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Review / Revisão

Private umbilical cord blood banks for family use, in Brazil - technical, legal and ethical issues for an implementation analysis

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Umbilical cord blood banks have been created worldwide after the discovery that umbilical cord blood (UCB) is a rich source of Hematopoietic Stem Cells (HSC) and an alternative to HSC from bone marrow for allogeneic transplantation. According to Brazilian legislation, banks for allogeneic use (government services) and exclusively autologous use (private services) can be created in the country. The storage of UCB units for direct donation (family use) can occur in public cord blood banks, hemotherapy services and transplant centers when there is a specific need to treat a known patient that is a member of the newborn's family. Even with the legislation being quite clear about the creation of cord blood banks and distribution of UCB units, ANVISA has identified an interest, demonstrated by the population and regulated sector, in the possibility of releasing UCB units, stored in autologous cord blood banks, with the purpose of clinical applicability to another family member other than the newborn owner of the cells. The objective of this study is to promote a discussion on a possible alteration in the legal parameters that support the implementation of autologous cord blood banks, towards the constitution of private banks for family use, pointing out the main issues. The study analyzed the technical and legal criteria related to cord blood banks, described the characteristics of HSC from different sources and types of transplant donations and procedures; discussed concerns related to Bioethical principles, current and potential clinical HSC applications, and possibly risks and benefits. Rev. Bras. Hematol. Hemoter. 2010; 32(4):317-328.

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Introduction

In the 1980s, researchers proved that, similar to bone marrow, umbilical cord and placental blood (UCPB) contain large quantities of hematopoietic progenitor cells (HPC) that

could be cryopreserved and then thawed without losing their capacity to form colonies *in vitro*.^(1,2)

The first allogeneic transplant of HPC from UCPB was performed in 1988.⁽³⁻⁵⁾ Thereafter this technique has been used extensively in the treatment of diseases, especially

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hematologic and oncological diseases, providing satisfactory results. Thus, UCPB is established as an excellent source of HPC and an alternative to the use of bone marrow cells, and so there is great interest in the storage of these cells.^(6,7)

The first public UCPB Bank, established in New York in 1992,^(2,8) encouraged the founding of other services worldwide. This fact is considered a strong factor in the search for compatible donors for patients needing a HPC transplant, particularly in pediatric settings. Private banks, commonly associated with biotechnology companies, have also been established with the objective of collecting and storing HPC for the donor child's own use (autologous storage) as well as for the use of the family.⁽⁹⁾

Brazilian law distinguishes two types of UCPB banks:⁽¹⁰⁾ collection and storage services for unrelated allogeneic use as part of the public network, BrasilCord,⁽¹¹⁾ that currently has nine units established throughout the country and has investment earmarked for another four units, and private services for autologous use, with 16 units in the country – one in the Central West, two in the South, three in the Northeast and ten in the Southeast. Additionally, the storage of UCPB for related allogeneic use, also called directed donation, can be carried out in public UCPB banks, hemotherapy services and transplant centers.⁽¹⁰⁾

Meanwhile, the National Health Surveillance Agency (Anvisa), linked to the Ministry of Health and responsible for the preparation and publication of technical and sanitary regulations relating to health services, has identified interest, primarily due to inquiries by the population and the regulated sector, about the possibility of releasing UCPB units, stored in autologous banks in Brazil, for the use of others, such as siblings or other relatives additional to the child donor.

Thus there is a need to encourage a systematic discussion on a possible modification of the legal parameters governing national UCPB banks for autologous use, making the HPC available for family use and also to estimate possible risks involved in this process. The inseparable reflection lies on an approach or comparison with the public entity, given the reciprocal consequences that government and private services encourage or restrict each other. Thus, this study addresses key legal, technical and safety criteria to regulate UCPB banks in the setting of current therapy and research involving multiple sources of HPC and the bioethical principles and other matters relevant to this subject.

Legal, technical and safety criteria

The Anvisa Resolution No. 153/2004 (issued by the Board of Directors), in force at the time of this analysis,^a deals with donor selection and the collection, transportation and processing, storage, release, and disposal of cells, and records, operations and quality control of UCPB banks⁽¹⁰⁾ according to the required biosafety standards and aims to minimize risks to patients, staff and the environment. It also determines that the services are licensed to operate or have a sanitary license issued by the local health department. According to the aforementioned ruling, strict sanitary technical criteria have been established for the collection and storage of UCPB for unrelated allogeneic use, including no hereditary diseases of the hematopoietic system, degenerative neurological diseases, metabolic diseases or other genetically related diseases in the family history; a minimum amount of cells, and absence of positive results in microbiological and serological tests.

