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CORD BLOOD BANKING: CURRENT DEVELOPMENTS AND FUTURE REGENERATIVE TRANSPLANT MEDICINE

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ABSTRACT

Since twenty years of the first successful cord blood transplantation, it is yet widely accepted that the cord blood is the major source of the stem cells for transplantation. Intensive research is being done on animal and *in vitro* models for differentiation of cord blood stem cells into various cell types that signs to be a future regenerative therapy. Results obtained in the animal models using cord blood therapy are supportive and encouraging to treat various diseases like cardiovascular, neuronal, diabetic, leukemia and orthopedic disorders. Recently, cord blood progenitor cells with stem cell properties were identified in umbilical cord blood, which indicates that umbilical cord blood transplantation is expanding to even non-hematological use. Cord blood is more advantageous than other sources because of easy availability, less chance of host-versus-graft disease, easy procurement, less transmission of infections and low risk to donor. Modern day research is focusing on various strategies to increase the cord blood progenitors and homing of stem cells for the successful transplantation. Cord blood will be a prime source of stem cells for regenerative medicine in near future. We review the current developments and future regenerative medicine in cord blood transplantation.

KEYWORDS: Stem Cells, Umbilical Cord Blood.

INTRODUCTION

Cord blood, also called placental blood, is the blood that remains in the umbilical cord and placenta . It is a rich and ethically accepted source of hematopoietic stem cells and considered as biowaste (Rubinstein et al., 1993). Cord blood contains various types of stem cells that include hematopoietic stem cells, Mesenchymal stem cells (MSCs) (Lee et al., 2004), Cord blood derived embryonic like stem cells (CBEs) (Greschat et al., 2008; Mcguckin et al., 2004), multi potent progenitor cells (MPPs) (Lee et al., 2007), and Unrestricted somatic stem cells (USSCs) (Kogler et al., 2004). Cord blood stem cells are being used for decades in treating diseases including leukemias, blood disorders, juvenile diabetes and brain injury. The first successful cord blood transplantation was performed in 1988 in a boy suffering from Fanconi's anemia (Gluckman et al., 1989).

ADVANTAGES AND DISADVANTAGES OF CORD BLOOD TRANSPLANTATION

Advantages of Umbilical cord blood (UCB) transplantation (Table 1) include rapid availability, good accessibility, low risk of infection transmission (although this is not completely eliminated as Epstein-Barr virus (EBV) cases have been reported), absence of donor risk, transplant possible for many recipients and the relatively lower risk of graft-vs-host disease (GVHD) with preserved graft-vs-malignancy effects (Alkindi and Dennison, 2011; Kogler et al.,1996).

The disadvantages of UCB transplantation (Table 1) are the limited cell dose (>60 Kg require two units), delayed engraftment or reduced survival, and lack of additional immune cells if donor lymphocytes are needed. It requires careful donor screening, testing for common hereditary blood and immune disorders. Controversial issues include, but are not limited to, immune reconstitution and risk of infections (Alkindi and Dennison, 2011; Gluckman and Rocha, 2006).

STEM CELL CLASSIFICATION

Umbilical cord blood contains circulating stem cells and the cellular contents of these cells are distinct as compared to bone marrow and adult peripheral blood. Cord blood stem cells are Multipotent and can differentiate into various cells. The number of umbilical cord blood hematopoietic stem cells equals or exceeds that of adult bone marrow and they are known to produce large colonies *in vitro*, have different growth factor requirements, have long telomeres and can be expanded in long term culture. Several research groups are focused on the development of protective drugs for the treatment of various diseases. Most diseases have complex pathological processes and the regenerative medicine need to find the cure. Intense efforts are involved in the understanding of the concepts of regenerative processes to protect physiological functions in disease conditions and the cell based therapies are best examples.

