HTA
Human Tissue Authority

Cord blood banking: A guide for parents

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Contents

Introduction

Umbilical cord blood, commonly referred to as 'cord blood', is the blood that remains in the umbilical cord and placenta following childbirth. Cord blood can be used to treat and cure many life-threatening diseases (Gluckman 2011). Cord blood may be collected at the time of birth and stored, so that it is available for the potential future treatment of the child or another person.

The HTA's role in cord blood banking

Since 5 July 2008, the HTA has regulated the collection, testing, processing, storage, distribution, import and export of cord blood. In the UK these are 'licensable activities' and can only lawfully take place under an HTA licence. Further information on HTA licensing can be found here: https://www.hta.gov.uk/policies/licensing-under-quality-and-safety-regulations.

We have created this guide to help parents to make informed choices about cord blood banking. It has been developed through engagement with cord blood experts and centres on our 'Three key messages about cord blood banking'.

Three key messages about cord blood banking

1. CONSENT

In order for cord blood to be collected for banking, the mother must give her consent. The cord blood bank, or someone acting on its behalf under a formal legal agreement, must clearly explain the options, benefits and risks to the mother.

2. SAFETY

All 'licensable activities' must be carried out by properly trained professionals on appropriate premises in a way that minimises the risks to the mother, the child, or any patient receiving the cord blood unit.

3. QUALITY

All HTA-licensed cord blood banks must meet the HTA's minimum standards for quality. It is important to note that beyond, these minimum standards practices can vary between cord blood banks.

Cord blood banking options

The HTA licenses both public and private cord blood banks in the UK. This section explains the different types of cord blood banking. Further information, including HTA inspection reports, on all HTA licensed cord blood banks can be found by searching for the bank's name on our website here: https://www.hta.gov.uk/establishments.

Public cord blood banking

Donating cord blood to a public bank is an altruistic act, as donated cord blood is made available to treat or cure potential recipients worldwide. The HTA considers a public cord blood bank to be a bank that provides cord blood units for use to the medical community through established national and international registries listed on the BMDW database (www.bmdw.org). The BMDW expects participating registries to adhere to the Standards, Guidelines and Recommendations of the World Marrow Donor Association (http://www.wmda.info) and participating cord blood banks are expected to adhere to the NETCORD/FACT Standards or equivalent standards.

There are two public cord blood banks in the UK: the Anthony Nolan Cord Blood Bank and the NHS Cord Blood Bank. Each bank operates independently, but both use the same quality and safety standards set by the HTA and NetCord-FACT. The UK public banks, along with public banks in other countries, list their cord blood units on national and international registries. This is to ensure that publicly donated cord blood units are made available to recipients worldwide. Treating hospitals search the registries to find cord blood units for recipients.

Donation of cord blood to a public bank is free of charge and donors are not paid. Only women giving birth at certain hospitals where one of these public banks operates are able to donate cord blood publicly.

Private cord blood banking

Banking cord blood privately means that the cord blood is collected and stored for potential future treatments. Privately banked cord blood is intended to be used only for the donor or a member of the donor's family. Units of cord blood banked privately are not listed on national and international registries.

There are several HTA-licensed private cord blood banks in the UK. Private cord blood banking is paid for by the client, i.e. the family expecting a baby. It can cost in the region of £2,000 for 20 years of storage, although costs and payment options vary between private cord blood banks.

Generally, private cord blood banks use third party mobile collection services, staffed by someone trained to draw blood (a phlebotomist). This means that the collection of cord blood for private banking can take place at most UK hospitals.

Cord blood banking for a specific medical need

In very few cases, there may be a specific medical need to bank a child's cord blood. In these instances, a consulting physician may be able to arrange the collection and storage of the cord blood, free of charge through the NHS or Anthony Nolan's directed donations service. If you feel this could apply to your situation, please consult your physician.

How is cord blood used today?

Cord blood has been shown to contain 'stem cells'. Stem cells are immature cells that have the potential to develop into different cell types. There are various conditions for which a cord blood stem cell transplant may be used, and there are also many potential uses under investigation.

