

Cord Blood Banking: Where are We?

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INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) offers the only hope of cure for a number of diseases of childhood both malignant and nonmalignant including thalassemia and metabolic-storage disorders.

In the US, 732 transplants are carried out per 10 million population; whereas in India, only nine transplants are done per 10 million population. Cord blood can be used to treat a variety of oncologic, genetic hematologic and immunodeficiency disorders.

Majority of such transplants are performed in children; however, the number of adults have been growing steadily in recent year. With a high birth rate and a large genetic diversity, India has potential to become the largest supplier of cord blood stem cells in the world.

CORD BLOOD STEM CELL BANKING

Umbilical cord blood (UCB), the blood remaining in umbilical cord and placenta following birth of baby, has emerged as a potential alternative source of hematopoietic stem cells (HSCs) in allogeneic hematopoietic stem cells transplantation (HSCT) as well as, at times, a last ray of hope for physicians.

The first umbilical cord blood transplantation (UCBT) was performed in 1988 in a patient with Fanconi anemia. This patient had a healthy human leukocyte antigen (HLA) identical sibling proven by prenatal testing to be unaffected by the disorder. The patient had no graft *vs* host disease (GVHD) and is currently healthy more than 20 years after UCBT, with complete long-term hematological and immunological reconstitution. Since the first UCBT, more than 20,000 UCBT have been reported worldwide and more than 600,000 cord blood units have been stored in more than 100 cord blood banks.

Net cord was created in 1998 to establish good practices in umbilical cord blood storage, facilitate donor search, improve quality of grafts, standardize excellence criteria on an international scale and important establish

procedures for cord blood bank accreditation. Net cord, the cooperative network of large experienced UCB banks, currently has more than 300,000 cryopreserved UCB and its ready for clinical use for unrelated recipients and more than 8624 grafts shipped.

The two main types of cord blood banks exist for the purpose of storing cord blood for future need of USBT, public cord blood banks and private cord blood banks.

Collection may be performed either prior to (*in utero*) or following (*ex utero*) delivery of the placenta *ex utero* collection is preferred, because it is technically easier to obtain the sample.

After collection, cord blood units should be tested, processed and stored for future use typically within 48 hours of collection. In general, public cord blood banks must perform more extensive testing in order to maintain databases searchable by various transplant centers world over.

Larger units (with at least 40 ml of blood) with higher total nucleated cell (TNC) numbers are preferred and a cut-off of 1×10^8 TNC per unit is commonly used to define a cord blood units with adequate TNC heavier babies and those that are meconium stained large placentas, and women with fewer previous live births have cord blood with higher TNC.

Legal aspects are actively evolving, and the ethical issues raised by both public and private banking have not yet been resolved.

Who owns a given cord blood unit, or should they be held for the person from whom they came until he or she reaches adulthood?

What should be the next step if the family stops paying the storage fees?

The American Academy of Pediatrics does not recommend that parents routinely store their infant's UCB for future use.

There is a one percent chance in 2700 that the same unit of UCB will be used for a child or family member. Parents should be warned that autologous cord blood will not be selected if the donor child develops leukemia as the cord blood is likely to have genetic markers of leukemia. Private cord blood banking is not allowed in the European countries, such as Italy and Spain.

India has a potential to become the largest collector of UCB in the world. The major obstacle for USBT in our country is cost involved in the procedure and the fact

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that majority of deliveries being done outside a tertiary care hospital setting.

CORD BLOOD STEM CELL TRANSPLANTATION

These stem cells can be used by the baby, the siblings, parents and even grandparents after HLA matching. Twenty-six years after the first cord blood transplant, approximately 3 million cord blood units are stored in family cord blood banks all over the world and 900 cord units were released for therapy over 650,000 umbilical cord blood units have been stored in public banks for transplants world wide. Over 30,000 cord blood transplants have been performed globally.

After the umbilical cord is clamped and cut, approximately over 80 ml of cord blood is very rich in stem cells, and after the removal of red blood cells, the stem cells are mixed with a cryoprotectant dimethyl sulfoxide (DMSO). These stem cells are stored liquid nitrogen at -196°C in liquid nitrogen and the shelf life of these stem cells is 21 years.

The advantages of cord blood are that it is easily available and has less graft *vs* host disease. In the coming decade, cord blood stem cells will be used extensively in the clinics and hospitals for various malignant and nonmalignant disorders (Table 1).

