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REVIEW


Will stem cells in cord blood, amniotic fluid, bone marrow and peripheral blood soon be unnecessary in transplantation?

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Abstract There are now various sources of stem cells. Those derived from blastocysts, named embryo stem (ES) cells, have attracted most attention and are highly multipotent. Human cord blood became widely used as a source of stem cells with differing properties to ES cells and their therapeutic application has grown steadily as they are stored in increasing numbers of stem cell banks. Other sources of human stem cells are derived from peripheral blood and amniotic fluid. They may arise from a common origin in epiblast. This review stresses the use of cord blood stem cells, but describes new approaches which may supersede the use of most stem cells. The advantages and disadvantages of these various classes are described in relation to potential methods involving gene conversion to change somatic cells to ES cells. 

KEYWORDS: amniotic stem cells, cord blood stem cells, embryo stem cells, grafting, peripheral blood stem cells, stem cell banks

Introduction

Various options have emerged in the world of stem cell therapy. The chief candidate for stem cells to date have been embryo stem cells (ES cells) prepared from the inner cell mass of the blastocyst. Tissue stem cells have gained in importance recently as it emerged that most tissues possess them, but they are believed to lack the pluripotency so characteristic of ES cells. Difficulties with ES cells emerged when their susceptibility to induced genetic change was found to be due to cell fusions or to other epigenetic changes *in vitro*. This finding tempered the use of ES cells for grafting, and alternative approaches were sought. Among these, the use of human umbilical cord blood has attracted much attention and has proved to be highly efficient, at least under some circumstances. This review details the advance of cord blood stem cells, estimates their value in clinical practice today, and queries if any other forms of stem cell technology may dominate in the future.

Development of umbilical cord blood stem cell banks

Emphasis is being placed on the storage of freshly collected stem cells from umbilical cord blood. Collected when an infant is delivered, they can be stored in case the child, or a family member, should suffer in later life from conditions such as leukaemia, Fanconi anaemia and other blood disorders. Ongoing research on cord blood stem cell technology also suggests that future therapies for such conditions as diabetes, heart disease and nerve damage are a possibility (**Table 1**) (Laughlin *et al.*, 2001). For some years, private companies have been holding cord blood stem cells in cryostorage for the child on a commercial basis. More recently, Richard Branson, of Virgin fame, has launched a similar company called Virgin Healthbank, and it includes a philanthropic aspect in dividing cord blood samples in half, keeping one half for family use and the other half made available for public use. The Virgin model of splitting cord blood units seems to rely heavily on future

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Table 1 Transplantation of unrelated umbilical cord blood in adults (adapted from Laughlin *et al.*, 2001).

Number of patients	68
Median age (years; range)	31.4 (17.6–58.1)
Median weight (kg; range)	69.2 (40.9–115.5)
Diseases (n)	
Haematological malignancy	54
Aplasia/MDS	14
Number of HLA loci disparity (n)	
0	2
1	18
>2	48
Median no. days to engraftment (range)	
ANC >500/ μ l	27 (13–59)
Platelet >20,000/ μ l	58 (35–142)
GVHD (n) (probability, %)	
Acute grade II–IV	33 (60)
Acute grade III–IV	11 (20)
Chronic/patients at risk	12/33
Median cell dose (range)	
N.C. infused ($\times 10^7$ /kg)	1.6 (0.6–4.0)
CD34 ⁺ cells infused ($\times 10^5$ /kg)	1.2 (0.2–16.7)
Event-free survival at 40 months (%)	26

cord blood stem cell amplification technology to ensure clinical efficacy. Such amplification technology is currently still under development, which raised doubts about the Virgin philosophy. This public/private approach is similar to that developed by Hollands in Toronto at the Victoria Angel Registry of Hope, but here whole units are processed solely for public use in parallel to a private service. Virgin Healthbank has attracted considerable press attention and the media and the health professions have discussed the need for this form of secure storage at some length.

Most commentators have devoted their comments to the basic facts involved in this form of storage. The idea of providing a newborn child with an 'insurance' against devastating diseases is obviously highly welcome (Table 2) (Reed *et al.*, 2003). When considered on a mass scale, however, doubts begin to emerge about the value of such a project. Critics stress that most privately stored samples will never be required since only one in 20,000 children up to the age of 20 will need it, despite evidence that one-fifth of stem cell transplants are carried out in young people with leukaemia. The Royal College of Obstetricians and Gynaecologists, London, also queries the need for this type of storage, advising midwives against collecting samples for commercial reasons instead of concentrating on the patients' immediate treatments. This College also stresses that, in any case, 5000 cord blood samples are stored annually by the UK National Health Service at their public cord blood bank in Edgware, London. Credit is nevertheless given to

Table 2 Post-processing haematological parameters of cord blood (adapted from Reed *et al.* 2003).