There are three sources of stem cells: adult stem cells, embryonic/fetal stem cells and cord blood (Figure1). Adult bone marrow possesses stem cells that are mesenchymal and hematopoietic in origin. Bone marrow stem cells have more plasticity and versatile because they are Multipotent and can be differentiated into many cell types both *in vitro* and *in vivo*. The bone marrow based cell therapy has some disadvantages such as it requires correcting human leukocyte antigens (HLA) match, and collection of bone marrow stem cells is uncomfortable, painful and tedious.

Embryonic stem cells are pluripotent derived from the inner cell mass of the blastocyst. These cells proliferate indefinitely and have ability to differentiate into most adult cell types. Cell therapy derived from human embryonic stem cells would be allogeneic by nature but is unacceptable due to ethical issues.

Cord blood is the richest source of stem cells and is ethically acceptable. UCB transplants are less prone to rejection than either bone marrow or peripheral blood stem cells. This is because these cells have not yet developed the features that can be recognized and attacked by the recipient's immune system. Multipotent non-embryonic stem cells are present in umbilical cord blood. These cells give rise

to cells obtained from the ectodermal, mesodermal and endodermal lineages. Along with hematopoietic stem cells cord blood contain non-hematopoietic cells that has been demonstrated by differentiation of UCB, MLPC, MSC and EPC into neuronal, cardiac, epithelial and hepatic lineages.

Mesenchymal Stem Cells (MSCS)

Mesenchymal stem cells are multipotentent and can differentiate in to chondrocytes, myocytes, adipocytes, osteoblasts and insulin producing cells. They can regenerate mesodermal tissues including bone, cartilage, marrow, muscle, tendon and fat (Kern et al., 2006; Kode et al., 2009).These cells are non-immunogenic and can modulate the immunogenic properties, which enable them important for cellular therapy, so there is a less chance of graft versus host diseases (GVHD) and increase in the engraftment after transplantation (Romanov et al., 2003; Lee et al., 2010). Bone marrow is the source of MSCs, but the differentiation potential decrease with age. Umbilical cord blood contains more MSCs than bone marrow MSCs and they are more proliferative but umbilical cord blood contains more stem cells than bone marrow so it may be the cause of higher proliferation of umbilical cord blood MSCs. While stem cells are best defined functionally, a number of molecular markers have been used to characterize various stem cell populations. The cluster of differentiation (CD) is used as a cell marker in immunophenotyping, allowing cells to be defined based on what molecules are present on their surface. A list of CD markers expressed on various cord blood stem cells are given in Table 2. MSCs are positive for CD 105, CD73, CD44, CD90, CD71 and CD29. They are negative for CD 45, CD34, CD14, CD56, and CD 31 (Kogler et al., 2004).

Unrestricted Stromal Stem Cells (USSCs)

In 2004, Gesine Kogler *et al* reported $CD45^-$ cells from cord blood, which they termed unrestricted stromal stem cells (USSCs) (Romanov et al, 2003). These cells have *in vitro* proliferative activity and controlled differentiation in different lineages .From *in vitro* studies they showed that USSCs can differentiate into chondroblasts, adipocyte, hematopoietic, neural and osteoclast cells. In acute myocardial infarction, USSCs improve the left ventricular function and dilation and mostly paracrine effects observed in USSCs treatment (Kogler et al., 2004). USSCs are adherent and spindle shaped with 10-25 µm size. These cells are constitutively expressing transcription markers expressing M-CSF, GM-CSF, IL-1β, IL-6, IL-8, IL-15, IL-11, IL-12, SDF1, and low levels of HLA-A, B, C and CD10. USSCs are positive for CD13, CD29, CD44, CD99e, CD90, CD105 and negative for CD14, CD 33, CD34, CD45, CD49b, CD49c, CD49d, CD49f, CD50, CD62L, CD62P, CD106,CD117 and glycophorin A (Lee et al., 2010; Kogler et al., 2006).

