joanne pang foundation
cord blood for life

Umbilical Cord Blood Banking

From Yesterday's Medical Waste to Today's Medical Miracle

An Overview

in Support of

Northern California Umbilical Cord Blood Bank

P.O. Box 320636 San Francisco, CA 94132 (415)-786-3036 www.joannepang.org

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Executive Summary

The uses of the lifesaving stems cells in cord blood have increasingly become a common therapy in treating life threatening diseases today. Already being used to treat thousands of patients with various grave conditions, cord blood stem cell research continues to yield new results and therapies from what was once considered medical waste.

After a baby is born and the umbilical cord is cut, the remaining blood of the placenta and the portion of the umbilical cord that remains attached to it are no longer needed by the baby. This blood is called placental blood or umbilical cord blood: "cord blood" for short.

Cord blood is rich in hematopoietic (blood-forming) stem cells, similar to those found in bone marrow. However, cord blood offers distinct advantages that make it better for medical treatments and transplants than bone marrow and peripheral blood.

Stem cells from bone marrow or peripheral blood are hard to obtain, as donation requires surgery and donors often find themselves in considerable pain and discomfort after the operation. Cord blood stem cells are easier to collect from donors and collection is painless for both mother and child.

Furthermore, where bone marrow and peripheral blood transplants generally require a perfect match between donor and recipient, mismatched cord blood transplants are possible (and have been performed), making it easier to find a suitable match.

Cord blood, bone marrow, and peripheral blood stem cell research already have resulted in clinical treatments. Leukemia, Sickle Cell Anemia and Hodgkin's disease are among the diseases and conditions from which adults and children are currently being treated with stem cells derived from cord blood.

And the promise of cord blood stem cells is just beginning to be unlocked. Published studies in nonclinical models have shown that stem cells in cord blood in addition to bone marrow and peripheral blood can become other cell types, including nerve cells, heart cells and insulin-secreting cells. This offers the potential to yield a cure for non-blood related diseases.

Despite the fact that umbilical cords are a rich, non-controversial source of stem cells, hospitals still currently throw millions of them away each year. A shortage of staff trained in the procurement and handling of cord blood combined with a deficiency of storage capacity means that hospitals around the country have been discarding this rich source of stem cells for years.

The California Senate Bill No. 962-*Umbilical Cord Blood: Research* by Senator Carole Midgen as well as the California Assembly Bill No. 34-*Umbilical Cord Blood Collection Program* by Assemblyman Anthony Portantino, which were both approved by Governor Arnold Schwarzenegger on October 11, 2007, have come out strongly in support of storing your baby's cord blood in public banks.

Public cord blood banking is not only an altruistic move, but also a sensible move on your part as parents. You will be a part of the crusade against genetic diseases and incurable diseases like cancer if you decide to make your baby's cord blood available for use to needy people or even in research.

Technologies are helping researchers extract even more value from cord blood that was previously thought to be medical waste. With the increasing demand on the supply and the diversity, the benefits of this research will be exponential.

Fact Sheet: Cord Blood Banking and Donation

What is cord blood?

Umbilical **cord blood** or cord blood is the blood that stays in the umbilical cord and placenta after the birth of an infant. This blood contains **stem cells** that are special cells that can help treat diseases in children and adults. In the past, all cord blood was thrown away after the infant was delivered. Cord blood can now be donated or saved in cord blood banks for future use.

How is cord blood used?

Stem cells from cord blood can be used to treat various grave diseases in children and adults. The stem cells in the blood help to build new healthy cells and replace cells that have been damaged. Cord blood has been used to treat certain cancers, inherited diseases and diseases of the immune system. Scientists are also studying whether cord blood can be used to treat other common diseases like heart disease, stroke, and brain diseases.

Who can benefit from the stem cells in cord blood?

Cord blood can benefit children and adults with certain diseases and in need of a life-saving transplant. Another benefit of cord blood is that an exact match to the person receiving the cord blood is not required.

How is cord blood collected?

After the infant is born, medical staff collects the cord blood and places it in a special container that is then sent to the cord blood bank. The cord blood and mother's blood samples are then processed and tested. If the mother's blood sample identifies the presence of infectious disease, the mother will be notified. Once the cord blood bank determines the blood can be used, it is stored for future use.

What are the risks with cord blood collection?

There are no risks to the mother or infant when cord blood is collected. It is collected from the umbilical cord after the infant is born. Collecting the blood will not affect delivery or cause pain to the mother or infant.

Are stem cells in cord blood different from embryonic stem cells?

Yes, stem cells from cord blood are different from embryonic stem cells. **Embryonic stem cells** come from developing human or animal embryos. Cord blood stem cells do not involve the use of embryos.

Is there a demand for cord blood?

Yes, thousands of patients who might benefit from a cord blood transplant die every year waiting for treatment. There is an especially great need for more cord blood donations from ethnic and racial minorities. Tissue types among ethnic and racial minorities can vary; therefore, it is desirable to have a larger "pool" of donated stem cells to meet the needs of these populations.

What options are available for cord blood to be donated or saved?

Cord blood is collected at the hospital shortly after delivery. There are several options if families want to donate or save infant cord blood:

- donate it to a public bank, where it is made available to others, much like blood banks;
- save it through a family or sibling directed banking program so it will be available for family members;
- save it to a private bank so it will be available for family members.

Families can call their local hospital or health care provider to find out which options are available. Families that decide to donate or save cord blood should make plans with a cord blood bank and their doctor before their infant's delivery.

Is there a cost to donate or save cord blood?

There is no cost to donate infant cord blood to a public cord blood bank. There may be costs associated with family or sibling directed donor programs, if the unit stored is reserved for a family. Some parents choose to save or "bank" cord blood in a private cord blood bank so family members can use the blood if it is ever needed. If parents choose to store their infant's cord blood, private banks charge a collection fee that ranges from $900 to $2000 and an annual storage fee of approximately $90 to $150. These fees may vary between private banks.