The collection and storage of UCPB for related allogeneic use should be performed after strict assessment of the risks and benefits involved in the use of the collected cells in respect to the importance of their therapeutic properties and the difficulty to find a compatible donor for the patient.⁽¹⁰⁾ The established storage criteria for related use are, thus, differentiated and susceptible to derogation in regards to the minimum number of cells obtained and the microbiological safety (bacteria and fungi) of the material. In banks for autologous use, storage of serologically positive units is acceptable, however the minimum requirements of quality for this type of storage must be maintained, such as the minimum concentration of cells and absence of positive microbiological tests.⁽¹⁰⁾

It is important to bear in mind the correlation between the defined and regulated technical and sanitary criteria for the collection and storage of HPC from UCPB, the intended use, whether for the donor's personal use or for others, as well as the storage time. Following this reasoning, the criteria of directed donation intended for 1) patients diagnosed with a pathology which justifies the real and imminent use of these cells to promote, protect and restore the patient's health and at the same time consider the risk to the life of the patient due to the disease and 2) families with increased and proven risk of diseases treatable by HPC transplantation. The collection criteria for unrelated allogeneic and autologous use are based on, among other things, the current therapeutic indications of HPC and on storage for an indefinite period of time until use, which may never occur.

Several documents guide the creation of banks and the use of UCPB cells at an international level (Table 1). In general, international regulations are more wide ranging, with high amplitude and low specificity, whereas national documents seek to achieve social, cultural, economic and, possible local contexts, are more detailed.

¹ Brazilian National Health Surveillance Agency (Anvisa)

Note: In standing Anvisa Resolution No. 153/2004 being reviewed at the time of publication of this review article, emphasizes the importance of this. Changes and technical-sanitary updates should be consulted in respect to future resolutions/Anvisa.

In most countries there is respect for private initiative and freedom of choice of each citizen, and so an outright ban of these banks is not suggested. This is in spite of the extremely low probability that UCPB units stored in private banks will be used in the light of current scientific knowledge mainly because the therapeutic indications for use in autologous transplants are extremely limited and due to inherent characteristics of the autologous cells and the UCPB unit^(4,12-15) in addition to the lack of empirical evidence

and uncertainty about the safety and effectiveness of their use.^{6,16} In Italy, private services are prohibited and in France they do not exist although there is no legislation that explicitly prohibits them.^(4,12,17) Argentina recently determined that all units stored in private banks in the country should also be linked to the National HPC Register.⁽¹⁸⁾ Other countries, such as Belgium and Australia, have stated their desire to prevent and even prohibit the creation of banks for commercial purposes, and thus veto

Table 1 - Key documents that guide the establishment of umbilical cord blood and placental banks and the use of Hematopoietic Progenitor Cells

Type of the Document	Title	Year
Legislation		
21 CFR Parts 16, 1270 1271	Current Good Tissue Practice for Human Cells, Tissues, and Cellular and Tissue-Based Product Establishments. FDA. Estados Unidos	2004
Directive 2004/23/EC	On setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells (of The European Parliament and of The Council)	2004
Directive 2006/17/EC	Implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells	2006
Real Decreto 1301/2006	Establecen las normas de calidad y seguridad para la donación, la obtención, la evaluación, el procesamiento, la preservación, el almacenamiento y la distribución de células y tejidos humanos y se aprueban las normas de coordinación y funcionamiento para su uso en humanos. Espanha	2006
Ordinanza del Ministero del Lavoro, della Salute e delle Politiche Sociali	Disposizioni in materia di conservazione di cellule staminali da sangue del cordone ombelicale. Italia	2009
Resolución INCUCAI n.069-09	Normas para la actividad de captación, colecta, procesamiento, almacenamiento y distribución de Células Progenitoras Hematopoyéticas provenientes de la sangre de cordón umbilical y de la placenta para uso autólogo eventual. Ministerio de la Salud. Argentina	2009
Recommendations		
Rec(98)2	Of the Committee of Ministers to member states on provision of haematopoietic progenitor cells (adopted by the Committee of Ministers of the Council of Europe)	1998
Rec(2004)8	Of the Committee of Ministers to member states on autologous cord blood banks and explanatory memorandum. (adopted by the Committee of Ministers of the Council of Europe)	2004
INCUCAI	Recomendación del Comité de Bioética sobre Banco de Células Progenitoras Hematopoyéticas con fines comerciales. Argentina	2005
Standards/Guidelines		
NMDP	National Marrow Donor Program. 19 th Edition Standards	2004
AABB	Cell Therapy and Cellular Product Transplantation. AABB Technica Manual Chapter 25	2005
WHO	Key safety requirements for essential minimally processed human cells and tissues for transplantation	2006
Council of Europe	Guide to safety and quality assurance for the transplantation of organs, tissues and cells - 3 rd ed.	2006
Standards/Accreditation Programs		
AABB	Standards for Cellular Therapy Product Services	2005
JACIE	Standards for Haematopoietic Progenitor Cell Collection, Processing & Transplantation 2 nd ed. adapted	2005
FACT / NETCORD	International Standards for cord blood collection, processing, testing, banking, selection and release. 3 rd ed.	2006

