# Cord blood stem cells

***Khalil E. Rajab,*** *FRCOG, FFFP,* ***Reginald P. Sequeira,*** *PhD, FCP.*


## ABSTRACT

إن اكتشاف مصدراً جديداً للحصول على الخلايا الجذعية من دم الحبل السري بدلاً من استخراجه من أنسجة الجنين، من الدم، أو من نخاع العظام، قد جدد الاهتمام بهذه التقنية الجديدة واحتمالاتها العديدة في علاج الأمراض المستعصية. خطط الباحثين في هذا المجال إدخال هذه التقنية في علاج بعض الأمراض العصبية المعقدة، الأمراض الوراثية، المناعية، أورام الدم السرطانية، التشوهات الخلقية للأعضاء، وأمراض شرايين القلب بالإضافة إلى تحقيق الحلم القديم في تأخير الشيخوخة. وقد وازا هذا الاهتمام الذي انصب على أبحاث الخلايا الجذعية ظهور فكرة إنشاء بنوك تجارية لتخزين دم الحبل السري المأخوذ عند الولادة. وتهدف هذه المراجعة إلى تقديم عرض ملخص للاستعمالات الطبية للخلايا الجذعية بصورة عامة وتلك المأخوذة من دم الحبل السري بوجه خاص مع استعراض لمناقشة الادعاءات والاعتراضات التي صاحبت ظهور فكرة فتح بنوك تجارية من أجل حفظ وتخزين دم الحبل السري. وانتشرت الآن هذه البنوك في الدول الغربية والعديد من الدول الآسيوية. وتجدر بنا الإشارة إلى ضرورة التمييز بين هذه البنوك والبنوك العائلية أو بنوك الدم الرسمية أو الإقليمية التي تحتوي على قواعد للمعلومات حول زرع الأعضاء، فصائل الأنسجة، دم النخاع، واستخدام الخلايا الجذعية. ونقدم هنا هذه المراجعة التي تلخص الوضع الراهن لمميزات واستعمالات الخلايا الجذعية بصورة عامة وتلك المستخرجة من دم الحبل السري، كما وستتم مناقشة الادعاءات التي تطرحها شركات بنوك دم الحبل السري والاعتراضات التي أثيرت حولها، ومدى تناسب إدخالها في دول مجلس التعاون عموماً وفي مملكة البحرين بشكل خاص.

The discovery that stem cells (SCs) can be obtained from umbilical cord blood instead of the more controversial source of embryonic SC's, has renewed interest on the new, exciting therapeutic potentials of this technology. Several therapeutic targets have been cited as candidates for treatment such as, malignant blood disease, hematological disorders, complex neurological illnesses, genetic and autoimmune diseases, benign and malignant blood diseases, skeletal anomalies, and the ultimate promise of using this technique in delaying the process of human aging. Parallel to this rise in popularity of SC research, SC banking has become a growing commercial enterprise. This review will attempt to present a concise account on the present status of the uses of SC in general, and cord blood (CB) in particular. An evaluation of the debate on the claims, and counter-claims in commercializing CB banking has been summarized.


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*From the Department of Obstetrics and Gynecology (Rajab), Faculty of Medicine, Arabian Gulf University, and of the Salmaniya Medical Complex, and the Department of Pharmacology and Therapeutics (Sequeira), Faculty of Medicine, Arabian Gulf University, Kingdom of Bahrain.*

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*Address correspondence and reprint request to: Prof. Dr. Khalil E. Rajab, Department of Obstetrics and Gynecology, Faculty of Medicine, Arabian Gulf University, PO Box 26752, Kingdom of Bahrain. E-mail: yonrajab@batelco.com.bh*