How do families decide if they want to save or donate cord blood?

The decision to donate or save cord blood is a choice that only expectant parents can make. It is important for expectant parents to talk to their health care provider so that they have all the information they need to make the decision that is right for their family.

Families do not have to donate or save infant cord blood.

About the Stem Cell Therapies

Stem Cell – a parent cell

Blood cell differentiation begins with multipotent hematopoietic progenitor cells (HPCs), which are located in the marrow spaces of the bone. These primitive cells undergo division and differentiation to form various peripheral blood cells. As the cells reproduce, they commit to a particular task or cell line and become known as *committed progenitor cells*. These committed progenitor cells are difficult to discern from the original multipotent cells but can be cultured to form colonies of specific types of blood cells[1], such as white blood cells, red blood cells, and platelets.

Cancerous Cells

When the cells can't function normally, they need to be replaced before they interfere with other organs.   A good example is Leukemia.

Leukemia is a cancer of white blood cells, or leukocytes. Like other blood cells, leukocytes are made in the bone marrow through a process that begins with multipotent stem cells. Mature leukocytes are released into the bloodstream, where they work to fight off infections in our bodies.

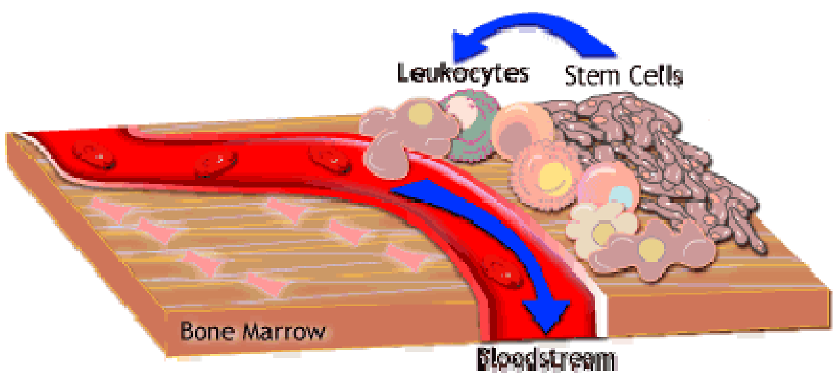

Figure 1: Bloodstream and Leukocytes

Leukemia results when leukocytes begin to grow uncontrollably and function abnormally, becoming cancerous. These abnormal cells cannot fight off infection, and they interfere with the functions of other organs.

Successful treatment for leukemia depends on getting rid of all the abnormal leukocytes in the patient, allowing healthy ones to grow in their place. The only way to do this is through chemotherapy, which uses potent drugs to target and kill the abnormal cells. However, oftentimes, chemotherapy alone can't eliminate them all.

Because of the potential of HPCs to reconstitute bone marrow and peripheral blood, they have been used for the treatment of various grave diseases including bone marrow damage, such as leukemia, for several decades. Several stem cell therapies are routinely used today. These include:

- Bone Marrow Stem Cell Transplant;
- Peripheral Blood Stem Cell Transplant;
- Umbilical Cord Blood Stem Cell Transplant.

Bone Marrow Stem Cell Transplant

Perhaps the best-known stem cell therapy to date is the bone marrow transplant, which is used to treat leukemia and other types of cancer, as well as various blood disorders.

In a bone marrow transplant, the patient's bone marrow stem cells are replaced with those from a healthy, matching donor. To do this, all of the patient's existing bone marrow and abnormal leukocytes are first killed using a combination of chemotherapy and sometimes radiation. Next, a sample of donor bone marrow containing healthy stem cells is introduced into the patient's bloodstream.

If the transplant is successful, the stem cells will migrate into the patient's bone marrow and begin producing new, healthy leukocytes, red cells and platelets to replace the abnormal cells.

Peripheral Blood Stem Cell Transplant

While most blood stem cells reside in the bone marrow, a small number are present in the bloodstream. These multipotent hematopoietic progenitor cells (HPCs) in peripheral blood stem cells or PBSCs, can be used just like bone marrow stem cells to treat leukemia, other cancers and various blood disorders.

Since they can be obtained from drawn blood, PBSCs are easier to collect than bone marrow stem cells, which must be extracted from within bones. This makes PBSCs a less invasive treatment option than bone marrow stem cells. PBSCs are sparse in the bloodstream, however, so collecting enough to perform a transplant can pose a challenge.

Umbilical Cord Blood Stem Cell Transplant

Newborn infants no longer need their umbilical cords, so they have traditionally been discarded as a by-product of the birth process. In recent years, however, the multipotent-stem-cell-rich blood found in the umbilical cord has proven useful in treating the same types of health problems as those treated using bone marrow stem cells and PBSCs.

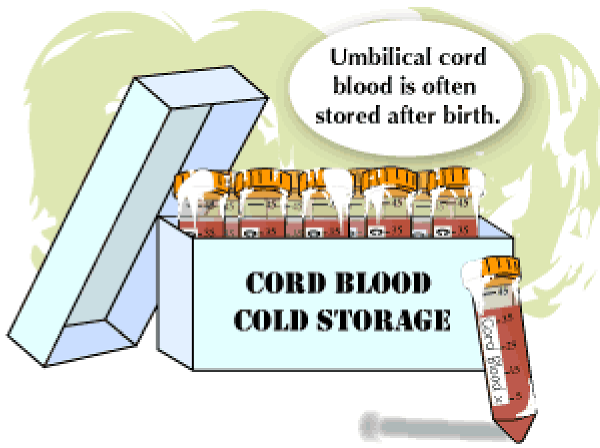

Figure 2: Cold Storage of Cord Blood

Umbilical cord blood stem cell transplants might be less prone to rejection than either bone marrow or peripheral blood stem cells. This is probably because the cells have not yet developed the features that can be recognized and attacked by the recipient's immune system. Also, because umbilical cord blood lacks well-developed immune cells, there is less chance that the transplanted cells will attack the recipient's body, a problem called graft versus host disease.