Cord Blood Derived Embryonic like Stem Cells (CBEs)

In cord blood, embryonic stem cell like adherent stem cells are reported and named as cord blood derived embryonic like stem cells (CBEs). CBEs are able to differentiate into bone, skeletal muscle, hepatic, fat, blood vessel and pancreatic cells (Mcguckin et al., 2004). CBEs express the embryonic stem cell transcription factor Oct4 involved in the inhibition of differentiation and self renewal (20). They can be used potentially for transplantation, drug testing and cell based assays. CBEs

are positive for CD34, CD164 and CD133 and are negative for glycophorin-A, CD38, CD45, CD7, CD56, CD16, CD33, CD3, and CD2 (Mcguckin et al., 2004; Lu et al., 1996).

Multipotent Progenitor Cells (MPCs)

A multipotent progenitor cell (MSC) is a cell that possesses the ability to differentiate into various but limited number of cell types, especially into cells of a closely related family of cells. (Lee et al., 2007). These cells have the capacity to differentiate into myoblasts, osteoblasts, hepatocytes, endothelial cells and germinal specific cell types (Moon et al., 2008). In hepatic injury in rat, MPCs successfully incorporated into liver and differentiated into functional hepatocytes and expressed CK-18 and albumin, a marker specific for hepatocyte (Kern et al., 2006). MPCs are the potential sources of cell-based therapies. MPCs are positive for CD14, CD44, CD45, CD 54, and CD31 and negative for CD34, CD90, CD104, CD133, CD49a, CD62e and CD73 (Lu et al., 1996; Lee et al., 2007).

APPLICATIONS OF CORD BLOOD

Cord blood stem cells have wide applications due to their capacity to differentiate into neural, epithelial, hematopoietic and endothelial tissues. Cord blood stem cells are able to treat various diseases like cardiovascular, neuronal, ophthalmic, endocrine, orthopedic and metabolic diseases.

Neurological Applications

Cord blood stem cells are potential for the treatment of the traumatic brain injuries. Lu.*et al* first documented the migration of transplanted cells to the site of brain injury which decrease the neurological damage (Lu D et al., 2002). Cord blood stem cells were used successfully in animal models for the treatment of other brain injuries including ischemic injury, heat stroke and cerebral overload of Nitric Oxide (Chen et al., 2006). These cells are also useful in the treatment of neurodegenerative diseases like Alzheimer's, Parkinson's and Amyotrophic lateral sclerosis (ALS). Cord blood derived MSC differentiated into dopaminergic neurons expressing the tyrosine hydroxylase and released dopamine into the medium (Fu et al., 2006). In Alzheimer's disease cord blood stem cells reduces the beta-amyloid plaques and astrocytosis in mouse model (William et al., 2008). Spinal cord injuries were also investigated by using these cells, transplanted cord blood stem cells were seen at the site of injury, but not at the uninjured site (Chen et al., 2001). Other studies reported that these stem cells improved the axonal regeneration, motor function and differentiated into various neural cells (Kuh et al., 2005). Clinically these cells are used to treat patients with spinal cord injury and they identified that cord blood stem cells improved sensory perception and mobility in the hip and thigh regions. In this study by computed tomography (CT) and magnetic resonance imaging (MRI), the regeneration of spinal cord was observed at the injured region (Kang et al., 2005).

Diabetic Applications

Diabetes mellitus type 1 (Type 1 diabetes or juvenile diabetes) results from autoimmune destruction of insulin-producing beta cells of the pancreas. The subsequent lack of insulin leads to increased blood and urine glucose. Cord blood stem cells are identified as Immunomodulating cells and are useful in the treatment of autoimmune disorders (Couri and Voltarelli, 2008). Cord blood derived MSCs have been shown to differentiate into insulin producing cells and expressing beta cell markers along with synthesizing and secreting functional proteins (Gao et al. 2008; Kern et al., 2006). It is reported that transplanted cells of cord blood are able to reduce the blood glucose and improve the renal neuropathy caused by diabetes. In addition, renal abnormalities were corrected suggesting their regenerative action in renal parenchyma (Ende et al., 2004; Naruse et al., 2005).