the advertising of any services offered, with the justification that "there is no proven use and such cord blood is unlikely to be used".⁽¹⁹⁾

A similar opinion has been stated by the World Health Organization and the Council of Europe to indicate that cord blood use in an autologous context is generally not recommendable.^(20,21)

Types of umbilical cord and placental blood donations: costs and opinions

Epidemiological data show the difficulties to find a compatible donor for a recipient in a timely manner. Overall, this chance is 25% within the family; outside the family this chance drops considerably and search success depends on donor records and a well-established selection of the genetic diversity of different races.^(22,23)

According to the world's largest database of potential HPC donors, Bone Marrow Donors Worldwide (BMDW), there are around 400,000 units of UCPB HPC stored in government banks around the world and available for transplantation as in December 2009 (www.bmdw.org/index.php?id=statistics_cordblood), while the global network of cord blood banks, NetCord, said that more than 8,500 unrelated allogeneic transplants are performed using HPC UCPB stored in government banks (www.netcord.org/inventory.html). On the other hand, there are few published reports of autologous use.⁽²⁴⁻²⁷⁾ Several papers have reported the successful use of UCPB cells in directed donation programs^(7,28,29) although international data on the number of such transplants are not available. Table 2 shows the possibilities of donating UCPB in Brazil and the costs to donor families. The opinions of researchers, health institutions and governmental and non-governmental organizations on the types of donation outlined, are unanimous in respect to the following and this should be carefully considered in the discussion proposed by this study:^(5-7,19,29-36)

1) Voluntary and altruistic donation is an act of clear benefit since it may be the only treatment option available to save the life of a patient with an incurable illness. If banks are established, they must be based on such gifts, and as public services, in particular, they should provide citizens with clinically proven and cost effective therapies as financial resources are limited;

2) Directed donation, by medical indication, is similar to altruistic donation and duly supported by the need of imminent use and is thus restricted to targeted populations. The costs borne by the public authorities associated with the collection, processing and storage of UCPB units are reasonable and comparable to other medical interventions;²⁸ the benefits to patients outweigh the investments involved;⁽³⁷⁾

3) the use of private autologous as well as directed donations in low-risk families are not offered by public services because they do not involve imminent use or an increased likelihood of future need and there is no scientifically proven basis at present to justify storage for autologous use;

4) Since both government and private banks are established, accurate, easily accessible and understandable information should be conveyed to the public explaining: a) the current indications and purpose of each service, b) the possible future uses of UCPB cells, as well as other sources of HPC in regenerative therapies and c) the research needed before this goal is achieved.

Characteristics of umbilical cord and placental blood hematopoietic progenitor cells

HPC, the most common type of adult stem cells isolated from UCPB, bone marrow and peripheral blood after mobilization with growth factors - have different properties. These properties influence the indication or restriction for use in the treatment of different diseases.⁽³⁸⁻⁴⁰⁾ Table 3

Table 2. Options for donating umbilical cord blood and placental blood in Brazil and the costs for the donor family

Type	proposal	Cost
Altruistic, voluntary donation or public	The donated unit will be available for use by a patient who needs in the general populationl	No cost
Directed donation by medical indication	Storage for families who already have one member, usually sibling, with diagnosed disease and in need of hematopoietic progenitor cells transplant as treatment	Typically provided by transplant centers at no cost, the storage may also occur in blood therapy services or government umbilical cord blood banks; private banks may pass the cost to the family ^a
Storage for private autologous use in low-risk family	Use of the newborn in family without prior indications that suggest preventive need of stored cells	Initial cost R\$3,000 to R\$4,500 Annual cost around R\$500