The researchers studied data taken from 314 patients treated at Duke between 1993 and 2007. The patients ranged in age from six months to 21 years and suffered from both malignant and non-malignant conditions. "We found that transplantation using 4/6 matched cord blood was effective and also carried a low probability of graft versus host disease, a complication caused by the attacking immune cells from the transplanted blood or marrow that perceive the recipient as 'foreign,' in the same way a healthy body's immune system might fight off a virus," said Vinod Prasad, M.D., a pediatric oncologist at Duke. "The incidence of other complications was low as well, and the data suggest that using 4/6 matched cord blood could improve access for all patients."

Both the versatility and availability of umbilical cord blood stem cells makes them a potent resource for transplant therapies.

A Critical Need to Expand Cord Blood Stem Cell Inventory

Difficulties in Locating a Matched Adult Donor for a Timely Life-Saving Transplant

In an attempt to make HPCs more widely available to the large number of patients who do not have an HLA-identical sibling, large international volunteer (bone marrow and peripheral blood donor) registries were created in the 1980s[2]. Unrelated adult donors are generally identified through these donor registries. Up to now, more than 20 million registered volunteer donors are listed in more than 40 registries worldwide[3].

These 40 registries of unrelated donors provide suitable donors for only about a third of the patients without a sibling donor; thus a shortage of suitable donors persists. In addition, the distribution of HLA alleles and haplotypes found in individuals varies among different ethnic and racial groups. Some alleles and haplotypes are common to several populations; others are predominantly confined to one population group. Thus, some populations are more likely to be underserved by these registries.

Registries maintain lists of the HLA types (and other clinically relevant information) of individuals willing to allow the harvesting of HPCs from their bone marrow or peripheral blood for transplantation should a need arise.

However, despite the large numbers of adult donors recruited over the past two decades, registries and transplant physicians still face several challenges, including:

- inability to identify fully or closely matched HLA donors for a significant proportion of transplant candidates, particularly non-Caucasian individuals;
- permanent or transient unavailability of some potential donors, even if that individual was identified in a registry on the basis of HLA match[4] ;
- prolonged interval between the time of a search request and the time of HPC acquisition. Currently reported median time is 2 - 4 months.

Discomfort in Extracting Stem Cells from Bone Marrow and Peripheral Blood Donors

<u>Discomfort Associated with Bone Marrow Donor</u>

The donation of HPCs is not without risk for adults. In the case of bone marrow donation[5], the bone marrow must be surgically removed, generally by large-bore needle aspiration while the donor is under general or spinal anesthesia[6]. Although fewer than 1 percent of donors experience serious complications, the procedure can result in significant postoperative discomfort to the donor at the aspiration site and may be a factor in recruiting donors to a registry[7].

Discomfort Associated with Peripheral Blood Donor

Alternatively, HPCs can be collected from peripheral blood through a process called leukapheresis after the administration of drugs to mobilize HPCs so that they move out of the bone marrow and into the bloodstream. One can typically collect up to 10x the number of stem cells in the blood vs. a bone marrow collection. However, leukapheresis can be associated with bone pain from the mobilization drugs, hypocalcemia, decreased platelet counts, spleen enlargement or (rarely) rupture, and complications from venous catheter placement.

Inadequate Cord Blood Inventory

In 2007, Umbilical Cord Blood transplants accounted for about a quarter of the 4,000 stem cell transplants performed in the United States. Based on current estimates by the Health Resources and Services Administration (HRSA) that sponsors the National Cord Blood Inventory, approximately 50,000 cord blood units (CBUs) useable for clinical transplant, are now available through existing public banks in the USA. HRSA projects the need for at least 100,000 more. The larger the inventory, the greater the likelihood that a patient will be matched to a suitable unit and receive an optimal dose of cells.

Umbilical Cord Blood Banks and Banking

Collection, Storage, Search, and Transplantation

A cord blood bank is a center whose central mission is to maintain a supply of cord blood for therapeutic use in transplantation. Figure 3 depicts the various aspects of the collection, storage, search and transplantation processes.

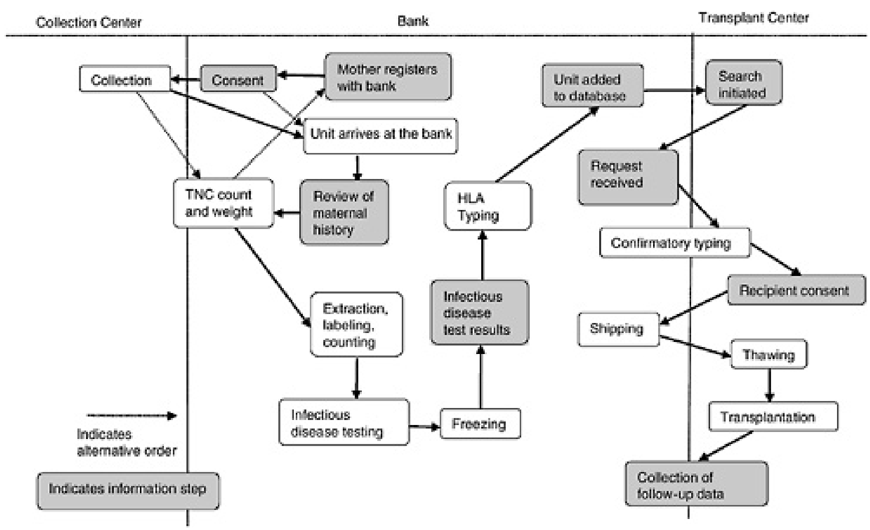

Figure 3: Major Components in the Process of Cord Blood Collection, Banking, and Transplantation.