	Mean value	SD	Range
Volume (ml)	103.1	32.7	42–256
Total nucleated cells (n)	8.9×10^8	6.0	0.6–36.2
Total mononuclear cells (n)	4.9×10^8	3.6	0.3–27.2
Total CD34 ⁺ cells (n)	2.1×10^6	2.4	0.1–21.2
Total CFU (n)	1.4×10^6	1.6	0.04–13.5
Nucleated cell recovery (%)	84.4	9.2	41.7–98.4

Virgin about their placing half of each sample in a national blood bank accessible to outsiders, which is a very welcome philosophy in the cord blood industry. It still remains to be seen just how practical this approach will be in providing sufficient cell numbers for both a public and a private transplant from one cord blood unit.

There is no doubt that haematopoietic stem cells (CD34⁺) existing in cord blood are invaluable to sufferers of various diseases. Cord blood units have been processed and stored in stem cell banks since the early 1990s, following the first transplant in Paris in 1988. There are currently hundreds of thousands of cord blood units stored worldwide, and there have been over 6000 transplants for 45 different diseases. Cord blood may even have efficacy as a transfusion in conditions such as acute stroke and multiple sclerosis. The rationale here is that whole cord blood contains oxygen rich fetal haemoglobin, anti-inflammatory cytokines, and of course stem cells, which all may help in stroke and multiple sclerosis. A clinical trial using cord blood stem cell transfusion in stroke is currently being planned in Canada (Bhattacharya, 2004; Chaudhuri *et al.*, 2007).

Mesenchymal stem cells in cord blood can, in theory, produce all tissue in the body thus providing a non-controversial source of stem cells for research and future therapy. Liver and insulin secreting pancreatic beta cells have already been derived from these cells. Cord blood stem cells differ from bone marrow in demanding less stringent tissue matching allowing cord blood transplants to be carried out with up to a 50% mismatch at the major HLA loci. They are reported to cause fewer complications and have lower risks of rejection via graft versus host reactions than bone marrow grafts. They have offered primary care for inherited diseases including haemophilia, haemoglobinopathies and sickle cell disease. This illustrates the possible unique immunological properties of both embryonic stem cells and umbilical cord blood stem cells, and also mouse embryo stem cells grafted to irradiated and non-irradiated recipients (Hollands, 1988).

It is essential to consult experts in the field to understand the significance of these debates, as described by Edwards (2004). Cells from human

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cord blood were tested for their efficacy as progenitors capable of colonizing bone marrow in mice with severe combined immunodeficiency (SCID) (Wang *et al.*, 1997). Quantitative comparisons between different sources of haemopoietic and mesenchymal stem cells revealed respective frequencies of 1 in 9.3×10^5 cells in cord blood, 1 in 3.0×10^6 in adult bone marrow and 1 in 6.0×10^5 in cells mobilized from peripheral blood. These cells proved to be primitive human haemopoietic cells capable of engrafting lymphoid and multilineage myeloid cells.

A classic example of the advantages of cord blood stem cells arose when they were involved in a case involving Fanconi anaemia. It formed the basis of so-called 'designer babies'. It arose when a family delivered a child with this disorder who, by the age of 5 or thereabouts, was succumbing to the disease. The parents wished to have another baby free of this disease, and were advised that it may be possible to cure the elder sibling. This would involve typing numerous embryos to find those with the closest HLA types present in the sick elder sibling.

The intention was to identify embryos free of Fanconi anaemia for transfer to the mother, and then extract cord blood stem cells if the pregnancy grew to term (Verlinsky *et al.*, 2000, 2001). Preimplantation genetic diagnosis was used by removing a single blastomere in order to select embryos free of disease and HLA compatible with the elder sibling. Close matches were discovered after numerous embryos diagnosed as free of Fanconi anaemia were classified for HLA types that were compatible with the elder sibling. The transfer of these selected embryos to their mother resulted in the birth of an offspring free of Fanconi anaemia and HLA compatible with the dying sibling. Its cord blood cells were collected and transplanted to the sick sibling. Symptoms of Fanconi anaemia rapidly declined and the donated stem cells initiated their repair functions within a few days (Verlinsky *et al.*, 2000, 2001). The astonishing recovery by the grafted sibling stands to this day as a wonderful example of the power of restoration achievable by cord blood stem cells.