^aThe transplant centers, both government and private, must be duly licensed by the competent Health Surveillance Organ and authorized by the General Coordination of the National Transplant System of the Ministry of Health (CGSNT/MS)

highlights the main advantages and disadvantages of using UCPB HPC transplants, compared to the use of bone marrow cells.⁽⁴¹⁻⁴⁵⁾ Apart from the particularities inherent to HPC, there are other factors that can have repercussions on the success or relapse of the transplant which include: age and body weight, disease and risk group related to the malignancy, genetic origin or not of disease and biological characteristics of the underlying disease, stage of remission and prior treatment.⁽⁴⁶⁻⁴⁸⁾

Thus, on contextualizing the characteristics of each patient in relation to the type of disease and the availability of donor/cells for treatment, a sample stored in an autologous bank may be inconvenient; it may be preferable to opt for treatment with cells of a related donor, when available, or unrelated, with the goal of having the benefits of the so-called "graft versus leukemia" effect and therefore a reduced likelihood of relapse, a result that is not obtained in autologous cell transplantations.^(41,42) Various aspects are subject to discussion, some of which are presented below.

Research and perspectives - an overview

HPC are being studied in respect to the repair of damaged organs and tissues in a field called regenerative medicine (www.stemcells.nih.gov/info/scireport/2006report.htm), mainly due to their plasticity – the ability to differentiate and contribute to the formation of different types of body tissues.⁽⁴⁹⁾ The treatment of neurodegenerative diseases such as Parkinson's, Alzheimer's and even spinal cord injuries are the main research areas⁽⁵⁰⁻⁵⁴⁾ together with treatment of strokes and autoimmune diseases such as lupus erythematosus, rheumatoid arthritis, multiple sclerosis and other diseases.⁽⁵⁵⁻⁵⁹⁾ In the area of tissue bioengineering, protocols involving the development of

skin, cartilage and bone cultures and the repair of muscles and organs such as the liver and pancreas have been developed.^(55,59-61) Other studies focus on the exploitation of other cell populations to HPC present in bone marrow and UCPB including mesenchymal precursor cells and endothelial cells, for example, for *in vitro* differentiation into osteoblasts, chondrocytes and adipocytes and in angiogenic therapy,⁽⁶²⁻⁶⁷⁾ and the development of induced pluripotent stem cells (iPSC) – reprogrammed adult stem cells engineered to have characteristics of embryonic cells (pluripotency), which promise to represent an ideal source of cells for future regenerative therapies in both autologous and allogeneic transplants.⁽⁶⁸⁻⁷⁰⁾

The Federal Government of Brazil, through the Ministries of Health, and Science and Technology, has been financing, since 2005, the Multicenter Randomized Study on Cell Therapy in Heart Disease.⁽⁷¹⁾ This study has shown that satisfactory results are achieved with improvement in cardiac function and quality of life as had already been suggested by isolated studies.⁽⁵⁵⁾ In the same year, the funding of 41 basic, preclinical and clinical research projects related to the development of therapeutic procedures using bone marrow and cord blood HPC and embryonic stem cells was also approved.^(72,73)

As can be seen in the wide range of research reported most studies are still at an early stage and are being developed in animal models. Of the research using HPC in humans, most is being developed with cells from the patient's own bone marrow, collected at an appropriate time, in sufficient quantity and with adequate cell viability (and other desired characteristics); much research uses allogeneic cells – with the possibility, in this case, of using cell units from government UCPB banks; research using other sources of adult stem cells (skeletal muscle, liver, pancreas, cornea, brain, dental pulp, adipose tissue and

Table 3. Advantages and disadvantages of the use of Hematopoietic Progenitor Cells (HPC) from umbilical cord and placental blood in transplants compared to the use of bone marrow cells

Advantages	Disadvantages
Less restrictions in HLA compatibility and, consequently, lower rejection;	Small volume of material available for collection and, consequently, limited number of cells, generally insufficient to treat an adult or even big child;
Possibility of use of one or more cells of donors with different HLA antigens;	Increased risk of genetic disease transmission;
HPC in more primitive state of development, resulting in a higher proliferative potential;	Delayed kinetics in respect to engraftment;
Lower incidence and severity of chronic graft-versus-host-disease;	Impossible to collect more donor cells in cases of engraftment failure or disease recurrence;
Lower incidence of viral transmission;	High storage costs.
Readily availability with no donation refusal;	
Material more easily collected.	

salivary glands),^(39,49) are ongoing and, similar to research involving HPC are also promising regarding their future use in the cure of diseases and injuries.

