Cord Blood Stem Cells: An Overview

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What are they?

Umbilical cords have traditionally been viewed as disposable biological by-product. Cord blood, however, is rich in multi-potent hematopoietic stem cells (HSCs). Recent medical advances have indicated that these stem cells found in cord blood can be used to treat the same disorders as the hematopoietic stem cells found in bone marrow and in the bloodstream but without some of the disadvantages of these types of transplants. Cord blood is currently used to treat approximately 70 diseases including leukemias, lymphomas, anemias, and Severe Combined Immunodeficiency (SCID). Six thousand patients worldwide have been treated with cord blood stem cell transplants, although the FDA considers the procedure to be experimental. These multipotent stem cells also show promise for the treatment of a variety of diseases and disorders other than those affecting the blood.

Use of Cord Blood in Transplants

Up to 180 mL of blood can be taken from an umbilical cord for use in stem cell transplants. Due to the experimental nature of cord blood transplants, such transplants are considered on a case-by-case basis. This blood is collected from the umbilical cord, processed,[1] and cryogenically preserved shortly after the umbilical cord is clamped. This blood can be cryogenically preserved for public or private (family) use. Public registries store cord blood donated for availability to the general public for transplantation. Private registries store cord
blood on behalf of families who wish to use this blood for the donor infant, siblings, or other family members. Private cord blood banks charge a collection fee (ranging from $1,000-2,000) and an annual storage fee (approximately $150 per year).

The Stem Cell Therapeutic and Research Act was passed in 2005, which supports building a public reserve of 150,000 cord blood units from ethnically diverse donors in order to treat more than 90% of patients in need of HSC transplants. Donors from ethnic minority patients are particularly in need due to the greater variation of HLA-types in non-Caucasian ethnicities. Thirty-five percent of cord blood units go to patients of diverse ethnic and racial backgrounds.

**What are the advantages?**

Cord blood does not have to be as closely matched as bone marrow or peripheral blood transplants. Bone marrow transplants typically require a 6/6 HLA match. While a closely matched cord blood transplant is preferable, cord blood has been transplanted successfully with as few as 3/6 matches. For patients with uncommon tissue types, cord blood may be an option if a suitable adult donor cannot be found. Since cord blood is cryogenically preserved and stored, it is more readily available than bone marrow or peripheral blood from an unrelated donor, allowing transplants to take place within a shorter period of time. It takes approximately two weeks to locate, transfer, and thaw a preserved cord blood unit. Finding a suitable bone marrow donor typically takes at least two months.

Graft-versus-host disease (GVHD) is a common complication after an allogeneic transplant (from a source other than the patient) where the patient’s immune system recognizes the cells as foreign and attacks the newly transplanted cells. This can be a potentially life threatening complication. The risk for developing GVHD is lower with cord blood transplants than with marrow or peripheral blood transplants. Patients who do develop GVHD after a cord blood transplant typically do not develop as severe of a case of GVHD. Cord blood also is less likely to transmit certain viruses such as cytomegalovirus (CMV), which poses serious risks for transplant patients with compromised immune systems.

**What are the disadvantages?**

While the transplantation of cord blood has its advantages, its main disadvantage is the limited amount of blood contained within a single umbilical cord. Because of this, cord blood is most often transplanted in children. Physicians are currently trying to determine ways that cord blood can be used in larger patients, such as transferring two cord blood units or increasing the number of cells in vitro before transplanting to the patient. It also takes longer for cord blood cells to engraft. This lengthier period means that the patient is at a higher risk for infection until the transplanted cells engraft. Patients also cannot get additional donations from the same donor if the cells do not engraft or if the patient relapses. If this is the case, an additional cord blood unit or an adult donor may be used. While cord blood is screened for a variety of common genetic diseases, rare genetic diseases that manifest after birth may be passed on. The National Cord Blood Program estimates that the risk of transmitting a rare genetic disorder is approximately 1 in 10,000.

**What are the potentials for use in stem cell therapy?**

In addition to the use of cord blood stem cells for transplantation, cord blood stem cells are currently being investigated for use in stem cell therapy. Cord blood stem cells are multipotent and are believed to have greater plasticity (the ability to form into different stem cell types) than adult hematopoietic stem cells found in bone marrow. HSCs are being investigated for use in autoimmune diseases such as diabetes, rheumatoid arthritis, and
systemic lupus erythematos (SLE) in order to reprogram or reconstitute the immune system. Additionally, research is being conducted on differentiating HSCs into other tissue types such as skeletal and cardiac muscle, liver cells (hepatocytes), and neurons. HSCs are currently being used in gene therapy, due to their self-renewing properties, as a means of delivering genes to repair damaged cells. HSCs are the only cells currently being used in this manner in clinical gene therapy trials.

What are the advantages?