Cardiovascular Applications

Loss of cardiomyocytes and the scar tissue formation during heart attack results in irreversible damage to the heart function. Many cell types related to angiogenic and myogenic functions were used for the cell based therapy of myocardial diseases (Chachques et al., 2009). Cord blood contains different types of stem cells and studies reported that MSCs differentiate into cardiomyocyte like cells (Nishiyama et al., 2007). These cells have *in vitro* proliferative activity and controlled differentiation to different lineages such as hematopoietic cells, bone, cartilage, heart and neural tissue (Kim et al., 2005). In acute myocardial infarction, USSCs improved the left ventricular function and dilation (Ghodsizad et al., 2009). In animal models of myocardial infarction, cord blood stem cells have shown the ability to selectively migrate to injured cardiac tissue, improve vascular function and blood flow at the site of injury, and improve overall heart function.

Orthopedic Applications

There are several studies showing that stem cells from cord blood can differentiate into bone and cartilage to restore various parts of the joints such as cartilage, ligaments and tendons after an injury, but also bones after a bone fracture or break (Wang et al., 2004). Several investigators identified that that certain stimuli direct cord blood MSCs and unrestricted stromal stem cells (USSCs) to differentiate into osteoblasts (Jager et al., 2007) and also cells stimulated by 10- β- glycerol phosphate and dexamethason (Degistirici et al., 2008).

Epithelial Tissue Applications

Cord blood stem cells are also able to differentiate into epithelial cells. This could be therapeutically useful in diseases associated with dysfunction of epithelial cells in the cornea of the eye, to restore the skin after injury but also in other tissue recovery after injury, such as colon and lung. There are already studies attempting the repair of corneal and skin damage which militate in this direction. Previous studies reported that the MSC can reconstitute the cornea in rat models (Ma, et al., 2005). Corneal epithelium has the self-renewing capacity due to its stem cells which protects the cornea by covering its front. Deficiency of corneal epithelial stem cells leads to vision disabilities.

Keratoconjunctivitis sicca and aniridia are the epithelial tissue diseases. Studies conducted using cord blood stem cells as cell based therapies show that MSC are capable of forming cornea and bone marrow stem cells can heal skin wounds (Ma, et al., 2005).

HEMATOLOGIC APPLICATIONS

Umbilical cord blood transplantation is largely used to treat hematological malignancies and given the opportunity is able to perform transplantation even if the related HLA donor is absent. Several hundreds of children had undergone unrelated transplantation for hematological and oncological malignancies.

Acute Leukemia

Acute leukemia is the rapid growth of abnormal white blood cells that accumulate in the bone marrow and interfere with normal production of blood cells. It is a rare disease and about 1.2% cancer deaths in the US are due to acute leukemia. In acute leukemia, children were studied using one and two cord blood units for transplantation. The risk of relapse is lower in case of using two cord blood units for transplantation. One report compared the related and unrelated umbilical cord blood grafts and not found any differences in overall survival (OS), TRM (transplant related mortality) and relapse rate (Locatelli et al., 1999).

Chronic Myeloid Leukemia

Chronic myeloid leukemia is also known as chronic granulocyte leukemia and is due to uncontrolled, increased growth of myeloid cells in bone marrow and blood. It was reported that the event free survival was 20% and the overall survival is 20-40% (Arcese et al., 2006).

Lymphoma

Lymphoma is a cancer in the lymphoid cells of the hematopoietic system. In this application, the patient's own cancerous cells are destroyed by chemotherapy or radiation and they are replaced with cord blood stem cells. It was reported that 16 patients with follicular and chronic lymphocytic leukemia had one year progression free survival of 63% (Barker et al., 2005). In other report of 20 patients with Hodgkin lymphoma and non-Hodgkin lymphoma receiving umbilical cord blood, a year progression free survival is 50% (Yuji et al., 2005).