In most cases, a mother will register with a bank prior to giving birth. Upon adequate completion of the informed consent, the mother's obstetrician is informed of her wish to be a donor, and arrangements are made to collect the cord blood. This is either by providing the mother with a kit or, if the delivery hospital is affiliated with a bank, by noting it in the mother's chart. In most cases, the collected blood is then transported to the bank in order to obtain volume and cell count. If both are high enough, the unit is processed, and samples are taken for infectious disease testing.

If the review of the maternal history and infectious disease testing are both within the bounds established by the bank, another sample is sent for HLA testing. Because obtaining HLA type is the most expensive part of the process, this is generally not done until the unit meets the bank's requirements in all other ways and is the last step before listing in a database.

Cord Blood Banking Options

Cord blood banks have been established in response to the needs of different patient populations, and the motivation to store cord blood varies from person to person. For some, there might be an immediate need within the family to treat a disease amenable to transplantation, for example to a sibling or a closely matched family member. Alternatively, a woman or a couple might donate altruistically (as with blood donation) by offering the cord blood as a public resource to be available for others with the need for an immediate transplant. Finally, some donors choose to contribute to research. Table 1 summarizes the primary banking options available to new mothers.

Table 1: Cord Blood Banking Options

Type	Purpose	Fee
Option 1: autologous banking (banking for future use by the infant from whom the cord blood was obtained or immediate family members)	Maintain a stored unit in the event that donor or a family member needs a hematopoietic stem cell transplant	Variable; involves an initial banking cost ($1,000 to $2,000) and then a yearly maintenance fee ($50 to $150)[a]
Option 2: philanthropic donation	Unit will be saved for potential use by the general public	No fee
Option 3: research donation	Procurement directed to an institution researching the properties of umbilical cord blood units	No fee to family but some research organizations are charged
Option 4: directed donation [b]	Collection to serve a patient in need, usually a sibling or other family member	Usually offered by the transplant centers at no cost to the family; also offered by some public and private banks; transplant centers may be charged to procure the unit

[a]If there is a history of a genetic disease or condition or a malignancy within the family, it is possible that insurance will cover these costs.

[b]Cord blood banking options should be presented to the family if a family member has a current or a potential need to undergo a stem cell transplant.

Classification of Cord Blood Banks

Cord blood banks can be classified into three main categories as in Table 2.

Public banks

Public banks store unrelated cord blood units that are philanthropically donated for transplantation or research purposes. The relevant information (e.g. HLA types, cell counts, and in some cases, the donor's medical history) is then stored in a database made available to transplant centers searching for a cord blood unit for patients. Some public banks also store a limited number of units for autologous or family use when a disease that is treatable by cord blood transplantation is known to exist within the donor's family. In these circumstances, the blood is often stored for a short time and the bank provides the necessary processing and testing to aid the transplant physician. Units that do not meet standards for clinical use may be used for quality improvement or research.

Private banks

Private banks store cord blood units only for autologous or family use. These banks generally charge a fee for the collection, processing, and storage of the cord blood and leave any decisions regarding the use of the unit to the donor or the donor's family. These banks tend to describe their service as offering "biological life insurance" that provides peace of mind to families that might be concerned about future health conditions in the child or a close relative for which cord blood transplantation might be a possible treatment. If the family decides to discontinue banking the unit, with their consent it may be made available for research.

Mixed banks

Mixed banks not only collect unrelated units donated for transplantation to unrelated recipients but also operate facilities for cord blood banking for autologous use by family members. The money received from private banking activities can help to offset the costs of public banking activities at these facilities. Both public and private units are processed and stored at the same facility; however, as with fully private banks, the private units are the property of the donor's family and are not available for general use. As with fully public banks, units that do not meet quality standards may be used for quality improvement or research. If a family decides that it no longer wishes to maintain ownership of a unit, it is conceivable that the unit would then become available to the public for unrelated transplantation to patients unrelated to the family or for research, if the family consents.

Table 2: Representative Cord Blood Banks

PUBLIC BANKS American Red Cross North Central Blood Services Cord Blood Program JP McCarthy Cord Stem Cell Bank Michigan Community Blood Centers Cord Blood Bank National Cord Blood Program of the New York Blood Center New Jersey Cord Blood Bank South Texas Blood & Tissue Center St. Louis Cord Blood Bank University of Colorado Cord Blood Bank
PRIVATE BANKS Cord Blood Registry LifeStor Sibling Donor Cord Blood Program Children's Hospital Oakland Research Institute Viacord
BANKS THAT OFFER BOTH Carolinas Cord Blood Bank Children's Hospital of Orange County Cord Blood Bank Cryobanks International, Inc. ITxM Cord Blood Services Lifebank USA LifeCord Puget Sound Blood Center and Hawaii Cord Blood Bank StemCyte Inc. and Cord Blood Family Trust The Elie Katz Umbilical Cord Blood Program at Community Blood Services

Impartial Information to Expectant Mother

As an expectant mother's primary source of information about banking options is her obstetrician, it is very important that obstetricians fully understand the different options available, and be able to effectively convey that information to the mothers. Further, as the obstetricians are not reimbursed by the public banking system the way they are with many private banks, it is also important that they fully "buy in" to the advantages of the public system.

Clinical Uses of Cord Blood Stem Cell

Key Clinical Uses of Cord Blood

Cord blood transplantation as a treatment for children with hematological, immunological, metabolic, and neoplastic diseases has been highly successful. Today doctors use cord blood cells to treat various grave diseases, mostly anemias or cancers of the blood such as leukemias and lymphomas.

The advantage of cord blood transplants is the relatively low rate of graft-versus-host disease (GVHD) compared with the rates of GVHD that occur as a result of bone marrow or peripheral blood transplants. This low rate of GVHD related to cord blood transplantation allows for the use of partially human leukocyte antigen (HLA)-mismatched cord blood units.