In fact, the findings suggest that cell therapy will be the medicine of the future. However, there are important questions that still need to be answered for researchers to gain a full understanding of the mechanisms by which cells provide the benefits that are presented clinically: 1) which cell lines are important for tissue repair and what is the best source;⁽⁷⁴⁾ 2) in what quantities and which are the soluble factors involved in the recruitment and cell differentiation processes of tissues that need to be repaired; 3) what (is/are) the mechanism(s) for the regeneration of damaged tissue and 4) what is the proliferation capacity of each cell type and the tissue regeneration capacity and *in vitro* methods for cell expansion.^(32,75,76)

It is important to stress that expectations involved with cell therapies and regenerative medicine should be viewed with caution due to the panacea inculcated about stem cells. Scientists state that, until all the issues presented are not elucidated, the proposal of regenerative medicine to cure different tissues is restricted to the realm of hope.⁽⁷⁷⁾ And the possibility of cancer after this type of treatment can not be discarded.

Bioethics

In the context of bioethics, UCPB storage has been characterized as an "emerging situation",^(12,19,22,78) that is, related to a theme that recently appeared associated to issues that involve the individual's health coupled to technical and scientific progress in medicine and human rights, culminating in controversy and opinions about fundamental ethical principles.⁽⁷⁹⁾ In general, these issues are associated to the four pillars of principlist ethics – autonomy, beneficence, nonmaleficence and justice – which today are extended to other characteristics – protection, caution, solidarity, vulnerability, utilitarianism, the principle of proportionality, and individual and public responsibilities.⁽⁸⁰⁾ Starting from this conceptual expansion with the approval of the Universal Declaration on Bioethics and Human Rights of UNESCO in 2005 (www.bioetica.catedraunesco.unb.br), bioethics was established for evaluations and articulation of policy related to public health and social fields.⁽⁸⁰⁾

In addition to the bioethical principles, it is important to pay attention to the issue of property rights of this valuable material.⁽⁸¹⁾ Who holds the rights: the baby, who donated it, who, until coming of age, is represented by the parents or the State as a fundamental part of the mechanism of transplantation and the institution that defines health policy for the benefit of all needy citizens?⁽⁸²⁾ Here, one must remember that in the Constitution of 1988, art. 196. "Health is the right of everyone and the duty of the state to guarantee

through social and economic policies aimed at reducing the risk of disease and other health problems and the universal and equal access to programs and services for its promotion, protection and recovery" (www.planalto.gov.br).

On considering the right of ownership of UCPB in respect to the principlist theory, one study in particular held an interesting debate both from legal and philosophical points of view.⁽³⁷⁾ It was argued in this study that the principles of justice and equity should be formulated so that: unequal property rights are justifiable provided that all persons have a minimum possession and the inequalities do not harm one entire life in society. In addition, it was conjectured that property rights should maximize the usefulness and efficiency related to the use, possession, transfer of material and so on. In consequence, assuming a low probability of future use of the UCPB by the newborn donor together with the fact that the necessity of future use is virtually impossible to predict at birth, a plausible situation is that the parents or guardian would choose to donate the blood to a sibling who needs the cells or to a government UCPB bank. This study concluded that the bioethical issues related to the storage of such material can be solved, generally by utilitarianism.

On the other hand, the right of ownership of the UCPB is not absolute, but limited. For example, it is possible to exclude others from using the cells, but this does not imply that one has the right to sell or receive any other income from its use. In Brazil the Law nº 10.205/2001, art. 14, Chapter II prohibits payment for the donation of blood or commercialization of its collection, processing, storage and distribution. Only payment of the costs of the materials used such as reagents and disposable materials used in the collection, processing and storage procedures and the labor costs, including medical fees are allowed.⁽⁸³⁾ Therefore, at first glance, marketing for profit presents little danger. Yet there are indications about the high profitability of services offering private storage of UCPB.⁽⁸⁴⁻⁸⁷⁾ This is described in some reports, widely circulated in the media, which mention the objectives and investments already made in this area, as well as the expected financial returns (available at noticias.uol.com.br/ultnot/efe/2007/02/01/ult1766u20029.jhtm; oglobo.globo.com/ciencia/mat/2007/01/26/287569409.asp; brasil.business-opportunities.biz/2006/12/04/franquiamexicana-busca-negocios-no-brasil/).