In addition to the benefits related to transplanting HSCs derived from cord blood, HSCs are relatively easy to isolate, giving them an advantage over other adult stem cell types. Cord blood HSCs are also believed to have greater plasticity than HSCs found in bone marrow or the blood stream. The limits and possibilities of using HSCs to repair tissues and treat non-blood related disorders are currently being studied.

What are the disadvantages?

Similar to transplantation, the main disadvantage is the limited number of cells that can be procured from a single umbilical cord. Different ways of growing and multiplying HSCs in culture are currently being investigated. Once this barrier is overcome, HSCs could be used to create ‘universal donor’ stem cells as well as specific types of red or white blood cells. Immunologic rejection is a possibility, as with any stem cell transplant. HSCs that are genetically modified are susceptible to cancerous formation and may not migrate (home) to the appropriate tissue and actively divide. The longevity of cord blood HSCs is also unknown.

Annotated Bibliography on Umbilical Cord Stem Cell Plasticity:

Introduction to Hematopoietic Stem Cells: http://stemcells.nih.gov/info/scireport/chapter5.asp

Ethics of Cord Blood Stem Cells vs. Embryonic Stem Cells

Cord blood stem cells are classified as adult (or non-embryonic) stem cells. Embryonic stem cells (ESC) are believed to be more advantageous for the treatment of disease or injury due to their pluripotent nature; that is, they have the ability to differentiate into all the cells present in the human body derived from the three germ layers (endoderm, mesoderm, and ectoderm). Adult stem cells are multipotent, implying that they can only differentiate into a limited number of cells typically within the same ‘family’ (e.g., hematopoietic stem cells give rise to red blood cells, white blood cells, and platelets).

In the procurement of embryonic stem cells for research, the embryo from which the cells are harvested is destroyed. For those who believe that human life begins at conception this research is obviously unethical. In contrast, adult stem cells can be isolated from tissue from a consenting patient. While cord blood stem cells are classified as adult stem cells, they appear to have greater potency (ability to differentiate into other cell types) than other adult stem cells, making them a potentially valuable option for use in a variety of treatments and therapies. Cord blood stem cells offer some of the advantages of ESCs without any of the ethical drawbacks. Research into the use of cord blood stem cells for the treatment of disease and disability is a promising and ethical avenue of stem cell research.
Private vs. Public Banking

In the public arena there has been much discussion on the benefits of for-profit private cord blood banking over public banking. Numerous for-profit companies offer new parents the option of collecting and storing cord blood for future use by the donor infant, siblings, or other family members. Parents may choose to bank cord blood if they have a family history of a particular disease or disorder, or as a means of "biological insurance" in case their child or family member develops a medical condition or becomes injured requiring a transplant.

While many diseases can be treated with a cord blood transplant, most require stem cells from another donor (allogeneic). Cord blood cells taken from the patient (autologous) typically contain the same defect or precancerous cells that caused the patient to need the transplant in the first place. Most medical professionals believe the chance that cord blood banking will be utilized by the patient or a close relative is relatively low. Estimates range from 1 out of 1,000 to 1 out of 200,000.[2] From these estimates, privately stored cord blood is not likely to be utilized by the average family. The American Academy of Pediatrics has discouraged cord blood banking for self-use, since most diseases requiring stem cell transplants are already present in the cord blood stem cells.[3] Additionally, a recent study published in Pediatrics indicates that few transplants have been performed using privately stored cord blood. From the responses of 93 transplant physicians, in only 50 cases was privately banked blood used. In 9 of these cases the cord blood was transplanted back into the donor patient (autologous transplant).[4] One of the main selling points of private cord blood banks is the possibility of a future autologous transplant.

There is no significant opposition in the medical community to the public banking of cord blood. The donation of cord blood to public banks has generally been encouraged by the medical profession. The American Academy of Pediatrics encourages the public donation of cord blood with appropriate genetic and infectious disease testing, although they caution that parents should be notified that they will receive the results of this testing. They also recommend that parents be informed that publicly banked cord blood may not be available for future private use.

American Academy of Pediatrics Policy - Cord Blood Banking for Potential Future Transplantation?

Other Information

One oft cited argument against cord blood banking is that it is not known how long these cells can remain viable in storage. While it is not known if cells taken from an individual as an infant will be beneficial to them as an adult, units stored for up to 10 years have been transplanted successfully. This indicates that there is no reason to suggest serious deterioration in the quality of cord blood units stored for longer periods of time.

Resource List

General Information:

- http://www.nationalcordbloodprogram.org/
Public Cord Blood Banks:

- http://www.marrow.org/HELP/Donate_Cord_Blood_Share_Life/How_to_Donate_Co...
- http://parentsguidecordblood.org/content/usa/banklists/publicbanks_new.s...

Private Cord Blood Banks:

- http://parentsguidecordblood.org/content/usa/banklists/listusa.shtml?nav...

References

[1] During the processing stage excess red blood cells and plasma are removed reducing the volume to approximately 20 mL.


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