Other Clinical Uses of Cord Blood

In addition to treatment of blood and blood-related diseases, cord blood has been utilized as an effective therapy in certain genetic diseases.

<u>Immune Deficiency</u>

- X-linked SCID
- X-linked a-γ-globulinemia
- Wiskott-Aldrich syndrome
- Chédiak-Higashi syndrome
- Chronic granulomatous disease
- Adenosine deaminase (ADA) deficiency
- Purine nucleotide phosphorylase deficiency
- Gaucher disease, type 1

<u>Bone Marrow Failures</u>

- Osteopetrosis
- Thalassemia
- Sickle cell disease[8]
- Fanconi anemia
- Dyskeratosis

<u>Metabolic Storage Disorders</u>

- Adrenoleukodystrophy
- Metachromatic leukodystrophy
- Adrenoleukodystrophy
- Metachromatic leukodystrophy
- Mucopolysaccaridoses
    - Hurler syndrome
    - Hunter (X-linked)

  - Sanfillippo
  - Morquio
- Maroteaux-Lamy
- Lesch-Nyhan syndrome (X-linked)

Challenges

The rate of use of cord blood for transplantation has increased rapidly, and in the United States, Europe, and Japan exceeds the use of bone marrow for childhood transplants. Clinical investigations indicate promising results in a variety of settings, although utilization and success are limited by several obstacles as follows:

- relatively few total cell volumes (~100 milliliters) than bone marrow grafts. This can result in very low cell doses (the number of cells in the graft per kilogram patient weight) for larger children and adults;

- higher risk of slow engraftment due to the use of low overall cell doses ($<1.5 \times 10^7$ nucleated cells in the graft per kilogram of patient weight);

- rate of infection sometimes higher due to slower immune reconstitution.

Some data indicate that this can be overcome by combining cells from multiple units or by combining cord blood with highly purified HPCs from mismatched related donors[9-10]. Several investigators have also explored the ex vivo expansion of cord blood cells[11] with the use of certain growth factors, but no data supporting faster engraftment by this approach are available and few comparative studies of the clinical outcomes obtained by transplantation of HPCs from adult donors and cord blood have been conducted.

Social Benefit of Cord Blood Stem Cell

Only 30% of patients who need a stem cell transplant can find an adult donor in their genetic families[12]. The remaining 70% of patients who seek unrelated donors have an urgent need to find matching stem cells, whether from bone marrow, peripheral blood, or newborn cord blood.

Racial Distribution of Marrow Donors

The majority of adults who are registered as potential donors are Caucasians[13] as in Table 3. Thus, patients who come from racial or ethnic minorities are at a serious disadvantage in their ability to find a matching adult donor.

Table 3: Racial Distribution of Marrow Donors

Caucasian	52.4 %
African American	8.0 %
Asian/Pacific Islander	6.5 %
Hispanic	8.5 %
Native American	1.2 %
Multi-Racial	2.2 %
Unknown	21.1 %

Racial Distribution of Cord Blood Donors

Cord blood donors do not have to be as precisely "matched" to the patient as adult donors. Thus, cord blood makes stem cell transplants accessible to many more patients. For this reason cancer patients, and especially minority group cancer patients, have a vested interest in having parents donate their newborn's cord blood to a cord blood bank.

One major goal of cord blood banking is to increase the HLA diversity in the inventory, particularly the HLA types of ethnic and racial minorities. However, early efforts aimed at increasing the recruitment of minority populations as donors of cord blood encountered difficulties similar to those faced in the early days of the bone marrow registries, resulting in lower than desired representations of units from members of minority populations as in Table 4 according to the American Red Cross[14].

Table 4: Racial Distribution of Cord Blood Donors

Caucasian	64 %
African American	16 %
Hispanic	12 %
Asian/Pacific Islander	4 %
Native American	1 %
Unknown	3 %

Benefits of Increased Cord Blood Donor Pool

Two consumer groups would have a vital stake in a cord blood bank.

Patients who need blood stem cells

At present these are mostly patients who are in need of hematopoietic (blood) stem cell transplants from unrelated donors, to treat cancers and disorders of the blood and immune system. In the future, it may be possible to use stem cells for regenerative medical therapies.

Parents who might donate their newborn's cord blood to the program

Mothers who are in good health and expecting a single baby will be sought to donate their baby's umbilical cord blood. At present, due to a lack of funding, cord blood is only stored for the public good in a few regional banks and listed in existing donor registries. There is also a for-profit industry that offers private cord blood storage to families that can afford it. These two banking practices overlap, as some banks offer both public and private storage. The programs which accept public donations are regulated by the FDA, whereas strictly private banks are registered, but not regulated, by the FDA.

Challenges

These two consumer groups have distinct needs and priorities, which sometimes may conflict.

As noted above, cord blood transplants can help redress the disparity of minority patient access to matching stem cells. In the current US population, birthrates are higher among certain minority groups[15-16]. Thus, the very minority groups that are least likely to find matching bone marrow or peripheral blood stem cell donors, and hence could benefit more from cord blood donations, are also generating disproportionally more opportunities to harvest cord blood. Another population group that could benefit greatly from public cord blood banking are inter-racial people. Currently, 1 in 20 US babies, and 1 in 6 in some parts of the country, is considered inter-racial[17]. These inter-racial children are creating a growing population that is not represented by the adult members of stem cell donor registries.

Another demographic feature of potential donor families is that of socio-economic status (SES). Lower-income families in the United States tend to:

- have higher birthrates;
- give birth at younger ages;
- have less education;
- be more likely to be members of racial/ethnic minority groups including immigrants;
- be over-represented among the uninsured and medically underserved.

Larger and more accessible cord blood collections could resolve several of these issues, in part, because of the relative ease and safety of acquisition of cord blood and the potential to obtain cells from a broad cross-section of the population and the ability to have successful transplant outcomes with a somewhat greater degree of HLA mismatch than with bone marrow or peripheral blood HPCs.