Disorders of the blood (including certain blood cancers and immune deficiencies), and inherited metabolic diseases are currently the only indications for which a cord blood stem cell transplant is generally accepted by the medical community as an established treatment (EBMT 2015 and Gluckman 2011). In some cases, a person's own cord blood may not be a suitable treatment for him or her, for example if certain malignancies or other genetic problems are present. In this guidance, when we talk about 'transplants' we mean these established treatments.

The quantity and quality of cells in units stored at a cord blood bank will differ, and these factors are influenced by natural variation in the cord blood itself and the way that the cord blood is collected, transported, processed and stored. Well-controlled procedures during all phases of cord blood banking are important to the success of a cord blood stem cell transplant.

For a cord blood unit to be used in a transplant, it must contain enough stem cells (Querol 2010). In some cases where a cord blood unit does not contain enough cells, cord blood units from two different donors may be combined to treat one patient. Both public and private cord blood banks in the UK set their own thresholds for the number of cells a cord blood unit must contain in order for it to be banked.

Public banks will store only cord blood units that are likely to contain enough cells for a transplant, because they aim to bank as many cord blood units as possible for use in established treatments.

Private cord blood banks will usually store the cord blood unit even if it does not contain enough cells for a transplant, because private cord blood banks store cord blood units for transplants, clinical trials and for 'potential future use' (i.e. for as yet unknown therapies that may be available in the future).

Private cord blood banking: Understanding your cord blood unit's potential

For anyone considering private cord blood banking, it is important to understand the potential for a cord blood unit.

Doctors select cord blood units to use for transplants based on quality measures such as the number of:

- cells (referred to as 'total nucleated cells' or 'TNCs') present in each unit, and
- stem cells (CD34+ cells) present in each unit.

Most private cord blood banks provide this information to you shortly after the cord blood unit is received into the bank. It is important to understand how these measurements determine the potential for the cord blood unit so that you can make the right decision for you about whether or not to bank cord blood with a private cord blood bank.

The table on the following page, '*How could privately banked cord blood be used?*', will help you to understand the how these measurements determine the potential uses for a cord blood unit. The table has been developed by the HTA with stem cell experts, including UK transplant centres, to help you make decisions about private cord blood banking and is not meant to be a guide for clinical decision making.

Measurement	Increasing number of cells →		
TNC count (The number of cells in a cord blood unit before freezing)	Fewer than 500 million ($<5 \times 10^8$)[A]	More than 500 million ($>5 \times 10^8$)	More than 1250 million ($>1.25 \times 10^9$)
CD34+ count (Total number of stem cells in a cord blood unit before freezing)	Fewer than 4 million ($<4 \times 10^6$)	More than 4 million ($>4 \times 10^6$)	More than 10 million ($>1 \times 10^7$)
Potential use for the cord blood[B]	May be unsuitable for transplant[C] but may be stored for potential use in clinical trials or future therapies	May be suitable for child[D] stem cell transplant	May be suitable for adult[E] stem cell transplant

Table: How could privately banked cord blood be used?

This table has been developed by the HTA with stem cell experts to give you an idea of how measurements like the number of TNCs and CD34+ cells in your cord blood can determine how privately banked cord blood could be used. We hope that this will help you to interpret information that may be provided to you by private stem cell banks about your cord blood.

A '5 x 10^8' is another way to write '500 million'. You may see numbers written this way on reports from the private cord blood bank.

B Stem cells used for established treatments discussed in this section are prescribed according to the weight of the recipient patient.

C 'Transplant' refers to transplantation for current established treatments as described in this guidance.

D Based on a recipient weight of greater than 20 Kg. For children weighing less than 20kg, appropriate cell numbers may be estimated based on weight using >2.5 x 10^7 TNC / kg and >2 x 10^5 CD34+ cells / kg.

E Based on a recipient weight of greater than 50 Kg. For adults weighing less than 50kg, appropriate cell numbers may be estimated based on weight using >2.5 x 10^7 TNC / kg and >2 x 10^5 CD34+ cells / kg

Key cord blood banking information

The following information explains some of the key information about cord blood banking, including:

- important quality considerations for cord blood banking; and
- common terminology that you may encounter when considering cord blood banking.