The bone marrow derived stem cells (SCs) transplantation was developed by a team in the Fred Hutchinson Cancer Research Center, USA, between the 1950's-1970's, and was pioneered by Donnall E. Thomas whose work was later recognized with a Nobel Prize.[1] This primary work confirmed that bone marrow cells infused intravenously could repopulate the bone marrow, and produce new blood cells. This work also contributed to the reduction of the likelihood of developing life-threatening complication, namely, graft-versus host-disease.[1,2] Instead of the SC being derived from the bone marrow, it became possible later to obtain these cells from the peripheral blood after stimulation using growth factor such as, granulocyte monocyte-colony stimulating factor (GM-CSF), and granulocyte-colony stimulating factor (G-CSF).[3] The advantage of using peripheral blood technique (hemopoietic stem cell [HSC]), rather than the bone marrow transplantation was developed, because the peripheral blood procedure provides a larger pool, and does not require that the donor be subjected to general anesthesia to collect the graft. Hemopoietic stem cell transplantation, however, has many hazards and potential complications, and has always been reserved for patients with life threatening diseases.[4]

The relatively more recent discovery of embryonic stem cells (ES) played a part in developing a much wider use of SC in biomedical arenas. These cells are derived from the inner cell mass of an early stage embryo known as the blastocyst. Human embryos reach the blastocyst stage 4-5 days post-fertilization, at which time it consist of 50-150 cells.[5] The principal feature of the ES is that they are pluripotent, they are able to differentiate into all the derivatives of the 3 primary germ layers: ectoderm, endoderm, and mesoderm. A variety of cells derived from these layers include any of the 220 cell types, which form the cells of the body.[6] The ES cells are characterized by their pluripotency, which distinguishes them from other multipotent progenitor cells in the adult, which are only capable of forming of few cell types.[6] They are also capable of maintaining their pluripotency even if they undergo several cell divisions. This pluripotency is not confined to ES as recent research showed that pluripotent SC can be produced in cultures from adult fibroblast. This versatility of adult SC offers an exciting opportunity with regard to cell therapy. There was already many successful attempt by using 4 transcription factors on cells from the mouse, than in human adult fibroblasts by somatic cell nuclear transfer, which allows trans-acting factors present in mammalian oocyte to reprogram somatic cell nuclei to an undifferentiated state demonstrating therefore, that induced pluripotent stem cells (iPS) cells can be generated from adult fibroblast.[7,8]

In view of the capacity of EC for self-renewal, several potential therapies were suggested in the field of regenerative medicine and tissue replacement after injury or disease,[9] but so far no medically approved therapy was derived from SC research. Adult SC and cord blood (CB) SC have thus far, been the only SCs used successfully to treat any disease.[10] Reported conditions which were tried experimentally by non embryonic, or CB SCs include several hematological immunological diseases, cancers, and juvenile diabetes, Parkinson's disease, blindness, and spinal cord injuries.[11,12]

The discovery that CB has primitive cells with clinical potential, matching that of the far more controversial ES held the promise that many diseases could be treated with CB.[13] Furthermore, researchers discovered that CB SC can be harvested in large enough quantities to repair tissue damage in patients by using the new microgravity technology - originally developed by NASA for the International Space Station.[14,15]

The newly discovered human CB cells were not as primitive as ES, which can give rise to any tissue type of the body. But they appear to be much more versatile than adult SCs, such as those found in the bone marrow, which repair damaged tissue during life.[15] Most of the recent reports suggest that CB SCs have the distinct advantages of bringing together the essential qualities of both types of SC, have most of the characteristic surface markers of embryonic SCs, and the fact that it can be saved, stored, and multiplied without any of the ethical dilemmas facing embryonic cell use.[16] In addition to the ethical problems of obtaining SCs from the embryo however, there are still other technical problems of graft-versus-host disease associated with allogenic SC transplantation.[13]

New potential sources for harvesting SC such as the menstrual blood are already being explored,[17] the *in vitro* conversion of skin fibroblast into ES, the discovery of a gene which can switch normal cells into SCs, and which can eliminate also the problem of rejection, SCs obtained from human/animal hybrid embryos, and the improvement of the techniques for extracting ES without destroying the actual embryo are currently being explored.[18-21]

The historical landmarks on SC research so far are summarized in **Tables 1 and 2**.

