

Is the personal banking of umbilical stem cells justified?

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ABSTRACT

Hematopoietic stem cells (HSCs) are defined by their ability to repopulate all lineages of the blood system – they are multipotent with ten or eleven possible fates. They can self renew, which is important for maintaining a pool of stem cells that can continually renew the bodies blood cells, which have a finite life span – with red cells surviving for around 120 days, platelets for 7 days and granulocytes for 7 hours – leading to a high turnover rate. During fetal life there are multiple sites of hematopoiesis, but following birth – the bone marrow is the only site of new blood cell formation, so its continuing function is vital to life. Umbilical cord blood has a high concentration of hematopoietic stem cells. However, there is considerable debate about how we should store these cells. This article aims to provide some information about the area of HSC regenerative medicine and outline some of the core areas of ethical debate.

Key Words: haematology, medical ethics; stem cell banking

Introduction

Umbilical cord blood was previously considered to be a medical 'by-product', usually discarded as waste following birth. However over the past 20 years, research has shown it to be a valuable source of hematopoietic stem cells and more recently, mesenchymal, neural and even pluripotent stem cells have been found (see Appendix for a summary of stem cell basics).^{1,2,3,5}

Why are haematopoietic stem cells important?

Haematopoietic stem cells (HSCs) are defined by their ability to repopulate all lineages of the blood system. They are therefore described as being multipotent, with ten or eleven possible fates. As with all stem cells, they are capable of self-renewal and differentiation. This maintains a population of undifferentiated stem cells, whilst simultaneously ensuring a constant supply of terminally differentiated blood cells. This is important as human blood cells have a finite life span and a high turnover – with red cells surviving for around 120 days, platelets for 7 days and granulocytes for only 7 hours. During fetal life there are multiple sites of hematopoiesis but, following birth, bone marrow is the only site of new blood cell formation, so its continuing function is vital. Umbilical cord blood has a high concentration of hematopoietic stem cells.^{1,2,3}

What are they currently used for?

HSC transplants have been used for many years to treat patients who have hematological malignancies or other diseases of the blood and bone marrow.²⁻⁶ There are three ways to obtain HSCs for transplantation – (i) direct extraction from the bone marrow, (ii) peripheral blood stem cell collection following injections of granulocyte colony-stimulating factor (this leads to overproduction of HSCs in the bone marrow which makes them available in the peripheral circulation) or (iii) umbilical cord blood collection.^{1,2,4} Each have their advantages

and disadvantages, however over the past 10 years, peripheral blood stem cells have been preferentially used.⁴ Umbilical cord blood was first successfully transplanted into a child with Fanconi's anaemia in 1988 and since then, the technique has been increasingly used to treat a wide range of conditions (table 1).²⁻⁶

Table 1: Diseases that may be treated with HSC transplants.²

Haematological malignancies	Haematological diseases and bone marrow failures
Leukaemias	Anaemias
Lymphomas	Thalasaemia
Hodgkin's	Sickel cell disease
Non-Hodgkin's	Fanconi's anaemia
Mantle cell	Severe aplastic anaemia
Burkitt's	Sideroblastic anaemia
Multiple myeloma	
Other diseases	Immunodeficiency and metabolic diseases
Neuroblastoma	Common variable immunodeficiency syndrome
Systemic lupus erythematosus	X-linked lymphoproliferative disease
Amyloidosis	X-linked hyper IgM syndrome
Breast cancer	Severe combined immunodeficiency (SCID)
	DiGeorge syndrome

Advantages & disadvantages of using umbilical cord blood

Cord blood is a favorable option in a number of situations. Firstly, autogenic transplantation from bone marrow or peripheral blood in a patient with a malignancy carries the risk of transferring neoplastic cells alongside the healthy stem cells during the procedure. Secondly, locating an identically matched HLA allogenic donor (related or unrelated) is very time consuming and the chances of success are low, even with the rapidly expanding number of bone marrow donors. This process is even more challenging for certain ethnic minorities, who are especially poorly represented.³⁻⁸ Cord blood can overcome a number of these difficulties as it is available very quickly and the collection process is non-invasive, which eradicates the issue of donor attrition. HLA mismatches are better tolerated in allogenic grafts which reduces the frequency of graft-versus-host disease (GVHD) post transplantation.²⁻⁶ This will increase the number of possible matches available (as they no longer have to be exact), which is of particular significance to ethnic minorities and those with rare HLA types.^{2,6} Additionally, cord blood has been shown to contain numbers of hematopoietic progenitor and stem cells that are comparable to samples taken from the bone marrow and peripheral blood.^{2,3,6} The stem cells are thought to be better quality than adult stem cells as they have not been exposed to long term environmental 'wear and tear'.³