Key points about collection

Timely

Collection of cord blood involves clamping and removing the cord and placenta as usual, then draining the blood from the umbilical cord and placenta. Delayed umbilical cord clamping (not earlier than 1 minute after birth) is currently recommended by **NICE** and **WHO** to allow more blood to reach the baby and help prevent anaemia. Banks can still collect high quality units of cord blood following delayed clamping. However, it is important that the cord blood is drained as soon as possible following delayed clamping to maximise the potential volume

Clean

To minimise the risk of contamination, it is important that the collection area is clean and fit for purpose. It is also important that the collector cleans the cord itself using correct aseptic technique.

Trained professionals

To ensure the best quality collection, those collecting cord blood must be properly trained. Anyone collecting cord blood must act under the authority of an HTA licence.

Key points about transport

Time

Time in transit should be kept to a minimum. Increased time in transit is related to increased cell death and can result in poor quality cord blood units (Fry 2013 and Querol 2010). Cord blood units should be cryopreserved (frozen) as soon as possible after collection and certainly within 72 hours (NetCord-FACT 2013).

Temperature

Cord blood banks should ensure that cord blood units remain within validated parameters, which may include a defined temperature range that has been shown to maintain quality. Banks should use specific containers that have been demonstrated to maintain the appropriate temperatures and the integrity of the cord blood unit.

Key quality testing terms

Common methods for assessing the characteristics of a cord blood unit are explained here. You may encounter these terms when considering cord blood banking.

Microbiological contamination

There is a risk that microbiological contamination could occur during cord blood collection, despite appropriate precautions being taken. Contamination could prevent the cord blood unit from being used in a transplant. Screening the cord blood for microbiological contamination before it is cryopreserved provides valuable information to the doctors selecting the unit for transplantation.

Total nucleated cell count (TNC)

There are many different types of cells in a cord blood unit, including stem cells and other cells. TNC refers to the total number of nucleated cells in a cord blood unit. TNC does not give specific information about the number of stem cells present.

Viability

A cord blood unit, like the circulating blood, is expected to contain mainly living cells and some dead cells. An assessment of viability estimates the proportion of living cells in a cord blood unit.

CD34+ cell count

CD34 is a molecule present on the outside of some stem cells. Cells that have this 'marker' are often referred to as 'CD34-positive' (written as CD34+). The number of CD34+ cells is used to estimate the number of stem cells in a cord blood unit. The presence of a high number of CD34+ cells is one of several factors indicating a cord blood unit us suitable for transplantation.

Colony forming units (CFU)

For a cord blood unit to be useful, cells in a cord blood unit should be able to proliferate (increase in number) and differentiate (develop into different more mature cell types). A CFU assay is a way to assess the ability of the cells within the cord blood unit to proliferate and differentiate. Greater numbers of CFUs observed correspond to greater proliferative capacity of the cells in the cord blood unit. The different types of CFUs observed correspond to the potential of the cells in the unit to differentiate into those different cell types in the body. Some cord blood banks and transplant centres use CFU assays as part of their assessment of whether or not a cord blood unit can be used in a transplant.

Frequently asked questions

General

What is cord blood?
Cord blood is the blood found in the umbilical cord and placenta.

Why bank cord blood?
Like bone marrow, umbilical cord blood is a rich source of blood forming (haematopoietic) stem cells. The blood-forming stem cells from cord blood are potentially useful for treating diseases that require stem cell transplants.

What other tissues can be banked at private cord blood banks?
Some private tissue banks store umbilical cord tissue, dental pulp and adipose (fat) tissue to extract cells for potential future uses. There are currently no established medical uses for cells extracted from these types of tissue.

What donor eligibility criteria exist for cord blood donation?
There are mandatory screening and testing requirements for anyone who donates any kind of tissue or cells (Human Tissue (Quality and Safety for Human Application) Regulations 2007). As well as these, each cord blood bank may set its own eligibility criteria, and carry out its own additional tests.

I am considering going abroad for a stem cell treatment not offered in the UK. Where can I find advice on whether or not this is safe?
If you are considering travelling abroad for a treatment, you should first talk to a trusted medical practitioner, such as your GP or specialist, about the safety of unlicensed stem cell treatments or treatments only available overseas. Use caution with online searches and clinics that promise cures based on patient testimonials.