***Stem cell science - the basics.*** The SCs are found in all multi-cellular organisms. Their main feature is the ability to regenerate by cell division, and to differentiate into a variety of specialized cell types. There are 2 kinds of mammalian SCs: the embryonic SCs, which can be found in the blastocysts, and adult SCs usually derived from adult tissues. While in the early embryo, SCs can develop into any of the specialized tissues in the adult SCs, and progenitor cells function are mainly in the repair system for the body, replacing specialized cells, but preserving the natural turnover of regenerative organs, such as blood, skin, and intestinal tissues.[22-24]

As SC can be grown and transformed into specialized cells of various tissues such as, muscle or nerves in cell culture, their use in medical therapies has been proposed. In particular, embryonic cell lines, autologous ES generated through therapeutic cloning, and highly plastic adult SCs from the umbilical CB or bone marrow are touted as promising candidates.[25]

Stem cells by definition has 2 properties: self-renewal, or the ability to pass through many division, and potency, which is the ability to develop into specialized cell types. To be precise, this would requires SCs to be either totipotent, or pluripotent - in order to generate any mature cell type:[26] "Totipotent results from the fertilization of ova by sperm cell. So, cells of the morula are also totipotent. These cells can differentiate into embryonic and extra embryonic cell types. Pluripotent SCs are the descendants of totipotent cells, and can differentiate into cells derived from any of the 3 layers. Multipotent stem cell describes the state, in which these cells can generate only one type of cells, and usually from a related group (for example, HSC can differentiate into any of the blood cells. Unipotent cells can develop into

**Table 1** - Milestones in the history of cord blood application in therapy.

| Year | Event | Location |
|---|---|---|
| 1988 | Treatment of Fanconi's anemia[69] | Paris Hospital, France |
| 1993 | First unrelated CBT[70] | Duke University, Durham, N.C, USA |
| 1997 | CBT used in chronic myelogenous leukemia during a clinical trial[71] | University Hospital La Fe, Valencia, Spain. |
| 1998 | First CBT in a boy with sickle cell anemia[72] | Emroy and Grady Hospital Atlanta, Georgia, USA |
| 2000 | First CBT using PGD testing to insure perfect matching[73] | Fairview Med Centre, Minneapolis, USA |
| 2006 | More than 8000 CBT performed[74] | Worldwide |

CBT - cord blood transplant, PGD - pre implantation genetic diagnosis

**Table 2** - Evolution of cord blood banking.

| Year | Event | Location |
|---|---|---|
| 1992 | The opening of the first cord blood bank[75] | The Blood Center, New York |
| 1992 | The opening of the first family cord blood center[75] | University of Arizona, USA |
| 1992 | First Family CBB[75] | University of Arizona, USA |
| 1995 | First CBB registry[75] | Duke University, USA |
| 2004 | A year long study by IOM to make recommendations for CB program[75] | IOM, USA |
| 2005 | Publication of IOM recommendation[75] | IOM, USA |
| 2006 | The US congress passes National CB legislation[75] | Washington, USA |

CBB - cord blood banking, IOM - Institute of Medicine

only single cell type, but retain self-regeneration which distiguish them from non-stem cells.

***Methods of identification of SCs.*** Stem cells are able to regenerate tissues over a lifetime. While the fundamental feature for a bone marrow derived cells, or HSC is their ability to transplant one cell and save the patient, the SC is able to generate new blood cells of all lineages for a long period,. Additionally, isolation of SCs from the transplanted individual is possible, and can in turn be transplanted into another individual without HSCs, proving that SCs are capable of self-renewal. Stem cells plasticity have been demonstrated *in vitro*, using clonogenic assays, where single cells show their ability to differentiate, and self renew.[27]

The identification of SC is based on a special set of surface markers that include many transcription factors and surface proteins.[28] "The transcription factors Oct-4, Nanog, and Sox 2 form the core regulatory network that ensures the suppression of genes that lead to differentiation, and maintenance of pluripotency. The cell surface antigens most commonly used to identify human SCs are the glycolipids SSEA4, and the keratin sulphate antigens Tra-1-60 and Tra-1-81. The molecular definition of SC includes many more proteins, and continues to be a topic for further research.[29,30]