CORD BLOOD TRANSPLANTATION

Hematopoietic stem cell transplantation (HSCT) involves the intravenous infusion of autologous or allogeneic stem cells collected from bone marrow, peripheral blood, or umbilical cord blood to reestablish hematopoietic function in patients with damaged or defective bone marrow or immune systems. A recent survey shows that 20% of HSCT in younger patients and 50% of HSCTs from unrelated donors were being performed with cord blood cells (Bertaina et al., 2010). UCBT is more advantageous than bone marrow trans plantation, including lower incidence of graft versus host disease, prompter availability of cord blood cells, and the possibility of using donors having HLA disparities with

the recipient (Gluckman, and Rocha, 2004). Cord blood as a best reservoir of various stem cells, mostly hematopoietic cells which are useful for curative of variety of malignancies and non- malignant diseases. There are several reports of related and unrelated cord blood transplantations for treating leukemias, marrow failure syndromes, congenital immunodeficiencies and inborn errors of metabolism (Phuong and Nelson, 2010).

Cell therapy is based on transplantation of live cells into an organism in order to repair a tissue or restore lost or defective functions. Cells mainly used for such advanced therapies are stem cells, because of their ability to differentiate into the specific cells required for repairing damaged or defective tissues or cells. Regenerative medicine is potential multidisciplinary area, aimed at maintenance, improvement, or restoration of cell, tissue, or organ function using methods mainly related to cell therapy, gene therapy, and tissue engineering (Stanevsky et al., 2009).

Stem cells are emerging role treatment of different types of diseases particularly in cancer treatment, there are tissue specific stem cells in human body, which are able to regenerate the tissue, because stem cells have a property of self-renewal, and produce different progenitor cells. The potency of a cell specifies its potential to differentiate into different cell types such as:

Totipotent: able give rise all germ layers and extra embryonic layers.

Pluri Potent: able to differentiate any type of cells but not forms placenta and umbilical cord.

Multi Potent: able to differentiate specific number of cell types**.**

Unipotent: capacity to differentiate into only one type of cell type (figure: 2).

In transplant medicine, cord blood is widely used as an alternative source of the hematopoietic stem cells found in bone marrow (Gluckman and Rocha, 2004; Hollands and Mccauley, 2009). Clinical applications of cord blood transplantation include both the promises and limitations of cell-based therapies for tissue repair and regeneration. Allogeneic stem cell transplantation (AlloSCT) has been used as best potential for curing numerous malignant and non-malignant diseases in children and adults. Related and unrelated UCB has emerged as an alternative source of hematopoietic stem cells to the majority of patients who are unable to identify a fully matched donor. Hematological malignancies are the most common indication for AlloSCT in children. Unrelated UCBT has been used successfully in the treatment of ALL, AML, CML, myelodysplastic syndromes, neuroblastoma, Hodgkin lymphoma (HL), non-Hodgkin lymphoma (NHL), and other malignant diseases (Table 3). Efficacy of UCB grafts in the treatment of ALL and AML suggest that mismatched UCB grafts lead to acceptable outcomes in patients with acute leukemia (Liao et al., 2011).

PEDIATRIC CORD BLOOD TRANSPLANTATION

Many children have received cord blood transplants from related donors generally a sibling, for a variety of conditions such as marrow failure syndromes, congenital immunodeficiency's, metabolic disorders, hemoglobinopathies, hematologic malignancies, and solid tumors (Quillen, 2009).

The number of hematopoietic progenitors in UCB have a greater capacity for expansion than those in bone marrow (BM), suggesting that UCB might be a suitable HSC source. (Stanevsky et al., 2009).The world first UCBT from unrelated donors to two children with leukemia. Worldwide, around 600,000 of UCB have been banked and close to 20,000 of allogeneic/autologous UCBTs from unrelated/related donors have been performed for the treatments of patients with malignant and non-malignant (Wagner and Gluckman, 2010).