Furthermore, there is a lower chance of infection transmission (cytomegalovirus and Epstein-Barr virus), as dormant infections tend to amass throughout life.^{5,6}

The disadvantages of cord blood include the relatively small sample volume that can be obtained. The number of cells available is usually only sufficient to transplant a child or small adult. This can, however, be combatted by combining different units of blood or growing the cells in culture to expand the number of progenitors present. Other drawbacks include the delay in the integration of red and white blood cells (increasing the chance of infection) and the restricted number of HSCs (creating a challenge if subsequent transplantations are required).^{4,5}

Umbilical cord blood banking - public

Taking the above into consideration, there are many parties who have an interest in banking this blood. Since 1996, the National Blood Service (NBS) branch of the NHS has been responsible for collecting and storing the majority of cord blood. Potential altruistic donors are approached during the antenatal period by medical staff at selected hospitals in the UK (usually selected for the highly ethnic populations they serve). At least 40ml of blood is extracted from the umbilical cord during the third stage of labor or soon after birth.^{2,6,7} The sample is condensed by removing the red blood cells and plasma. Following this, the unit is screened and typed.^{2,6}

There are a host of reasons why an individual may choose to bank their blood. Public cord blood banks deal largely with non-directed, altruistic donations. Resources are merged with those of the bone marrow registries to maximize the chances of locating a match. As umbilical cord blood is usually discarded, donating it is not usually considered a controversial issue. Patients will receive a HSC transplant from a public umbilical cord blood bank if they are unable to find an appropriate related or unrelated bone marrow donor. Public banks also handle directed donations from families that have been deemed to be at high risk of a condition that is known to be heritable and treatable by HSC therapy. This ensures that the cells can be used for HLA compatible siblings or for the newborn child in future life.^{2,4,5}

Umbilical cord banking - commercial

Recent research has shown that mesenchymal, endothelial and neural progenitor cells and pluripotent stem cells are present in umbilical cord blood.^{2,3,5} With this discovery, there has been an emergence of commercial cord blood banks – companies offering to collect and store umbilical cord blood for a fee (table 2). This trend began in America and has since been taken on by the UK. These companies promote cord blood banking for autologous use (use of patients own stored cells), advertising the service as a form of healthcare insurance for your unborn child. They promote prospective treatments and cures that, at this point in time, are speculative and have no scientific support. Although stem cells have been identified in cord blood, their therapeutic potential has yet to be demonstrated.^{5,9}

Before possible uses for personal blood banking are considered, there are difficulties met when obtaining the blood. Because companies charge for collection, an outside party may be responsible for the process, which can create extra paperwork and stress for the maternity unit. It is possible for priorities to become distorted throughout the birthing process – if parents are paying a considerable fee to bank their cord blood, attention may be focused on that, which potentially detracts from care of the mother and baby and puts them at risk of obstetric complications.⁹ Some commercial banks even suggest that someone of a non-medical background can do the collection, which carries the risks of contamination and getting an insufficient sample volume.⁵

Table 2: Principal differences between public and commercial cord blood banking.

	Public	Commercial
Who is it available to?	Everyone	Everyone
Where does it happen?	Only selected hospitals have the resources to facilitate the collection process	Any hospital - companies can provide the necessary equipment and staff
What is the fee?	No fee	Collection and storage fee
What happens to the blood collected?	Donated blood is added to the national registry	Donated blood is stored privately
Who is the blood available to?	Altruistic donations are available to all patients Directed donations are preferentially available to families who are at known risk of HSC treatable disease	Donations are restricted to the family members of the donor

It is hard to estimate the chances of a child needing a transplant of his or her own blood where there is no known risk of HSC treatable, heritable disease. Although there is a relatively large store of privately banked blood, it is very rarely used.^{5,6,9} This seems like a wasted resource which prevents the identification of possible matches for those that are in need. The probability of needing treatment for hematopoietic disorders under 20 years of age is very low, with chances ranging from 1/20,000 to 1/2700, based on current clinical applications.^{5,6} It is usually the more favorable probabilities that are published by commercial companies and, while this may have some element of truth, it is impossible to say whether or not the 1 out of 2700 could be treated just as effectively with an allogenic transplantation.⁵ It has also been suggested that if the child did develop a hematological malignancy, that autologous blood may not be the best treatment option due to the possible persistence of leukemic cells or genetic predisposition to the disease, which would demand subsequent transplantation.⁶