*In vitro* culture conditions can alter the behavior of cells, making it unclear whether the cells will behave in a similar manner *in vivo*. Considerable debate exists currently, as to whether some of the proposed adult cell populations are truly SC.[31] In any case, the adult body has a small number of SC in many tissues and organs - where they lie dormant until activated by illness, or injury. Unlike ES, adult SCs have not proved to be able to morph into every kind of cell, and may be limited to becoming cell types within their tissue of origin. Adult SCs in hippocampus of the brain, for example, can become neurons or glial cells, but not a bone or liver cell. Similarly SC from a new-born's CB (considered adult cells because they are not from the embryos) produce only blood cells. Recently, though, cord tissue was found to contain mesenchymal cells capable of generating bone and cartilage.[32] In general, adult SCs are scarcer, and harder to culture than ES, yet large number is needed for therapies.[32]

Due to the pluripotency and versatility of ES, research was concentrated on producing embryonic cell lines in the laboratory, but the ever increasing demands, and the publicity on the use, and misuse of SCs technology at the turn of the millennium, leads to polarization of public opinion. While the proponents argue that it is unethical not to use leftover embryos to save lives, the opponents warned of a brave new world of "embryo farms". This controversy spiraled into a series of congressional debates, and presidential statements on the issue of unethical SC research.[33] The use of CB as an endless source for the "ethical stem cells" has became very popular, however, due to technical limitations with these cells alternative approaches were explored. Some frontiers examined recently were the prospect of finding new kinds of adult cells, which are as versatile as the cells found in the embryos. This has been achieved by cloning, and culturing adult skin fibroblast cells, and the most recent permission in the United Kingdom, to start hybrid technology as a potential source for SCs.[34] Another outcome for this debate was the congressional recommendation for the establishment of public, and private banking of CB in the USA.[35]

***The evolution of CB banking.*** To date, many official CB bank centers have been established in North America, Western Europe, Australia, Asia, Africa, South Korea, and the Middle East. In the private sector, many western

private firms also opened branches overseas for banking CB, or have encouraged the public to send samples of their CB to their main centers in Europe, or North America. It is reported now that over 8000 patients throughout the world have been treated so far using CB SCs therapy for mainly blood and immunological diseases.[36-38] These historical developments on CB as a potential source for SCs should be appreciated in the backdrop of the controversy of SC research.[39-41]

***Emergence of CB banking in North America and Western Europe.*** In the USA, the potentials of CB therapeutic applications prompted the government to authorize $10 million in 2004 for starting a National Cord Blood Stem Cell Bank to regulate the collection, distribution, and use of CB donations in the US. Based on this budget, Congress requested the Institute of Medicine (IOM) to investigate and review available CB programs, and present them with technical study, and guidance on the optional management, and benefit of a national banking program.[42] One year later, the IOM committee presented its report, "Cord blood: Establishing a National Hemopoietic Stem Cell Bank Program" to the US Department of Health and Human Services Resources and Services Administration, and the public. The committee emphasized that a national CB banking should aim at maximizing access to "high-quality CB SC" for patient therapy and research, in an efficient, cost effective, and in the most ethical way. They have also agreed on several key qualities for the program such as:[43,44] simplicity (the national program should be supported, and to avoid duplication of effort), quality (it should encourage the best possible chance of patient recovery), and patient and physician support (education is an integral and necessary part of the program).

***Key IOM recommendations. Education and ethics.*** The ethical issues associated with collection, storage, and use of donated tissue for transplantation, the committee emphasized that "before a donor consents to donate CB, she must fully comprehend: who has access to the CB once it is donated, where it will be stored, how her privacy will be protected, and whether the donor stands to gain, or be harmed by the donation". Two key recommendations in the study highlight the need for physicians, and other pre-natal care providers, to provide all expectant patients with an informed choice about the storage, or the disposal of their newborn's CB SC, and to provide a balanced education on all CB banking option prior to labor and delivery. Informed consent should be obtained before labor and delivery, and donors must be provided with clear information about their options. The information must include a balanced perspective on the different options for banking (family banking, or public donation). The information disclosed for donation should not include language that gives the impression that the unit will be available to the family after donation.