From the point of view of fairness and equity, there is discussion of other ethical issues: the existence of an unjust socioeconomic distance between those who can and those who can not pay for storage services of autologous UCPB.⁽²²⁾

The limitation of property rights also influences the definition of government policies. For example, it is not lawful for a government to determine the use of biological material needed by anyone without the proper consent of a parent or guardian through the signing of a consent form, a legal

doctrine with ethical basis that guarantees individual autonomy.⁽⁸⁸⁾

When conceptualizing autonomy, some theories state that, for an action to be autonomous, it is necessary that the person has a full understanding without being coerced.^(89,90) However, regarding several emerging situations, full knowledge becomes relative in the scope of scientific development. In this case, we assume that an autonomous action is one with a substantial degree of understanding and freedom from any coercion and that, at the same time, it is exercised responsibly, limited by respect for the dignity and freedom of others.⁽⁸⁸⁾ This means that the responsibility that each individual has for himself is not independent of what he should have for others, thus identifying the principle of solidarity with the inversion of individual values for collective values being the rule of thumb.⁽²²⁾

Advertising campaigns conducted by private UCPB banks are seen as a threat to individual autonomy because of the understanding they cause and the moment of probable vulnerability to which they are projected. Authors state that overall, the messages used consist of an exciting and persuasive speech to say that stockpiles of these services represent "real life insurance" or "biological insurance" in case the donor develops a serious illness during childhood or adulthood, and that the birth is the only moment that such material can be collected.^(35,91) The messages also suggest that "will" be able to use because of the discoveries of regenerative medicine in vogue in recent years⁴ thus interpreting the results of basic research and extrapolating them, often with excessive optimism, for their use in humans.^(30,33)

The advertisements, moreover, often fail to distinguish between the indications for allogeneic use and indications for autologous use, as well as to inform parents that in the cases of autologous transplantation or other treatments, these cells can be obtained from the bone marrow or peripheral blood of the patient after mobilization using growth factors, procedures that are already routinely being carried out. The fact is that doctors, employees and consultants of private UCPB banks may have potential conflicts of interest in the recruitment of customers due to their own financial gain;⁽⁹¹⁾ and parents tend to do everything possible for their child's good, and even blame themselves in cases of not doing so⁽⁵⁾ – see the testimonials of parents in the advertising material and sites of private UCPB banks – which possibly includes the acquisition of services based on promises offered by scientific advances and motivated by the ideology of consumption to be addressed later in this study.

Context of risk

The Brazilian National Health Surveillance System (SNVS) has identified, as part of its basic responsibilities for

decision making, the incorporation of the concept of risk and, specifically, to identify risks, whether in the production process, or when providing services and new technologies, or in the consumption process.⁽⁹²⁻⁹⁴⁾ In sequence it considers risk management with political and administrative guidance. At this point, reference is made to the State's regulatory role, to ensure the right of everyone to health and the common or public good and can even "intervene in the individual's activities when they prove against, inconvenient or harmful to those interests".⁽⁹⁵⁾

From the standpoint of autologous UCPB banks, changes in technical and health criteria that allow the release of stored units for family use can be considered interesting. The processes will need to be adjusted, primarily, to check other characteristics required in the storage of units for related allogeneic use, as listed in Table 4. Here, important questions should be asked in respect to storage units for directed donation: 1) what is the minimum number of cells that will be stored? 2) Is there a minimum which impedes storage as is established in the storage of UCPB for autologous use? 3) Will the amount of viable cells present in the unit be sufficient for any treatment, after the freezing process and storage for decades and then thawing? 4) Which microbial contaminants are allowed without causing harm to the possibly immunosuppressed recipient and in what concentrations would they be allowed? 5) Will the presence of these contaminants change the cell biology and expansion, commissioning and differentiation characteristics in various lineages?