In children, UCBT is used for malignant diseases, particularly for acute myeloid leukemia treatment. Non-malignant diseases can also be treated by UCBT, such as inherited metabolic disorders (IMDs), primary immunodeficiency diseases (PIDs), hemoglobinopathies and BM failure syndromes. Though UCBT was successful in children for treating several diseases with single dose of cells, but in adults the cell dose is limited, to overcome this problem double cord blood transplantation was used in treatment of variety of diseases (Richard et al., 2006).

CORD BLOOD BANKING

By knowing the fact that cord blood are the richest source of stem cells cord blood banks are established worldwide to collect and store the cord blood. First cord blood bank was established by H E. Boxmeyer and this cord blood bank provided the unit for first transplant (Gluckman et al., 1989). After successful transplantation of umbilical cord blood cells, it was accepted and the first unrelated cord blood bank was established by Rubinstein (Rubinstein et al., 1993). Cord blood banking process involves many phases to provide quality cord blood units. The phases are recruitment, consent, testing of donor and their previous medical history, collection, processing freezing t and releasing the cord blood unit to the transplantation centers for use (Broxmeyer et al., 1993).

CORD BLOOD BANKING PROCESS

Recruitment and Consent of Donor

Donor recruitment, consent, donor selection and testing are the issues related to the cord blood banking process and for to the ethical issues (Figure 3). Information should be provided to the mother in the form of posters, videos and presentations. The information should be provided in easily accessible way, so that she can make decision to donate or not. For the donors from the ethnic minority group information should be available in the suitable language. Discussion regarding to the banking issues with the mother should be in a language with which donor is comfortable. The importance of cord blood banking, benefits, risks and the right of the mother to decide either to donate or not should be explained to the donor (Warwick and Armitage, 2004). Consent from the donor should be obtained to collect the cord blood sample for processing, freezing, testing for diseases , storage, donor counseling, to test the medical records of mother and infant, saving the personal data, use of cord blood for research and development in case of not suitable for banking (Ballen, 2005).

Collection of Cord Blood

The aim of the collection of cord blood is to minimize the risk of contamination from maternal blood, secretions, bacteria, fungi and maximizing the volume of cord blood without interferring the normal delivery procedures. There are two methods of collecting cord blood i.e., *ex utero* and *in utero.* In the first case cord blood is collected before the delivery of the placenta while in the later process after the delivery of placenta. *Ex utero* collection is performed outside the delivery room after delivery of placenta and *in utero* collection of the blood takes place in the delivery room at the third stage of the labor while the placenta is present in the utero. *In utero* collection normally performed by trained obstetrician or nurse mid wife and the *ex utero* collection is performed by trained personnel from cord blood bank. *Ex utero* collection is less invasive and greater control over technique (Warwick and Armitage, 2004; Ballen, 2005). But there are no adverse effects recorded till now in *ex utero* or *in utero* collection.

Processing of Cord Blood

Long-term storage is the key to a successful banking and space considerations are predominant. Before storage, volume reduction procedures should follow. Many methods are practiced and the major one is removal of red blood cells and plasma (Warwick and Armitage, 2004). But in early years whole collected blood was frozen in 10% dimethylsulphoxide. Usually freezing of cord blood in 10% DMSO is in controlled rate freezers at the temperature of -4°Č followed by decreasing 1°Ċ per minute, then transferred to -80°Ċ and finally to liquid nitrogen freezers at -180°Ċ for long term storage.

The samples are tested for the full blood count and HLA typing after the donation. After processing, sample is tested for the full blood count to ensure the recovery of nucleated cells, CD 34^+ cells count and viability of cells. At the time of donation, sample from donor is tested for infectious diseases like HIV, hepatitis B, C, human T cell lymphotrophic virus 1 (HTLV-1), and syphilis. If a cord blood unit is selected for transplantation more sensitive tests are performed such as anti HBc, and hepatitis C, HIV, Cytomegalo virus are tested by nucleic acid technology. After addition of cryoprotectant small amount of cord blood is tested for bacterial and fungal contamination. If contamination is found or less than 80% of CD 34^+ cells observed than it is excluded from the banking.