After the recommendation of the IOM study, the house of representative agreed to the "Stem Cell Therapeutic and Research Act of 2005",[45] which created the new Federal program to collect and store CB, and expand the current bone marrow registry program, to also include CB. The IOM study assisted in guiding the health policy at the state level as well. To date, 12 states have passed some form of CB education legislation, which benefit about a third of the US population. Many states are developing similar legislation to assist doctors and pregnant women to understand the advantages, and disadvantages of banking CB SCs.[46]

With regard to commercial blood banking (family blood banking), there are several companies in the US, which provide the service at a cost of approximately $1500-2000. The samples are collected in a special kit provided by the company that also supplies educational materials. Some of these companies expanded their commercial CB banking interests abroad to many other countries. Cryo-Save Company for instance, has outlets in over 36 countries including the Middle East: Turkey, Iran, Pakistan, Kuwait, Lebanon, Qatar, and Bahrain.[47-49]

In the United Kingdom (UK), an opinion paper was issued by the Royal College of Obstetricians and Gynecologists (RCOG) Scientific Committee on CB banking in 2001, and then revised in June 2006, which is summarized as: "Cord blood banking started in 1996 as banking of the HSC within the National Blood Service (NBS), and funded initially through research and development funding. Women in selected maternity units in the UK are approached during antenatal period, and offered the option to donate CB to the NHS Cord Blood Bank (NCBB). Appropriate consent is obtained by trained NBS staffs, and blood is collected by trained NBS operatives. These donations are sent to NCBB for processing and storage for future potential use in unrelated transplantation, in similar way to bone marrow donations. The donations are tested for a variety of parameters including markers for infection, and for human leucocytes antigen (HLA) types. The tissue types of both unrelated CB and bone marrow donors are available for the search for matching any patient, anywhere in the world, for those who may require HSC transplantation. This established non-directed, or altruistic CB banking service is to be distinguished from directed, family, or autologous CB storage now being offered commercially by a number of companies trading in the UK". Private CB banks offer expectant mothers the service to store their cord HSC for a long period in case, "the child, or his/her siblings ever develop a metabolic, immunological, or

hematological disease that could only be treated by autologous, or related cord blood SC transplantation". Additionally, with the possibility of SC therapy, it may heal or improve degenerative diseases, private CB banks have used this possibility to advocate the personal storage of CB.

In the UK, the supplies of CB for storage are: free donations (non-directed) donations, directed donations in at-risk families, and non-directed donation from low-risk families. In the last group however, it is difficult to estimate the likelihood that a directed donation from low-risk family would ever be used.

The RCOG states "that many of the projected usages of non-HSCs remain speculative, and subject to research yet to be undertaken. At present, much more research is needed, including clinical trials on the use of these cells in the treatment of non-hemopoietic disorders, before any realistic estimate can be made as to the potential use of umbilical SCs in cellular therapy and regenerative medicine, and on the utility of directed donations. Few of commercially banked units have been used in transplantation, but this number is likely to increase, as more become available for this purpose, and as the population of those donating ages".[50]

***The key advice and recommendations of the RCOG.***[51-54] Cord blood is an accepted alternative to bone marrow transplantation, particularly in large spectrum of diseases of children, and young adults. Cord blood banking for therapeutic purposes will require a license from the Human Tissue Authority under the terms of the Human Tissue Act, which stipulates that: at-risk family CB donation is an acceptable procedure, if it is carried out in a public CB bank. There is no proof so far, to recommend commercial CB collection, and banking in low-risk family. Cord blood banking for possible future use is still uncertain, but if some patients wish to go through this, it should be carried out safely, depending on the facilities in the unit where the delivery will take place, maternity units and health centers providing perinatal care need to develop a policy on how to respond to clients' request for CB storage through local or regional commercial banks, and how to recover costs. Printed pamphlets stating the unit's policy on CB banking should be given to all maternity patients on their first visit.