Consent

Who can consent to cord blood donation?
In all cases, consent for cord blood collection must come from the mother.

Who controls the use of the preserved cord blood stem cells?
If the cord blood has been given to a public cord blood bank then the public bank retains control. If the cord blood has been banked with a private bank then usually the parents retain legal control over the cord blood. In BOTH cases, the mother can withdraw her consent for donation / storage at any time. In some cases, legal

control of the cord blood unit may be transferred to the child when he or she reaches a specified age.

Collection

How is the cord blood collected?
The umbilical cord is clamped and cut in the same manner as it would be for normal delivery of the baby. Blood is then drawn from the umbilical cord into a cord blood collection bag. By law, anyone collecting cord blood must be appropriately trained and working under the authority of an HTA licence. The premises where the cord blood is collected must be risk assessed by a trained individual as fit for purpose and this assessment must be documented.

How soon after collection should the cord blood be stored?
For optimal viability it is recommend that the cord blood is stored as soon as possible following collection, and certainly within 72 hours. (NetCord-FACT 2013). Minimising time between the birth and cryopreservation (storage) is important to maintaining the quality of the cord blood unit.

Who is legally allowed to collect cord blood?
Since 5 July 2008, any person collecting cord blood must be acting under the authority of an HTA licence. The main responsibility for complying with HTA requirements lies with licensed establishments and organisations acting on their behalf. However, it is also important for parents to be familiar with this legal requirement so that they do not unknowingly allow collection by an unauthorised person. It would be unlawful for an unauthorised midwife or birthing partner to undertake the collection.

What happens to a cord blood unit that is collected unlawfully?
Licensed establishments are required to report all instances of unlawful cord blood collection to the HTA. Using an unauthorised person to collect cord blood may lead to contamination of the cord blood or inadequate collection. The HTA can require the disposal of any unlawfully collected cord blood.

Transport

What are the requirements for the transportation and storage of cord blood?
Cord blood banks should ensure that critical transport conditions such as temperature and time limits are defined, validated and maintained to preserve the

quality and safety of tissues and cells, and that only packaging and containers that have been validated as being fit for purpose are used.

Safety

Is the cord blood screened for infectious diseases?
By law, donors of umbilical cord blood (the mother) must be screened and tested for evidence of infection with certain transmissible diseases.

The donor screening process typically involves the mother answering a series of health and lifestyle questions, designed to determine which tests are needed. A sample of the mother's blood is then taken after the birth. Usually, this is at an appropriate time on the same day as the birth, but if that is not possible then the mother's blood sample must be taken for testing within seven days after she has given birth.

Certain tests are mandatory for all donors. Diseases that must be tested for include: Human Immunodeficiency Virus (HIV), Hepatitis viruses B and C (HBV, HCV) and Syphilis. In certain circumstances, other tests such as Human T-lymphotropic virus Type I (HTLV-I) testing may be required, depending on the information provided during the donor screening process.

After collection

What happens to the cord blood once it is collected?
After the cord blood is collected, it is sent to the cord blood bank for processing, quality control testing, and storage. Processing procedures, quality control tests and storage procedures can vary from bank to bank.

How do processing methods differ?
An unprocessed cord blood unit contains different components, including plasma, red blood cells, white blood cells and stem cells.

Cryopreservation of 'whole blood' refers to freezing and storing the cord blood unit without removing any red blood cells or plasma.

Red blood cells have been associated with harmful or fatal side effects if too many of them are used in a transplant (FACT Spring 2013). This means that some of the red blood cells need to be removed from the unit before it can be used in a transplant, and this can be done before or after cryopreservation. 'Red cell depletion' (also called 'red cell reduction') refers to the removal of most of the red blood cells before cryopreserving the cord blood unit. Units stored without red cell

depletion must be washed after they are thawed and before use in a transplant (FACT-JACIE Cellular Therapy Standards).

Plasma does not contain any stem cells. To reduce the space required for the storage of cord blood, plasma is removed before cryopreserving the unit, and this process is referred to as 'volume reduction'.