Economic Benefit of Stem Cell Transplant

Rising Cost of treating Cancer

Cancer was once assumed to be a death sentence because the disease was often incurable. The crisis for many today is paying for available treatments due to high cost of treating cancers.

The medical cost in the United States rose from an estimated $72 billions in 2004 as in Figure 4 to an estimated $89 billions in 2008 according to the fact sheets from the American Cancer Society. When combined with the indirect morbidity costs (cost of lost productivity due to illness) at $18.2 billions and the indirect mortality costs (cost of lost productivity due to premature death) at $112.0 billions, the total cost due to cancer in 2008 was calculated to be $219.2 billions.

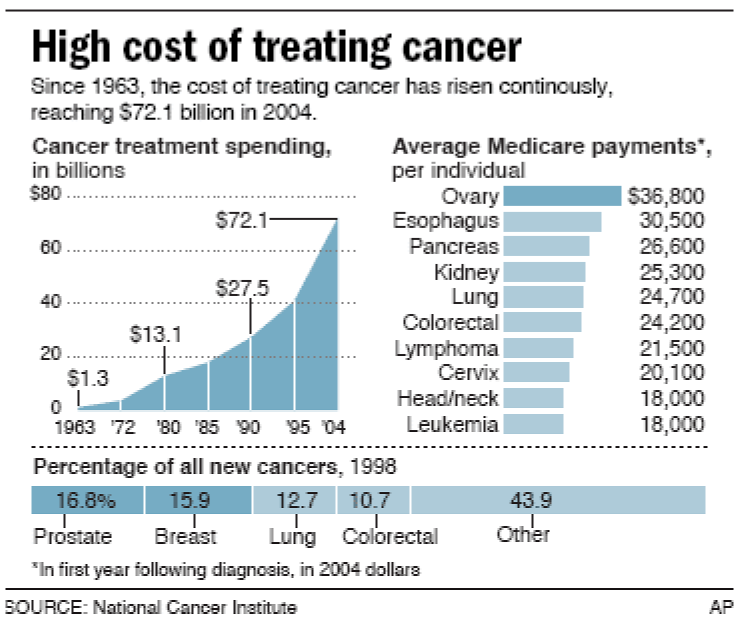

Figure 4: High Cost of Treating Cancer

"It is a big surprise that 20 percent of people with health insurance can't afford to have the cancer therapy they need to save their lives," said John Seffrin of the American Cancer Society. The survey, jointly conducted by ACS and the Kaiser Family Foundation, includes 20 profiles of cancer patients and their struggles to find affordable medical coverage according to the CNN news “Cancer treatment can save most lives but many can't afford it” dated on February 5, 2009. Also mentioned in this article, the cost of treatment and medicine for a ten-year-old Taylor Wilhite since last March is now approaching the lifetime limit of $1 million from her father's family health insurance plan. Taylor has leukemia in bones and blood.

Incidence & Mortality

It is estimated that 1,437,180 men and women (745,180 men and 692,000 women) will be diagnosed with and 565,650 men and women will die of various cancers in 2008 according to National Cancer Institute's SEER (Surveillance Epidemiology and End Results) Cancer Statistics Review[18]. For leukemia alone, it is estimated that 44,270 men and women (25,180 men and 19,090 women) will be diagnosed with and 21,710 men and women will die of leukemia in 2008.

US Incidence

The US incidence rate for all forms of cancer in all races in 2001-2005 were 549.3 per 100,000 men and 411.0 per 100,000 women as in Table 5.

Table 5: Incidence Rates by Race from All Cancers

Race/Ethnicity	Male	Female
All Races	549.3 per 100,000 men	411.0 per 100,000 women
White	551.4 per 100,000 men	423.6 per 100,000 women
Black	651.5 per 100,000 men	398.9 per 100,000 women
Asian/Pacific Islander	354.0 per 100,000 men	287.8 per 100,000 women
American Indian/Alaska Native	336.6 per 100,000 men	296.4 per 100,000 women
Hispanic	419.4 per 100,000 men	317.8 per 100,000 women

The US incidence rate from leukemia alone in all races in 2001-2005 were 16.0 per 100,000 men and 9.5 per 100,000 women as in Table 6.

Table 6: Incidence Rates by Race from Leukemia

Race/Ethnicity	Male	Female
All Races	16.0 per 100,000 men	9.5 per 100,000 women
White	16.7 per 100,000 men	9.9 per 100,000 women
Black	13.0 per 100,000 men	8.0 per 100,000 women
Asian/Pacific Islander	9.1 per 100,000 men	5.9 per 100,000 women
American Indian/Alaska Native	7.9 per 100,000 men	6.9 per 100,000 women
Hispanic	11.7 per 100,000 men	8.0 per 100,000 women

US Mortality

The US mortality rate from all forms of cancer in all races in 2001-2005 were 234.4 per 100,000 men and 159.9 per 100,000 women as in Table 7.

Table 7: Death Rates by Race from All Cancers

Race/Ethnicity	Male	Female
All Races	234.4 per 100,000 men	159.9 per 100,000 women
White	230.7 per 100,000 men	159.2 per 100,000 women
Black	313.0 per 100,000 men	186.7 per 100,000 women
Asian/Pacific Islander	138.8 per 100,000 men	95.9 per 100,000 women
American Indian/Alaska Native	190.0 per 100,000 men	142.0 per 100,000 women
Hispanic	159.0 per 100,000 men	105.2 per 100,000 women

The US mortality rate from leukemia alone in all races in 2001-2005 were 9.9 per 100,000 men and 5.6 per 100,000 women as in Table 8.