***Advice to obstetricians and neonatal pediatricians.*** No alteration is necessary in the usual management of the third stage of labor, collection of CB should be made from the ex-utero (separated) placenta, a third party (not the attending obstetrician or midwife) should perform the collection, and should meet the European Tissue and Cells Directive, and bank collection should not be made if there is contraindication, such as all preterm deliveries, nuchal cord, or maternal hemorrhage. The health authority should consider making CB collection for families with genetic disorders, or families with a member with an acquired disease that is treatable by HSC transplantation, in order to provide broad coverage.

***Approved clinical uses of umbilical CB.*** The principal uses of umbilical CB so far, have been in pediatric hematological malignancy. This has been a technical advancement on bone marrow, as a source for allogeneic transplantation with the following advantages in clinical practice:[53,54] a) rapid and easily accessible compared with the highly specialized and expensive bone marrow grafts, b) abundant availability of CB. It has the feature in transplantation of tolerating a mismatch of tissue type between donor and the recipient, much more than is acceptable with bone marrow, or peripheral blood. Ethnic diversity has a positive role among donors of CB, because it provides higher frequency of HLA haplotypes in comparison with bone marrow registries, 3) less effect of graft versus host disease, 4) less viral transmission: particularly cytomegalovirus (CMV), and Epstein-Barr virus.

The side effects of cord blood transplantation (CBT) are: 1) relatively less SCs in each CB donation, which can lead to delayed engraftment. Cord blood bank deal with this problem by the use of multiple units of CB for transplantation, and by efforts to expand the progenitor pool, 2) shortages of obtaining CB from the same donor of SC, or lymphocytes from the graft donor, if the disease relapses.

***Present uses of cord blood.*** a) the CBT is successful from HLA identical sibling specially in children with sickle cell anemia, b) the CBT from unrelated donors has been complicated with sustained engraftment, and a low incidence of graft versus host disease, c) report on HSC transplants from unrelated donors in adult with leukemia, published in 2004,[55] is encouraging. The incidence of chronic graft versus host disease, transplant related mortality, relapse, mortality, and leukemia-free survival were not significantly different between those receiving CB, compared to adult donation of HSC d) the number of SCs in CB grafts is vitally important, for speed of engraftment and survival following unrelated CB transplantation, particularly in adults. One unit was found insufficient for any patient over 50 kgs in weight. Researches therefore, need to concentrate on enlarging the pool of donors, and put new plan to increase the dose of HSC ex-vivo, and the giving of more CB units.

***Future possibilities.*** There are tantalizing possibilities about the use of CB, and non-HSC in the treatment of variety of acute and chronic conditions, but there is increasing evidence of the use of fetal-derived SC in the treatment of neurological diseases and a number of preclinical studies, which suggest an improvement in

cardiac function following infusion of umbilical CB cells for acute myocardial infarction. There have also been reports of the infusion of CB SC in a patient with long standing spinal cord injury, cases of hemoglobinopathies, and in a case of Fanconi's disease (rare genetic disease due to bone marrow failure, associated with increased incidence of solid tumors, and skeletal anomalies).[55,56]

Commercial CB banks are citing such preliminary research as further potential uses in their literature. In addition, websites are now offering cell therapy using CB cells ahead of formal clinical trial for variety of conditions, such as chronic neurological diseases, asthenia syndrome, motor neuron diseases, diabetes type-I, and even aging.

***Critique on CB banking.*** Embryonic stem cells taken from aborted fetuses have proven their versatility in laboratories, by first demonstrating their ability to undergo generic multiplications, and secondly to produce perpetual SC lines. Furthermore, it has an innate ability to differentiate under special conditions to any of the 220 varieties of specialized cells present in body organs.[57] Their agility, plasticity, and compatibility to easily develop in suitable biological environments, made it the ideal candidate for SCs therapy, and research.[55] However, since the turn of the millennium, the issue of extraction of SCs from discarded embryos has resulted in contentious ethical, moral, and religious debates. It has furthermore been politicized, and widely publicized in the media, political parties, and in the American Congress, and the European parliaments. Hence, this controversy also affected research funding, and scientist began to look for other non-controversial sources of SCs. The so-called adult SCs has in contrast to ES, been known for a long time, and include bone marrow stem cells, HSC, the umbilical cord, placenta, and more recently from menstrual blood SCs. More up to date methods to obtain adult SCs are cloning the adult skin fibroblasts, to produce ES. New but more controversial experiments also have recently been licensed in the UK, to produce hybrid embryos from human and animal cells as a source for ethical embryonic cells.[58,59] Since, these sources are less controversial than the human ES used for storage and research, and because of the dwindling of laboratory cell lines obtained in the past directly from human embryos, CB is stored now by both public and private CB banks in many countries. The essential feature of public CB banks is that they bank CB for the use of the general public, and currently most Europeans, US, and UK banks coordinate through their data bases, and laboratories the matching CB to patients through the National Marrow Donor Program. The commercial CB banks are for-profit establishments, which bank the CB for the private use of donor, or his relatives.[60]