Release of Cord Blood Unit for Transplantation

When processing and testing are completed, an official inspects the donor and information related to the donor and decides to store in bank or not. Then the donated units are available on the registries for searching. The information related to volume, total cell count and HLA type are provided.

CONCLUSIONS

Cord blood transplantation has emerging role in future medicine. Cord blood has different types of stem cells, which provide new progenitor cells for disease treatment. Currently, most hematopoietic stem cells are transplanted into patients who have been treated with high doses of chemotherapy with or without radiation to kill diseased or cancerous cells. Utilizing the process of stem cell banking, cord

blood cells show great promise for potential future applications including treatment and repair of non-hematopoietic tissue, gene therapies and mini transplants. Regeneration of neurons is not possible now, but in future, we can induce the stem cells in brain to differentiate into neurons just like vaccines to give antibodies. Thus, Stem cell therapy is useful in future regenerative medicine for treating many diseases.

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Table: 1. Advantages and Disadvantages of Cord Blood Transplantation

Advantages	Disadvantages
1. Decreased risk to donor	1. Difficult to achieve sufficient total nucleated cell dose in larger recipients using single Cord blood unit
2. Faster procurement	2. Delayed engraftment and increased risk of graft failure
3. Lower incidence of grade IIIV acute GVHD	3. Delayed T-cell immune reconstitution
4. Enhanced ability to cross donor-recipient HLA disparities	4. Increased risk of transplant-related mortality
5. Immediate availabity when emergent HST is needed	5. Increased costs of hospitalization
6. Easy delivery process compared to the freshly harvested Bone Marrow(BM)	6. No obvious cell source for post-transplant donor lymphocyte infusions.
7. Low risk of viral transmitting (12).	**7.** CB unit with a nucleated cell count less than 23 million perkgbwt of the recipient has successfully engrafted adults. The time to neutrophil and platelet engraftment is slow (11).

Table: 2. CD Markers on Umbilical Cord Stem Cells

CD	MSC	USSC	CBE	MPC	HSC
CD45				+	+
CD34			+		+
CD14				+	
CD105	+	+			
CD73	+				
CD44	+	+		+	+
CD90	+	+			+
CD71	+				
CD29	+	+			
CD56					
CD133			+		+
CD49a		+			

Table: 3 Diseases Treated with Umbilical Cord Blood Transplantation

Malignant disorders	Non-malignant disorders
Neuroblastoma	Aplastic anemia
• Non-Hodgkin lymphoma	· Fanconi anemia
· Hodgkin disease	· Severe combined immunodeficiency
• Acute myeloid leukemia (AML)	· Thalassemia major
· Medulloblastoma	• Diamond-Blackfan anemia
· Germ-cell tumors	· Sickle cell anemia
• Multiple myeloma	· Wiskott-Aldrich Syndrome
· Acute lymphoblastic leukemia (ALL)	• Osteopetrosis
• Chronic myeloid leukemia (CML)	• Inborn errors of metabolism
· Myelodysplastic syndromes	• Autoimmune disorders
• Chronic lymphocytic leukemia	• Amyloidosis