Are cord blood collections ever rejected?

Yes. Both public and private cord blood banks may choose not to store the cord blood unit based on their acceptance criteria for cord blood quality. Public cord blood banks in the UK operate strict acceptance criteria, so that they can maximise the number of high quality cord blood units that can be banked. Acceptance criteria vary between private cord blood banks, but it is rare for a private cord blood bank to reject a cord blood unit if the family wishes to continue storage. Some banks will not store cord blood units if the mother's blood tests positive for a disease such as HIV.

Where a privately banked cord blood unit has been identified as not meeting a bank's acceptance criteria, the reasons for this and any implications on the clinical usefulness of the cord blood should be discussed with the family. This will help the family to make an informed decision about continuing storage of the cord blood. If a bank decides to discontinue storage based on their own policies, the family is normally entitled to a full or partial refund according to the terms of the storage agreement.

In addition to storage for established transplant treatments, private cord blood banks market cord blood banking services for potential future uses, including clinical trials and stem cell therapies that have not yet been developed. Private cord blood banks should provide families with sound scientific and medical information to assist them in making informed choices about whether to store their cord blood for potential future uses yet to be investigated or proven.

Can rejected cord blood be used for research?

Cord blood rejected by a public or private cord blood bank can be used for research, but only if the mother has given her specific consent for this. Otherwise, the cord blood that is unsuitable for banking will be disposed of using normal hospital disposal procedures.

Storage

What is cryopreservation?
Cryopreservation refers to freezing and storing at low temperatures.

How long can cord blood be stored?
The absolute length of time for the successful storage of cord blood has not been determined. Under appropriate storage conditions, it may be possible to preserve the cells for many decades.

Uses of stored cord blood

Will public cord blood only be used in the UK?
No. It can be used worldwide. Once the cord blood unit has been frozen, it will be stored until required. By consenting to bank your cord blood publicly, you are agreeing to its being registered on national and international databases such as the British Bone Marrow Registry, Bone Marrow Donors Worldwide and the European Marrow Donor Information System (EMDIS). Organisations worldwide can search these databases to find a suitable match for a patient who needs a stem cell transplant.

Are there any limitations associated with the use of cord blood?
Yes. The quantity and the characteristics of cells in the cord blood unit influence how the cord blood unit may be used. For example, a transplant containing too few stem cells may fail.

How likely is it that my child would need to use their stored cord blood?
Some private cord blood banks provide statistics to illustrate the likelihood that an individual will need to use their banked cord blood. However, estimates of the probability of an individual needing a stem cell transplant tend to vary according to the source and are based on uncertain assumptions. The estimates cannot be directly translated into the likelihood of an individual using their own cord blood unit since this would also depend on other factors such as the number of stem cells within the unit, the quality of the cells and the availability of alternative sources of stem cells such as peripheral blood stem cells (Pasquini 2005).

Is cord blood the only source of stem cells?
Although cord blood storage is a unique opportunity to preserve the stem cells within cord blood, it is not an individual's only opportunity to access their own stem cells since peripheral blood stem cells and bone marrow stem cells may also

be available. Stem cell technologies are developing rapidly, and it is likely that there will be future developments that will find new uses for stem cells. It is, however, by no means certain that these uses will rely entirely on individuals having their own cord blood stored

How successful are cord blood transplants?

The HTA is not able to give advice about the effectiveness of treatments using cord blood.

Feedback

At the HTA we want to make sure that the information we provide to the public and those we regulate is relevant, useful, and up to date. We would greatly appreciate it if you would help us to achieve this by giving us your feedback on this guidance here: enquiries@hta.gov.uk.

Resources and references

http://www.closerlookatstemcells.org/

http://www.macmillan.org.uk/information-and-support/treating/stem-cell-and-bone-marrow-transplants

Bone Marrow Donors Worldwide (BMDW). http://www.bmdw.org/index.php?id=97.

European Society for Blood and Marrow Transplantation (EBMT) 2014 Annual Report (2015) https://www.ebmt.org/Contents/Resources/Library/Annualreport/Documents/Forms/AllItems.aspx

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