Many human examples have followed this initial case, and are evidently highly successful. Perhaps the most astonishing is the Canadian patient who developed leukaemia during pregnancy and was told that she would die. She insisted that her baby's cord blood was collected and she received it as a transplant, which cured her leukaemia. Both mother and baby are alive and well today and the child gives her name to the Victoria Angel Registry of Hope in Toronto (Hollands, unpublished).

In some aspects, cord blood cells are less efficient than marrow stem cells. They need longer intervals for haemopoietic repair (especially platelets) and recovery in human recipients as compared with the

use of bone marrow, and this has restricted their use by some physicians. A trial divided children into two groups, one being given grafts of cord blood and the other adult bone marrow (Frassoni *et al.*, 2002). Blood neutrophils and platelets multiplied in both groups. A more rapid rise in neutrophils and platelets was found in bone marrow recipients, although more marrow cells were necessary to achieve short-term protection. Cord blood recipients had produced more committed and early progenitors, which improved the restoration of their haemopoietic progenitor cell reservoirs as reprogramming was achieved after initial delays.

The comparative recovery of recipients grafted with stem cells from cord blood or peripheral blood (PBSC) mobilized by cytokines was studied by Schipper *et al.* (2003). Qualitative differences in content and quality of stem cells and megakaryocyte progenitors were assessed in relation to their haemopoietic composition, distributions of mature and immature megakaryocyte progenitors and their kinetics *in vitro*. Differences *in vitro* during their maturation included the transient expression of CD34⁺CD41⁺ in peripheral blood cells as compared with their absence in cord blood stem cells, until megakaryocytes were formed carrying these markers. This delay led Schipper *et al.* (2003) to decide that cord blood cells should be cultured for 2 weeks before grafting, as they differentiated to produce immature cord blood subpopulations expressing CD34⁺CD41⁻ and containing >98% of megakaryocyte progenitors. CD34⁺CD41⁺ cord blood cells did not form megakaryocytes, although their progenitors formed 7% of all PBSC. Phenotypic differences resulted because megakaryocyte progenitors in peripheral blood expressed CD34⁺CD41⁺ *in vitro*, whereas slight variations resulted as cord blood progenitors differentiated into CD34⁺CD41⁺ megakaryocytes.

Capacities for colonization by grafted mesenchymal stem cells from cord blood, adult bone marrow, and peripheral blood were also compared (Wexler *et al.* 2003). Properties for self-replication, proliferation and differentiation into mesenchyme tissues including bone, fat, tendon, muscle and bone marrow stroma were assessed. Confluent cultures of bone marrow mesenchymal stem cells after 10–14 days maintained a non-haematopoietic phenotype of HLA class 1⁺ CD29⁺CD44⁺CD90⁺CD45⁻CD34⁻CD14⁺ in successive passages, and comprised ca. 1 in 3.4×10^4 cells capable of producing adipocytes and osteocytes. In contrast, mononuclear cells in cord blood and peripheral blood cultured over three or more passages under mesenchymal stem cell conditions produced adherent, non-confluent fibroblast-like cells with the haemopoietic phenotype CD45⁺CD14⁺CD34⁻CD44⁺CD90⁻CD29⁻. When seeded with cord blood cells enriched for

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CD34⁺ to produce colony-forming units of granulocytes/macrophages but not functional mesenchymal stem cells (MSC), cultured bone marrow MSC and mature stroma produced colony-forming units of granulocytes/macrophages. Adult haemopoietic stem cells thus provided mesenchymal stem cells, whereas cells from cord or peripheral blood did not, although it is possible that very small populations had gone undetected.

Highly pluripotent CD45⁻ somatic cells isolated from human cord blood are named unrestricted somatic stem cells (USSC) (Kögler *et al.*, 2004). They share similarities with fetal MSC, and have different properties from human adult MSC as they vary in lacking HLA class II and being able to migrate to heart and form Purkinje fibres and cardiomyocytes. USSC can be expanded to 10¹³ cells without any loss of their pluripotency after adhering to substrates. They can also be induced to differentiate into osteoblasts, chondroblasts, adipocytes, haemopoietic precursors, and neural cells including astrocytes and neurons, each expressing their relevant markers. Persisting for 3 months in brains of recipient adult rats, those that migrated resembled neurons. Differentiating along mesodermal and endodermal pathways in animals, they assisted bony reconstruction in rat femurs and displayed chondrogenic activity in mouse recipients. They form human haemopoietic tissue in fetal sheep, and albumin-producing hepatic parenchyma in atria and ventricles of sheep hearts (Kögler *et al.*, 2004). Tumours were absent in all recipients, and the cells seemed to be immunosuppressive and non-immunogenic. This valuable information shows how cells such as these have immense therapeutic possibilities.