Table 8: Death Rates by Race from Leukemia

Race/Ethnicity	Male	Female
All Races	9.9 per 100,000 men	5.6 per 100,000 women
White	10.2 per 100,000 men	5.7 per 100,000 women
Black	8.5 per 100,000 men	5.2 per 100,000 women
Asian/Pacific Islander	5.1 per 100,000 men	3.0 per 100,000 women
American Indian/Alaska Native	5.7 per 100,000 men	4.1 per 100,000 women
Hispanic	6.3 per 100,000 men	4.0 per 100,000 women

Cost Effective with Stem Cell Transplant

Stem cell transplant can be very expensive. Although it may vary, the total costs for the procedure can easily reach $100,000 or more in average today according to the American Cancer Society from about $60,000[19] in 1989 as in Figure 5 for acute myelogenous leukemia (AML), severe combined immunodeficiency (SCID), severe aplastic anemia (SAA), and chronic granulocytic leukemia (CGL). The total costs include medical supplies, pharmaceutical products, blood products, lab/x-ray, procedure, and nursing cares.

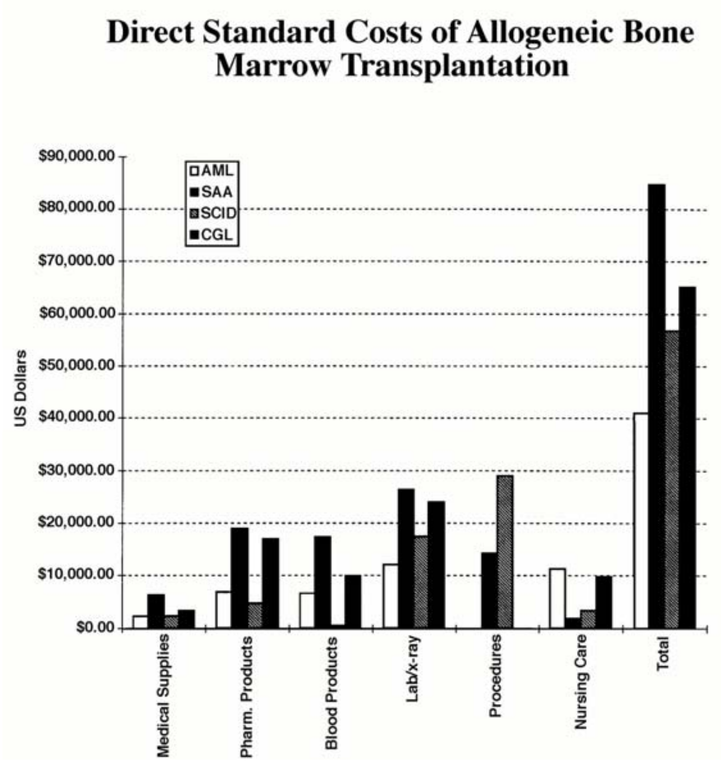

Figure 5: Direct Costs of Allogeneic Bone Marrow Transplantation

Stem cell transplant is a lengthy and intensive treatment. Its cost, when taken at face value, appears very high. However, costs and resource utilization associated with the transplant and traditional chemotherapy are similar when evaluated over a five-year period. When the improved survival obtained with the transplant is considered, transplant is more cost-effective than chemotherapy treatment.

There are a number of categories that could be included in the definition of costs. A full accounting of costs could include dollars associated with five variables. These five variables are

- The medical procedure and ancillary procedures and services
- Diagnosis and treatment of side effects caused by the procedure
- Savings resulting from the ability to avoid other procedures
- Savings resulting from the ability to prevent morbidity
- A net value attached to the effect of prolonging life (both the costs associated with treating new medical conditions that could occur and savings accruing from increased productivity, a percentage of which an be returned to the resources available for health care).

Conclusions

The real issue facing new parents is not whether to donate their cord blood, but where to donate it. Forprofit private cord blood banks are increasingly clamoring for their business. An autologous (self) transplant can also be done if a child's umbilical cord blood has been stored in a private cord blood bank, and that may seem very attractive to new parents.

Conversely, many expectant parents are driven by the desire to protect their own offspring, before any altruistic urge to benefit society. At the same time that all Cord Blood Programs will attempt to recruit parents as potential donors, there are private cord blood banks that will market to parents as potential customers. For those parents who can afford it, private banks offer the option to preserve their child's cord blood for family use. The parents retain control over the disposition of the cord blood.

A child's own cord blood is guaranteed to be a perfect match for that child. This means there's theoretically no chance that the cells will be rejected after transplantation. But in the case of some diseases, doctors consider it unwise to use a child's own cord blood cells for treatment, says Columbia University's Kritstine Gebbie.

Gebbie chaired a panel that advised the U.S. federal government regarding cord-blood banking. "The cells may already carry in them the seeds of the cancer that you are trying to treat in the child," she said. In other words, in cases of some genetic diseases, including many leukemias, doctors fear they would end up transplanting cells that would later become cancerous if they used a patient's own cord blood for the procedure.

Parents can also donate their baby's umbilical cord blood to a public bank for free where it will be used for research and transplants to treat a variety of diseases.

There is a great deal of debate over the degree of "medical insurance" that is realistically provided by family banking of cord blood. Regardless of current claims, the fundamental fact is that no one can confidently predict the future of medical advances. Thus, expectant parents feel torn between the advice of professional societies versus the medical research advances publicized in the media.

Citations and Acknowledgements

Source Citations

[Ref.1] Guyton A, Hall J, eds. 2000. Red blood cells, anemia, and polycythemia. In: *Textbook of Medical Physiology*. 10th ed. Philadelphia, PA: W. B. Saunders and Co. Pp. 382–391.

[Ref.2] Beatty PG, Dahlberg S, Mickelson EM, Nisperos B, Opelz G, Martin PJ, Hansen JA. 1988. Probability of finding HLA-matched unrelated marrow donors. *Transplantation* 45(4): 714–718.

[Ref.3] BMDW (Bone Marrow Donors Worldwide). 2004. *Bone Marrow Donors Worldwide Annual Report 2003*. Leiden, The Netherlands: Europdonor Foundation.