We can identify some of these issues today compounding doubts concerning the storage and use by relatives without answers to these questions. And even so such use is not imperatively prevented. You can then, on the other hand, given the doubts expressed, suggest that the criteria remain the same as those for the storage of UCPB for autologous use (e.g. minimum number of cells and absence of microbiological contamination, etc.) and only then would the private banks be given a permit to supply units for family use. This decision would create different measures for the same purpose: storage criteria for family use in government versus storage criteria for family use in private UCPB banks, which, from legal and technical standpoints is not permissible and even less justifiable.

Considering the expansion of services offered by private banks, one can imagine that this may lead to more advertising of these services with consequent increase in demand and a reduction in potential donors for government banks. However, on analyzing this question less emotionally, it appears that it becomes questionable from the structuring point of view of advertising campaigns of the BrasilCord network,⁽¹¹⁾ which should focus on underrepresented populations in order to optimize financial resources. This means that, as the network of government UCPB banks become duly supplied with a large variety of human

Table 4. Technical-sanitary legal criteria (RDC / n.153/2004 ANVISA) for the donation of umbilical cord blood and placental tissue for non-related allogeneic use, using autologous and directed donation for use related

Criteria	Donation for non-related allogeneic use (BrasilCord)	Donation for autologous use (private banks)	Directed donation for use in relatives
Donor selection	- age between 18 and 36 years old - least two documented prenatal consultations - gestational age > 35 weeks	- gestational age > 32 weeks	- collection after indication by the physician responsible for patient care ^a
Delivery data	- membrane rupture < 18 hours - uneventful labor		
Exclusion criteria ^b	- fetal weight < 2000g - severe fetal distress - fetus with congenital abnormality - infection during labor - maternal temperature > 38°C during labor - infectious processes during pregnancy or diseases that might interfere with placental vitality - pregnant women taking hormones or drugs that are deposited in tissues - pregnant women with personal or family histories of autoimmune diseases, cancer, hereditary hematopoietic system diseases, among others - pregnant women at increased risk for transmitting blood-borne infections or with one or more positive results ^c - positive bacterial or fungal culture results	- severe fetal distress - infection during labor - maternal temperature > 38°C during labor - infectious processes during pregnancy or diseases that might interfere with placental vitality - positive bacterial or fungal culture results	- positive markers of HIV 1 and 2 or Hepatitis C infection
Quarantine	Unit is released after: - clinical reassessment of the newborn between 2 and 6 months of age - Repeat testing for markers of blood-borne infections ^c (maternal blood)		- units with < 5 x 10 ⁸ nucleated cells, other tests positive for blood-borne ^e infection markers e or positive bacterial or fungal culture results can be used ^a
Other laboratorial analyses	- minimum of 5 x 10 ⁸ nucleated cells - ABO / Rh - HLA antigens - toxoplasmosis serology - hemoglobin electrophoresis - CD34 ⁺ cell and CFU-GM counts - Cell viability	- tests for markers of blood-borne infections ^{c, d}	- ABO / Rh - HLA antigens - CD34 ⁺ cell count - hemoglobin electrophoresis

^a Joint decision between the services that collect and process the material, the patient's physician and the transplantation center; ^b The unit will not be collected if or should be discarded after the collection procedure if any of these criteria exist; ^c HIV 1 and 2, HTLV I and II, Syphilis, Chagas, Hepatitis B and C, CMV IgM; ^d If one or more results are positive, disposal should be considered in a joint decision with the mother; ^e HTLV I and II, Syphilis, Chagas, Hepatitis B, CMV IgM and Toxoplasmosis IgM

leukocyte antigens, including rare antigens, representative of the biodiversity of the country's ethnic population, any individual will have the chance of finding a compatible donor.

In analyzing the socioeconomic context, it is interesting to stress the characteristic of growing

consumption of modern societies, in which the ideology of consumption promotes the internalization of production impositions on individuals or the community, to "whittle down their freedom of choice and the real idea of 'quality', 'effectiveness' or even 'need' of what is being bought."⁽⁹⁵⁾ Consequently, if production, in this case the offer of a

health service, aims at, even though it is not explicitly stated, the needs of the capitalist production and profit system, many risks to the individual and collective health could be generated due to these processes. Even if no direct risks exist, then, serious "risks" to the consumer economy may emerge, given its vulnerability in the consumer market tied to the high investment required. This possibly may also involve the risk of disappointment, delusion and despair on needing a service based on scientific evidence and its promises.