The medical community usually approve of public CB banking. While private CB banking which are currently spreading, is usually not advisable unless the donor has a family history of specific genetic diseases.[61] Commercial CB banking is still illegal in France, and Italy, and opposed by the European Group on Ethics in Science and New Technologies. Indeed, CB harvesting remains a controversial practice (see the guidelines of the British RCOG-2006 statement on CB in practice, and the American Academy of Pediatrics 2007 statement on cord blood banking).[62] One of their interesting observations is that, children of parents who banked their CB are unlikely to ever use it (the odds of ever using it is 1:2700-1:20,000), and that most of the claims made by private CB banks of insuring the future family health against a multitude of diseases through storing CB are unsubstantiated.

Establishing CB bank services therefore, in the underdeveloped, or developing countries where sophisticated hematology services or SC research is lacking, can prove both costly, and wasteful exercise. At the private level, concerned companies may argue that this is in violation of free choice, and that those who are going to bank their CB are the affluent, that should not be denied access to family CB banks. Moreover, who can predict the range of possibilities of SC therapy, 30 years from now, when the children of donors will be in their early middle age, and may need it.

Private CB banks are managed around the world by major conglomerate companies, which have branches divided on the main regions of the world. As far as the experience of GCC states with bone marrow storage centers, public, or private CB banking, it is still basic with the exception of probably, King Fahad Specialist Hospital in Riyadh, Saudi Arabia. As for the rest of GCC states, there is now a branch for the American 'Cry-Save Arabia' in Dubai,[63] Bahrain, and Kuwait. The Qatar Ministry of Health have been approached in 2007-2008 to open local CB banks. Private companies have even gone a step further, by providing donors with blood collection kits that can be collected locally, and sent to the nearest overseas bank.[64]

Other considerations in private CB collection is the cooperation of the Obstetrics, Medical, and Midwifery staff in executing this collection, and at what stage of labor (before or after the delivery of the placenta, for example, *in utero* or *ex utero*), and how to store it until collection. It is not clear yet, if private banks would screen the blood against virus infection, sexually transmitted diseases, and whether they do tissue typing, like in public banks.[65] Quality storage is a necessary issue because it involves cryopreservation (initial freezing to -90$^0$C, then deep freezing with liquid nitrogen), and regular quality control.

As of 2007, the cost of private CB banking is approximately $2000 for collection, and $125 per year for storage.[66] A further difficulty with CB banking is the volume of the specimen, whether it was adequate at collection (ideally between 70-100 ml), or not.[67] Recent improvements however, was reported from the University of Toronto, to increase the yield of CB SCs to enable their use in treating adults, as well as children.[68] As for starting public or regional centers for SC storage, therapeutic applications, and research will be useful in the GCC states, particularly in countries with biological research facilities, and registry system to match CB for those in need. In Bahrain, we propose a joint venture by the Ministry of Health, to establish initially a well-staffed National Blood Bank Center with Hematopoietic Stem Cell and Transplant Services, and equipped with registry-database of donors. This center is to work jointly with the Al-Jawhara Center for Molecular Medicine and Genetics, in the College of Medicine-Arabian Gulf University. A joint national project like this will have a positive contribution to the health and scientific development in the Kingdom of Bahrain, and the GCC States in the Gulf Region.

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