Table 1: Diseases treated by stem cell therapy

<i>Leukemias (all therapies are allogeneic)</i>
<ul style="list-style-type: none"> • Acute leukemia <ul style="list-style-type: none"> – Acute lymphoblastic leukemia – Acute myelogenous leukemia – Acute biphenotypic leukemia – Acute undifferentiated leukemia • Chronic leukemia • Chronic myelogenous leukemia • Chronic lymphocytic leukemia • Juvenile chronic myelogenous leukemia • Juvenile myelomonocytic leukemia • Myelodysplastic syndromes refractory anemia • Refractory anemia with ringed sideroblasts • Refractory anemia with excess blasts • Refractory anemia with excess blasts in transformation • Chronic myelomonocytic leukemia
<i>Lymphomas (all therapies are allogeneic)</i>
<ul style="list-style-type: none"> • Hodgkin's lymphoma • Non-Hodgkin's lymphoma (Burkitt's lymphoma) • Other disorders of blood cell proliferation (all therapies are allogeneic) • Anemias • Aplastic anemia • Congenital dyserythropoietic anemia • Fanconi anemia • Paroxysmal nocturnal hemoglobinuria

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<i>Lymphomas (all therapies are allogeneic)</i>
<ul style="list-style-type: none"> • Pure red cell aplasia • Inherited red cell abnormalities • Beta thalassemia major • Blackfan-Diamond anemia • Pure red cell aplasia • Sickle cell disease • Inherited platelet abnormalities • Amegakaryocytosis/congenital thrombocytopenia • Glanzmann's thrombasthenia • Inherited immune system disorders—severe combined immunodeficiency (SCID) • SCID with adenosine deaminase deficiency (ADA-SCID) • SCID which is X-linked • SCID with absence of t-cells and b-cells • SCID with absence of t-cells (normal b-cells) • Omenn syndrome • Inherited immune system disorders—neutropenias • Kostmann's syndrome • Myelokathexis • Inherited immune system disorders—other • Ataxia-telangiectasia • Bare lymphocyte syndrome • Common variable immunodeficiency • DiGeorge syndrome • Hemophagocytic lymphohistiocytosis • Leukocyte adhesion deficiency • Lymphoproliferative disorders • Lymphoproliferative disorder, X-linked • Wiskott-Aldrich syndrome
<i>Myeloproliferative disorders</i>
<ul style="list-style-type: none"> • Acute myelofibrosis • Anogenic myeloid metaplasia (mylofibrosis) • Polycythemia • Essential thrombocythemia
<i>Phagocyte disorders</i>
<ul style="list-style-type: none"> • Chediak-Higashi syndrome • Chronic granulomatous disease • Neutrophil actin deficiency • Reticular dysgenesis
<i>Bone marrow cancers (plasma cell disorders)</i>
<ul style="list-style-type: none"> • Multiple myeloma • Plasma cell leukemia • Waldenstrom's macroglobulinemia • Transplants for inherited disorders effecting the immune system and other organs (all therapies are allogeneic) • Cartilage-hair hypoplasia • Gunther's disease (erythropoietic porphyria) • Hermansky-Pudlak syndrome
<i>Bone marrow cancers (plasma cell disorders)</i>
<ul style="list-style-type: none"> • Pearson's syndrome • Shwachman-Diamond syndrome • Systemic mastocytosis
<i>Transplants for inherited metabolic disorders (all therapies are allogeneic)</i>
<ul style="list-style-type: none"> • Mucopolysaccharidoses

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Transplants for inherited metabolic disorders (all therapies are allogeneic)

- Storage diseases
- Hurler's syndrome
- Scheie syndrome
- Sanfilippo syndrome
- Morquio syndrome
- Maroteaux-Lamy syndrome
- Sly syndrome, beta-glucuronidase deficiency
- Mucopolysaccharidosis ii (i-cell disease)
- Leukodystrophy disorders
- Adrenoleukodystrophy/adrenomyeloneuropathy Krabbe disease (globoid cell leukodystrophy)
- Metachromatic leukodystrophy
- Pelizaeus-Merzbacher disease
- Lysosomal storage diseases
- Niemann-Pick disease
- Sandhoff disease
- Wolman disease
- Inherited metabolic disorders
- Lesch-Nyhan syndrome
- Osteopetrosis
- Solid tumors not originating in the blood or immune system (autologous therapy)
- Retinoblastoma

CORD BLOOD TRANSPLANTATION IN THALASSEMIA IN INDIA

Transplantation of stem cells offers the only hope of cure for a number of diseases of childhood, both malignant and nonmalignant, including thalassemia. The preferred donor is a matching sibling; but with a growing number of one child family and only a one in four chance of a sibling being a match, there is an increasing need for match unrelated.

Ideally, the cord blood unit should be 6/6 HLA match with the patient, but 5/6 are also accepted. The required total nucleated and CD 34 cell dose depends on the recipient body weight. The disease-free survival rate varies between 80 and 95% in beta thalassemia.

CORD BLOOD TRANSPLANTATION IN INDIA

The cost of autologous transplant in India is \$12,000 and allogeneic transplant is \$18,000 to \$20,000. The chance of finding a matching family donor is 25%, whereas it is one in a million in unrelated donors. In India, there is no bone marrow donor registry and, hence, patients in India, face a problem in finding a donor. Due to fungal infections approximately, 5% of the transplant patients are lost in India.

CONCLUSION

It is expected that cord blood transplantation will be the mainstay in the therapy for malignant and nonmalignant disorders.

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