Current Stem Cell Research

The possible benefits to private blood banking are dependent on the success of current and future research and there has already been some promising work done in the area. Developing stem cell therapies has been an area of interest for some time now, however, the use of embryonic stem (ES) cells is shrouded by ethical concerns and they have shown a high risk for teratoma formation.¹¹ Induced pluripotent stem (iPS) cells were thought to be an ethically sound alternative to ES cells, but the risk of teratomas remains alongside concerns about using virus' to make the cells.¹¹ Unrestricted umbilical cord somatic stem cells (USSC) appear to have several advantages to ES and iPS cells. Although found less frequently (in 30-35% of cord blood samples as opposed to 100% of bone marrow samples), they have been shown to have a much greater capacity for proliferation and differentiation than the mesenchymal stem cells found in bone marrow aspirates.¹⁰⁻¹² A study looking into

what exactly is responsible for this wide range of differentiation showed that it may be attributed to elongated telomeres and certain epigenetic signatures found on important pluripotency regulating genes.¹⁰ USSC cells have been shown to develop into adipocytes, neurons, chondrocytes and the three separate germ cell layers in vitro.¹¹ They are easily expandable, without sacrificing karyotype or potency. Recent studies have also shown in vivo differentiation of cells to myocardiocytes and purkinje fibers. Animal studies have demonstrated potential for the treatment of neural and bone injuries. Studies on pigs and rats have shown that, following injection into infarcted cardiac tissue, USSCs differentiated into cardiac progenitor cells causing thickening of the ventricular wall and promoting angiogenesis. This resulted in an overall improvement in cardiac function, with specific improvements in perfusion and wall movement of the affected area.^{10,13,14}

Conclusion

Is the personal banking of umbilical cord blood justified? There are persuasive arguments for and against banking. While there is a lot of promising research being undertaken in the field, it is impossible to predict when this research will yield results that can be clinically and therapeutically applied. It is evident that there have been many recent advances, however these usually carry caveats, yet to be ironed out. It is hoped, *but not known*, that autologous transplants could be used for treatments in the future. Even if successful therapies are developed, it is hard to predict whether autologous cells will have any great advantage over allogenic cells. At this moment in time, with so many uncertainties, 'if's' and conditions attached to the promises being made – it is hard to justify charging money to bank umbilical cord blood. There are many patients who are in desperate need of blood for lifesaving treatment and the more blood that is banked commercially as opposed to publicly – the lower the chance of finding a match. However, in the future, if research continues to be successful and clinical therapies based around autologous stem cells are developed – this should be a resource that is open to everyone, not just those that can afford the expense of private blood banking.

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Appendix – Stem Cell Summary

Appendix : Stem cell summary.

What is a stem cell?

Stem cells are undifferentiated cells that are capable of dividing to produce identical daughter stem cells (self-renewal) **AND** differentiated cells.

They can be further defined by their differentiation potential, i.e. the number of differentiated cell types that they can form. This property is known as 'potency'.

- **Totipotency** – can make ALL cell types (eg. cells in the zygote and those produced from the first few divisions of the fertilised egg)
- **Pluripotency** – can make all adult cell types, however cannot contribute to the placenta (eg. cells found in the inner cell mass of the developing blastocyst)
- **Multipotency** – can make multiple, though limited, cell types (eg. haematopoietic stem cells)
- **Tri/Bi potency** – can make two or three cell types (also known as **progenitor cells**)
- **Unipotency** – can make one cell type (also known as **precursor cells**)

There are two distinct types of stem cells:

Embryonic stem cells

These cells are **ONLY** present in the inner cell mass of the blastocyst in embryonic development. They are pluripotent and will differentiate into all adult cell types to produce a fetus.

Tissue (adult) stem cells

These cells are found in almost all tissues. They can self-renew and produce all cell types found within their specific tissue. They are particularly important in tissues with a naturally high turnover or tissues that are easily damaged (eg. the skin, the blood, the gut).

Somatic cells can be manipulated into a stem-like state using retro-viral transduction. These cells are called **induced pluripotent cells** (iPS cells).