Transplantation of cord blood stem cells has attracted optimistic assessments (Ooi *et al.*, 2004). Eighteen patients in their 40s who suffered from acute myeloid leukaemia were grafted with cord blood stem cells from unrelated donors. Seventeen survived, one died and three showed relapses in the first 2 years post-grafting. Virtually all recipients displayed rising neutrophil counts, an indication that myeloid reconstruction was in progress. Four patients treated with cyclosporin and methotrexate to avoid graft-versus-host reactions displayed continuing evidence of this condition, although overall, 76% of patients were alive and disease-free after 2 years. Almost all of these cases were alive and free of disease after 4 years.

A highly optimistic survey on the use of human umbilical stem cells has also been presented by Ghen *et al.* (2006). They stressed the abundance of their clinical applications as they write: 'Other than haematopoietic progenitors, there are mesenchymal, endothelial stem cells and neuronal precursors in varying quantities, that are found in human umbilical cord blood. These may be useful in diseases such

as immune deficiency and autoimmune disorders. Considering issues of safety, availability, transplant methodology, rejection and side effects, it is contended that a therapeutic stem cell transplant, utilizing stem cells from human umbilical cord blood (HUCB), provides a reliable repository of early precursor cells that can be useful in a great number of diverse conditions. Drawbacks of relatively smaller quantities of mononucleated cells in 1 unit of cord blood can be mitigated by in-vitro expansion procedures, improved in-vivo signalling, and augmentation of the cellular milieu, while simultaneously choosing the appropriate transplantation site and technique for introduction of the stem cell graft.'

This summary is backed up by their detailed descriptions of the potential clinical applications of HUCB cells. They are readily available, and involve low costs in testing for HIV, hepatitis A, B and C, cytomegalovirus, toxoplasmosis, blood typing, Rh factor and tests possibly needed for endemic diseases. A wealth of growth factors and accompanying stem cells are present in cord blood and have distinct advantages over adult stem cells, since they are involved in earlier cell cycle phases, and do not have to obey a challenge associated with adult stem cells, namely their decreased capability for differentiation (stemness) due to their harvesting in a later cell cycle phase (Ghen *et al.*, 2006). Such long-standing environmental abuse as lifetime exposure to pesticides, insecticides, preservatives, heavy metals, allergens and volatile organic compounds may contribute to loss of effectiveness in adult stem cells, and may be reasons why human cord blood cells are useful for numerous disorders, since they contain haematopoietic progenitors, mesenchymal progenitors, endothelial cell progenitors and non-haematopoietic stem cells.

Ghen *et al.* (2006) stress that umbilical cells have some drawbacks. These include the relatively low total counts of mononucleated cells, problems in matching appropriate human leukocyte antigens which arise especially in minority groups, the large quantities of cells required to reconstitute the entire immune system, and the toxicity experienced by patients undergoing bone marrow or human stem cell transplantation. Political and religious organizations have accepted that using human cord blood is morally and ethically satisfactory for establishing repositories of stem cells, and Ghen *et al.* (2006) explain the full extent of their value.

Some other possible approaches to stem cells

The above evidence implies that human umbilical stem cells will be an excellent pathway to follow, and

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Richard Branson may have a winner as he establishes his company designed for the use of human cord blood stem cells. Yet, even while paying tributes to the potential of cord blood, bone marrow and peripheral blood stem cells, the future may lie in a different direction.

Alternative forms of stem cells

One example concerns the source of stem cells. Very recently, another source of multipotent ES cells emerged in a recent study by De Coppi *et al.* (2007). They were discovered among tissues collected from the amniotic cavity during amniocentesis in humans and rodents, and those cultured *in vitro* were discovered to multipotent. Named AFS cells, they were few in numbers but could be purified. Displaying clear evidence of induction, they produced adipogenic, osteogenic, myogenic, endothelial, neurogenic and hepatic lineages *in vitro*, which covers tissues formed in the three primary embryonic germ cell layers. Early primitive forms were induced to differentiate into neural lineages when exposed to nerve growth factor (NGF) and they were then able to engraft mouse brain in a manner resembling that attained by neural stem cells.