[Ref.4] Wagner JE, Barker JN, DeFor TE, Baker KS, Blazar BR, Eide C, Goldman A, Kersey J, Krivit W, MacMillan ML, Orchard PJ, Peters C, Weisdorf DJ, Ramsay NKC, Davies SM. 2002. Transplantation of unrelated donor umbilical cord blood in 102 patients with malignant and nonmalignant diseases: Influence of CD34 cell dose and HLA disparity on treatment-related mortality and survival. *Blood* 100(5):1611–1618.

[Ref.5] Gluckman E, Rocha V, Boyer-Chammard A, Locatelli F, Arcese W, Pasquini R, Ortega J, Souillet G, Ferreira E, Laporte JP, Fernandez M, Chastang C. 1997. Outcome of cord-blood transplantation from related and unrelated donors. Eurocord Transplant Group and the European Blood and Marrow Transplantation Group. *New England Journal of Medicine* 337(6):373–381.

[Ref.6] Locatelli F, Rocha V, Chastang C, Arcese W, Michel G, Abecasis M, Messina C, Ortega J, Badell-Serra I, Plouvier E, Souillet G, Jouet JP, Pasquini R, Ferreira E, Garnier F, Gluckman E. 1999. Factors associated with outcome after cord blood transplantation in children with acute leukemia. Eurocord-Cord Blood Transplant Group. *Blood* 93(11): 3662–3671.

[Ref.7] Buckner CD, Clift RA, Sanders JE, Stewart P, Bensinger WI, Doney KC, Sullivan KM, Witherspoon RP, Deeg HJ, Appelbaum FR. 1984. Marrow harvesting from normal donors. *Blood* 64(3):630–634.

[Ref.8] Mazur M, Kurtzberg J, Halperin E, Ciocci G, Szabolcs P. Transplantation of a child with sickle cell anemia with an unrelated cord blood unit after reduced intensity conditioning. *J Pediatr Hematol Oncol,* 2006. 28(12): p. 840-4.

[Ref.9] Latour R, Rocha V, Robin M, Rodrigues C, Rea D, Laghero J, Traineau R, Ribaud P, Ferry C, Devergie A, Gluckman E, Socie G. Double Cord Blood Transplantation in Bone Marrow Failure Syndromes. *Blood (ASH Annual Meeting Abstracts)* 2007 110: Abstract 2018.

[Ref.10] Ballen K, Wang B, Rosenthal J, Nademanee A, Karanes C, Jaing T, Graham M, Tan P, Gjertson D, Petz L, Forman S, Chow R. An International Multi-Institutional Study of

Double Cord Blood Transplantation in a Racially Diverse Population. *Blood (ASH Annual Meeting Abstracts)* 2007 110: Abstract 2017.

[Ref.11] North T, Goessling W, Armant M, Kao G, Silberstein L, Ritz J, Zon L. Ex Vivo Treatment of Human Cord Blood with dmPGE2 Can Safely Increase the Potential for Hematopoietic Engraftment. *Blood (ASH Annual Meeting Abstracts)* 2007 110: Abstract 1190.

[Ref.12] Donor Recruitment (from the Marrow Foundation).
About 30% of patients in need of a transplant are able to find a matching donor from within their own family.
(http://www.themarrowfoundation.org/DONOR/donor_idx.html)

[Ref.13] National Marrow Donor Program - Minority Facts & Figures.
Because patients are most likely to find a compatible donor within their own ethnic group, a diverse group of potential donors is needed. As of 31Dec2002, over 4 million volunteers have joined the National Marrow Donor Program, but persons of color are in the minority.
(http://www.marrow.org/NMDP/minority_facts_figures.html)

[Ref.14] Ballen KK, Kurtzberg J, Lane TA, Lindgren BR, Miller JP, Nagan D, Newman B, Rupp N, Haley NR. 2004. Racial diversity with high nucleated cell counts and CD34 counts achieved in a national network of cord blood banks. *Biology of Blood and Marrow Transplantation* 10(4):269–275.

[Ref.15] Births: Final Data for 2002.
National Center for Health Statistics, National Vital Statistics Reports.
(http://www.cdc.gov/nchs/births.htm#Tabulated)

[Ref.16] Child Health USA 2002.
statistics compiled by The Health Resources and Services Administration's Maternal and Child Health Bureau (MCHB).

[Ref.17] Mavin Foundation.
Founded in 2001, MAVIN's MatchMaker is the only national program dedicated to mixed race bone marrow donor recruitment and education.
(http://www.mavinfoundation.org)

[Ref 18] Ries LAG, Melbert D, Krapcho M, Stinchcomb DG, Howlader N, Horner MJ, Mariotto A, Miller BA, Feuer EJ, Altekruse SF, Lewis DR, Clegg L, Eisner MP, Reichman M, Edwards BK (eds). *SEER Cancer Statistics Review, 1975-2005*, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2005/, based on November 2007 SEER data submission, posted to the SEER web site, 2008.

[Ref 19] Viens-Bitker C, Rery-Lemonnier E, Blum-Boisgard C. Cost of allogeneic bone marrow transplantation in four diseases. *Health Policy* 1989;12:309–317.

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The Joanne Pang Foundation, a 501(c)(3) tax exempt organization, is committed to transforming a dream into reality-the establishment of Northern California Umbilical Cord Blood Bank (NCUBB), the first non-profit, public umbilical cord blood bank in Northern California, within the vicinity of a world-class blood and marrow transplant center at the UCSF Children's Hospital.

The ethnic diversity of the San Francisco Bay Area region means that the cord blood units from NCUBB will have a broad genetic mix which will help benefit Asian, African American, Caucasian, and Hispanic patients of all ages.

In addition to establishing the NCUBB, the Joanne Pang Foundation is dedicated to promoting education and awareness of various blood and marrow diseases, supporting the advancement of clinical research and providing patient assistance and family support.