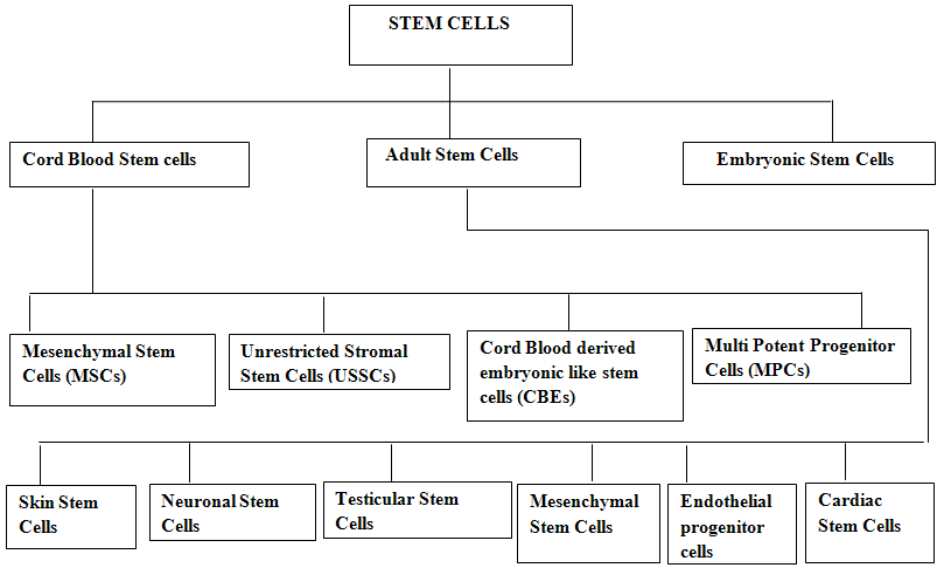

Figure: 1. Classification of Stem cells

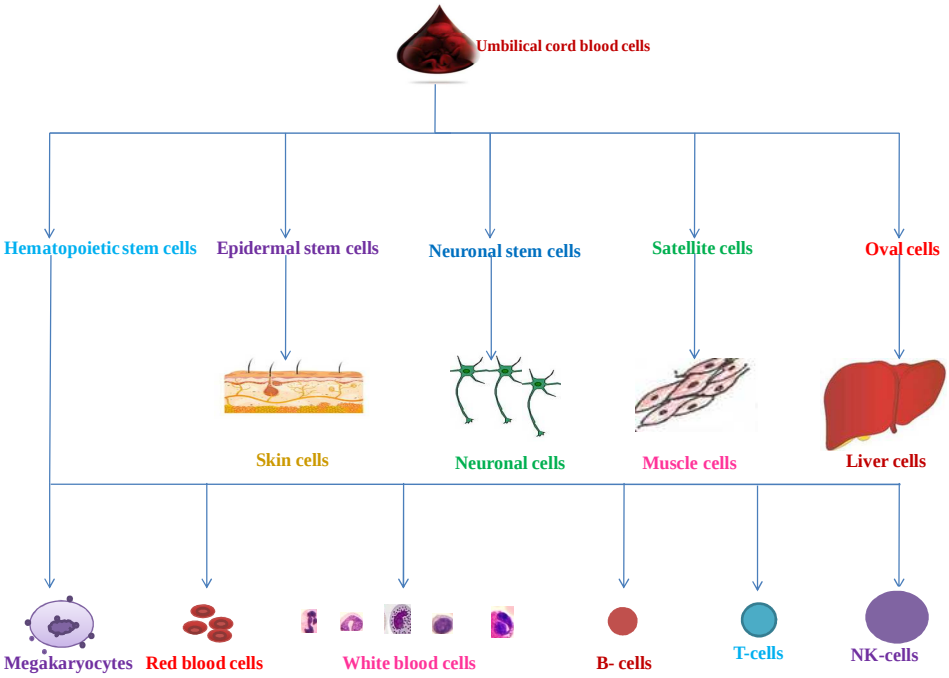

Figure: 2. Umbilical Cord Blood Cells Differentiate into Different Types of Cells

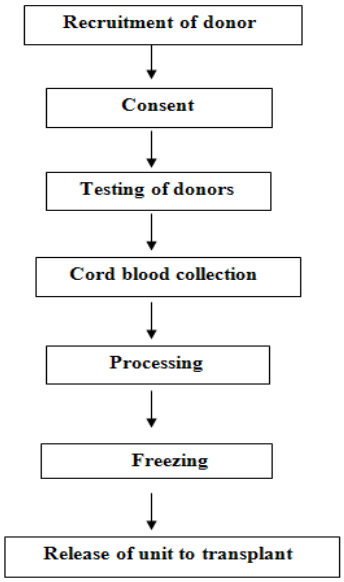

Figure: 3. Cord Blood Banking Process.