AFS cells expressed c-kit (CD117), which is the receptor for stem cell factor (Zsebo *et al.*, 1990). The c-kit population in many human samples collected during amniocentesis could be identified and expanded in culture as stable AFS cells. They divided every 36 h, did not need feeder layers, expressed class I major histocompatibility antigens, but showed no sign of spontaneous differentiation. They expressed mesenchymal and neural markers but not markers of ES cells such as CD29, CD44, CD73, CD90 and CD105 (De Coppi *et al.*, 2007). Their undifferentiated state was confirmed by their expression of Oct-4, but they differed in one sense from ES cells, which grow as teratocarcinomas when implanted into recipients whereas AFS cells did not. *In vitro*, they remained diploid after 250 generations and could be cloned. This and other evidence led De Coppi *et al.* (2007) to conclude that AFS cells resembled multipotent stem cells.

The cellular products of AFS cells possess distinct therapeutic properties. One of these includes their induction to neuronal lineages, as 80% of the original population became positive for nestin. Some cells that were induced and grafted transformed to dopaminergic neurons expressing the *GIRK2* gene. When injected into lateral cerebral ventricles of newborn mice, the AFS cells participated seamlessly in the development of the central nervous system by 1-month post-injection and survived efficiently over a 2-month period in periventricular areas and olfactory bulb. Likewise, they were able to colonize hepatic lineages over 45 days. AFS cells placed in osteogenic

medium to differentiate in-vitro-produced functional osteoblasts. When seeded on scaffolds which had been implanted subcutaneously into immunodeficient mice, they produced blocks of material resembling bone. In their conclusion, De Coppi *et al.* (2007) stress that AFS cells can be obtained from routine amniocentesis which may be a convenient source for autologous therapy in later life.

It is remarkable that the data presented by De Coppi *et al.* (2007) has close resemblances with other types of stem cells reported in the literature, including the capacities of embryo stem cells prepared from rabbit inner cell mass (Cole *et al.*, 1966). Isolated cells divided for 200 and more generations while remaining faithful to their specific enzymic content, diploid chromosomes and morphologies. They clearly awaited an inducer, and this was achieved by culturing rabbit blastocysts intact except for the removal of their zona pellucidae. Outgrowths of cells now differentiated into muscle, neurones, blood islands, connective tissues and others. This is exactly what De Coppi found for their AFS cells. Such a curious link may have been due to the differentiation of early epiblast and precursors of the amniotic cavity in rabbit inner cell mass cultured *in vitro*. It is possible that all ES cell lines form this way, since ES cells are made from inner cell mass cells which may contain such precursors.

Improving the acceptance of allografts

Another unusual example of the properties of bone marrow stem cells emerged in 2004, when Tilly and his colleagues reported that they could form stem cells capable of producing oocytes and restoring ovarian function (Johnson *et al.*, 2004, 2005). Bone marrow grafts given to female mice, and possibly humans, could produce new follicles and oocytes in a recipient's ovary, and it seemed that these grafted tissues shared genes typical of germ cells (Johnson *et al.*, 2004). This evidence led to proposals that bone marrow stem cells could migrate to and colonize ovaries and so maintain a plentiful stock of oocytes for reproduction. This situation was postulated as a means of replenishing ovarian follicles when numbers in the ovary were declining to very few. Johnson *et al.* (2005) later detected follicles and oocytes in recipient ovaries within 24–36 h post-grafting of marrow grafts, which persisted in this form for several months. Grafted cells expressed stage-specific antigen (SSEA1), a marker of germline, while other typical markers that were expressed included *Oct-4*, which is characteristic of a lack of differentiation. Curiously, genes for synaptonemal complex protein (*Scp3*), growth differentiation factor 9 (*Gdf9*), and a zona pellucida protein (*Zp3*) could not be found in the cells, and germline genes such as *Mvh* were also absent from preparations of grafted tissue. This evidence queried

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whether these cells were 'true' oocytes despite positive morphological evidence. They were not haemopoietic stem cells (HST) since ovarian tissues containing Mvh cell lines were $\text{lin}^- \text{c-kit}^+ \text{Sca-1}^-$ whereas typical HST express both lin^+ and Sca^+ (Johnson *et al.*, 2005). Nevertheless, one gynaecologist commented that his patients given ovarian transplants ovulated longer than expected, adding some support to the hypothesis.

