. Language services are available. For more information, please:

- Call: (800) 955-4572 (M-F, 9 a.m. to 9 p.m. EST)
- Email: infocenter@LLS.org
- Live chat: www.LLS.org
- Visit: www.LLS.org/informationspecialists.

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Información en Español (LLS information in Spanish). For more information, please visit www.LLS.org/espanol.

Telephone/Web Education Programs. LLS offers free telephone/Web education programs for patients, caregivers and healthcare professionals. For more information, please visit www.LLS.org/programs.

Online Blood Cancer Discussion Boards and Chats. Online discussion boards and moderated online chats can provide support and help cancer patients to reach out to others in similar circumstances, and share information. For more information, please visit www.LLS.org/chat or www.LLS.org/discussionboard.

LLS Community. LLS Community is an online social network and registry for patients, caregivers, and supporters of those with blood cancer. It is a place to ask questions, get informed, share your experience, and connect with others. To join visit https://communityview.LLS.org.

Sign Up For an E-newsletter. Read the latest disease-specific news, learn about research studies and clinical trials, and find support for living with blood cancer. Please visit www.LLS.org/signup.

LLS Chapters. LLS offers community support and services in the United States and Canada including the *Patti Robinson Kaufmann First Connection Program* (a peer-to-peer support program), in-person support groups, blood cancer conferences and other great resources. For more information, please

- Call: (800) 955-4572
- Visit: www.LLS.org/chapterfind.

Clinical Trials (Research Studies). New treatments for patients are ongoing. Patients can learn about clinical trials and how to access them. For more information, please:

- Call: (800) 955-4572 to speak with our LLS Information Specialist who can help conduct clinical-trial searches.
- Visit: www.LLS.org/clinicaltrials.

Advocacy. The LLS Office of Public Policy (OPP) engages volunteers in advocating for policies and laws that encourage the development of new treatments and improve access to quality medical care. For more information, please:

- Call: (800) 955-4572
- Visit: www.LLS.org/advocacy.

Other Resources

AABB
www.aabb.org

This international nonprofit organization, formerly known as the American Association of Blood Banks, works to advance the practice and standards of transfusion medicine and cellular therapies to optimize patient and donor care and safety. The AABB maintains a list of accredited facilities that are responsible for procuring, processing and storing umbilical cord blood stem cells that can be used for transplantation. To access this list, visit http://www.aabb.org/sa/facilities/celltherapy/Pages/CordBloodAccrFac.aspx.

Center for International Blood and Marrow Transplant Research (CIBMTR)
www.cibmtr.org

CIBMTR collaborates with the global scientific community to advance hematopoietic cell transplantation and cellular therapy research worldwide. A combined research program of the National Marrow Donor Program®/BeTheMatch® and the Medical College of Wisconsin, CIBMTR facilitates critical observational and interventional research that has led to increased survival and an enriched quality of life for thousands of patients.

Foundation for the Accreditation of Cellular Therapy (FACT)
www.factwebsite.org

A nonprofit corporation that establishes standards for high-quality medical and laboratory practice in cellular therapies. FACT is cofounded by the International Society for Cellular Therapy (ISCT) and the American Society of Blood and Marrow Transplantation (ASBMT) for the purposes of voluntary inspection and accreditation in the field of cellular therapy.

International NETCORD Foundation
www.netcord.org

The mission of the International NETCORD Foundation is to promote the highest quality in cord blood products through worldwide standards and accreditation, to balance global supply and demand for umbilical cord blood, to encourage and facilitate the use of cord blood transplants by promoting laboratory and clinical research and providing professional and public education.

National Marrow Donor Program (NMDP)
www.bethematch.org

The NMDP is a global leader in bone marrow transplantation. NMDP conducts research to improve transplant outcomes and provides support and resources for patients who need life-saving bone marrow or cord blood transplants. NDMP operates Be The Match, a registry of bone marrow donor volunteers and a registry of cord blood donations.

New York Blood Center's National Cord Blood Program (NCBP)
(866) 767-6227
www.nationalcordbloodprogram.org

This public cord blood bank collects, processes, tests and stores donated cord blood for use by anyone who may need it. The NCBP supplies information for patients, their families and caregivers, healthcare professionals, expectant parents and the general public.

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US Department of Health and Human Services Food and Drug Administration Center for Biologics Evaluation and Research. *Guidance for Industry: Biologics License Applications for Minimally Manipulated, Unrelated, Allogeneic Placental/Umbilical Cord Blood Intended for Hematopoietic and Immunologic Reconstitution in Patients with Disorders Affecting the Hematopoietic System.* Office of Communication, Outreach and Development (OCOD), (HFM-40), 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448. March 2014.