Finally, in reference to the Precautionary Principle – restrictions in the use of a product, technology or implementation of a specific healthcare service until hard evidence is acquired regarding the characterization of risk,⁽⁹³⁾ many people claim, would result in the stagnation of Science. However, one must remember that the use of this principle also has in its concept authority to support decision making of socioeconomic order.⁽⁹⁶⁻⁹⁹⁾ "And, above all, to promote political responsibility at the highest level as it requires a competent assessment of the economic and social impact arising from the decision to act or to refrain from acting."⁽⁹⁷⁾

Conclusions

This study succinctly addressed the main arguments, data and opinions on this issue, outlining political questions, the basis for decision making according to health policies defined for this area. For this a thorough study of every aspect - technical, legal and ethical - and a real evaluation of the impact of each one were made.

In particular, a study on storage of autologous UCPB was emphatic when reporting that this material is wasted with the random storage by low-risk families. Directed donation is defended when there is medical indication. It also makes an analogy with the storage of blood: if blood therapy services decided to save blood for the exclusive use of the donor or his family, blood transfusions, as they are today, with the enormous power to save lives, would not be effective, resulting in obvious catastrophic consequences for many patients.⁽¹⁵⁾

As conclusions of this study, we highlight:

- from an advertising point of view, private UCPB banks are characterized as healthcare services; the supply of this type of service to the public should not be seen as totally harmless. Several problems may be associated with an unwarranted acquisition of this service involving social, emotional, psychological and financial questions;
- estimates of the need to use cells stored in private banks (random storage for low-risk families), added to the statistics on the use of these cells and bioethical issues, currently indicate there is no justification to implement these services or a demand for them;
- information that is clear, accurate, and easy to access and understand related to the purpose of each service, the current therapeutic indications, research and possible

future use of stem cells from different sources in therapies should be conveyed to the population with the objective of enabling individuals to arrive at a conclusion as to whether or not to store UCPB, either in government or private services, as well as a better understanding on the ownership of cells stored in private banks: does this imply there will be access to the necessary treatment when needed? or would not having cells stored in a private service exclude a patient from access to cell therapy and regenerative medicine in the future if and when the clinical use has been proven?

- the State has, as one of its responsibilities, to protect and preserve public health, a role that can not be neglected with the establishment of proper cost/benefit-risk as an essential process in decision making related to healthcare policies;⁽⁹⁷⁾
- in addition to quality, efficacy and safety of a healthcare service, access and cost must also be considered to limit the vulnerability attributed to socioeconomic differences and one should guarantee to society that public structures aimed at maintaining fair access to health services and compliance with the principles and guidelines of the Brazilian government healthcare system.⁽¹⁰⁰⁾

Resumo

Os bancos de sangue de cordão umbilical e placentário foram criados a partir da comprovação de que o sangue de cordão umbilical e placentário (SCUP) é uma fonte rica em células progenitoras hematopoéticas (CPH) e alternativa às células provenientes da medula óssea para transplante, fato que gerou o interesse pelo armazenamento das células nele contidas. A legislação brasileira distingue bancos para uso alogênico não aparentado (públicos) e para uso exclusivamente autólogo (privados). Por sua vez, o armazenamento de SCUP para uso familiar (doação dirigida) pode ser realizado em bancos de sangue de cordão umbilical e placentário públicos, serviços de hemoterapia ou centros de transplante, quando há um membro da família do nascituro com doença diagnosticada e que necessite de transplante de CPH como tratamento. Apesar de a legislação ser clara, a Anvisa tem identificado o interesse sobre a possibilidade da liberação de unidades de SCUP, armazenadas em bancos autólogos, para a utilização de outrem, familiar, além do recém-nascido beneficiário. O objetivo do trabalho visa promover a reflexão sobre uma possível modificação dos parâmetros legais nacionais que regem os bancos de SCUP autólogo, tornando-os bancos com vistas ao uso familiar, por meio da exposição dos principais elementos relacionados ao tema. O estudo analisou os critérios técnico-sanitários legais para regulamentação dos bancos; descreveu as características das CPH de diversas fontes e tipos de doação para transplante; contextualizou a relação com os princípios da Bioética; avanços sobre terapia e pesquisas relativas às CPH; e discutiu possíveis riscos envolvidos no processo. Rev. Bras. Hematol. Hemoter. 2010;32(4):317-328.

Palavras-chave: Cordão umbilical; Bioética; Legislação; células-tronco.

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