Johnson *et al.* (2005) assessed other concepts that might explain their findings, including trans-differentiation that can occur under certain circumstances, induced by factors such as epigenesis or cell fusion. These factors did not appear to be incriminated in the reported relationship between bone marrow and ovary. A different explanation explored by the investigators concerned the many ES cells that migrate to genital ridge in immature mice. One-half of them fail to colonize it and migrate elsewhere. They could be stem cells which become localized in many tissues. Large amounts of data have shown inner cell mass cells are highly plastic, especially when forming chimaeric mouse embryos, and single inner cell mass cells placed in the blastocoelic cavity in mice form chimaeras and colonize many tissues (Gardner, 1968). Such evidence might lessen the surprise at the claim that pluripotent marrow cells can colonize germline.

Bypassing rejection

Improved methods may prevent the rejection of organ allografts and so offer a much wider scope for transplanting cells between incompatible donors and recipients. If this can be achieved, there would be a reduced need for cord blood stem cells. An approach to this end involves using a specific orally active inhibitor of the Janus kinase 3 (JAK3) system named CP-690,550 (Changelian *et al.*, 2003). It lengthens survival of mice in a model of heart transplantation without impairing the proliferation of cells in grafted heart tissue. It is free of side-effects typical of many existing therapies, and enabled mouse recipients to survive with kidney grafts over 3 months as their haemoglobin concentrations were fully restored. Studies with doses three times weekly were also effective in *Macaca fascicularis*. The JAK3 system offered an equal efficiency and lack of side effects in this species as it had invoked in mice. Therapeutic strategies may be developed for human application, although tests are still needed on embryo implantation.

A distant future?

Finally, it is increasingly possible that soon there may be no need for any donors in the cure of haemopoietic and other disease. Scientific attention now concentrates on very different pathways as transdifferentiation and reprogramming cells open new opportunities. This has been approached by

transferring four factors, namely *Oct 3/3*, *Sox2*, *c-Myc* and *Klf4* into adult fibroblasts shown when these four genes typifying ES cells were injected into somatic cells. Some of the injected cells converted to ES cells (Takahashi and Yamanaka, 2006). These modified cells could partake in embryonic development in mice and colonize all three germ layers.

It is beginning to appear that, if the necessary genes are known, one cell type can be converted into another. Imagine at the age of 50 making a small preparation of one's own blood cells, identifying haemangioblasts and then injecting them with genes establishing nerve cells, blood cells, muscle cells or whatever else is needed. Would haemangioblasts be the best option? They are very close to constituent cells of the inner cell mass and might revert to another cell class more easily than the highly differentiated recipient cells utilized by Takahashi and Yamanaka (2006). This whole approach offers a simple approach using self cells which are easily available, fresh, have never seen an incubator and should not be expensive.

Other approaches that may be closer than imagined also emerge in routine work on cord blood cells. To this end, it is well worth quoting a section of the conclusions drawn by Chaudhuri *et al.* (2007) in their recent paper on the application of umbilical cord transfusion in acute ischaemic stroke: 'Umbilical cord blood transfusion in stroke may have the potential to reduce the burden of disability in stroke and possibly other brain diseases. There are, however, many unanswered questions regarding its therapeutic value and the practicality of its use. Umbilical cord blood can be obtained in large quantities at birth, can be used without risking the ethical objections of embryonic and fetal stem cell therapy'.

Summary

This review presents a glimpse into the world of cord blood stem cells and their possible use in therapies. They might even replace the potential of ES cells which raise ethical and technical problems and are bound to be expensive. Cord blood stem cells now offer major advances in therapies for most body tissues, and their clinical role will undoubtedly expand. The recent discovery of pluripotent amniotic stem cells may challenge the value of cord blood stem cells, although they both make demands on women in the middle or at the ending of their pregnancy. Perhaps those great tanks of umbilical cord stem cells, haemopoietic precursors and peripheral blood cells will soon be obsolete as new means of genetically modifying the properties of somatic cells may ultimately replace all other approaches. If it becomes practical, people will carry basic cells for conversion in their own blood.

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As this paper was being prepared, Takahashi et al. (2007) claimed that under some circumstances umbilical cord blood transplants are equally as safe and effective as transplants using related bone marrow or peripheral blood. Their study involved treating patients with haematologic malignancies by a myeloablative conditioning regimen. According to a note in an online oncology resource centre, Cancer Consultants (see <http://professional.cancerconsultants.com/print.aspx?id=39055>), this treatment gave advantages when treating patients for treatment-related mortality, relapse, disease-free survival for standard-risk and high-risk patients and less frequent graft-versus-host disease. This report clearly adds to the advantages of cord blood.

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