



# PROGENICS CRYOBANK

## *Startup Checklist*

### Registration

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- **HOW SOON SHOULD I REGISTER WITH PROGENICS?**

We recommend that our clients register at least TWO months before their expected due date. In certain circumstances you can still register with Progenics as long as there is enough time to deliver a collection kit to you before you give birth to your baby. Simply call Progenics' office for further details regarding the registration process.

- **WHAT SHOULD I DO AFTER REGISTERING WITH PROGENICS?**

- ✓ Pick up a collection kit at Progenics or, if you prefer, a collection kit will be shipped to your home or work once your online registration, over the phone, emailed, mailed or faxed registration is approved. It takes 1-2 business days to courier the kit to you. Normally, there is no charge for shipping a kit.
- ✓ If a kit is shipped to you, open the outer brown cardboard box and take out either the white collection kit or the blue collection kit. The type of kit you receive depends on how the kit will be shipped back to Progenics after the cord blood or cord blood and cord tissue are collected.
- ✓ After you open the brown cardboard box, take out the envelope and read the "Instructions for Parents". Keep the cord blood collection kit (either the white box or blue case) at room temperature (15° to 25°C) and do not freeze or overheat the kit.
- ✓ Bring the cord blood collection kit to your delivery hospital and give it to your attending labour nurse when you are admitted to the Labour and Delivery Ward (or Birthing Unit). Remember to take the kit out of your luggage if you have placed it inside. With the exception of clients delivering at North York General Hospital, call the designated medical courier when you are admitted to the hospital so that they can have a courier on standby to pick up the cord blood.

**Note:**

If you forget to bring your collection kit to the hospital, please ask your nurse or physician to use an emergency kit (only if your delivery hospital is North York General Hospital or hospitals which have our emergency supplies). For other hospitals in which emergency supplies are not available, please call the designated medical courier at 1-866-882-8865 to request that they deliver a collection kit to you if they can. On short

notice, it is not guaranteed that they will be able to ship the collection kit to you in time before you give birth, and a fee could be charged. Contact us to find out if your hospital carries our Progenics Emergency Kits.

### Cord Blood Shipping

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- **HOW WILL CORD BLOOD BE SHIPPED TO PROGENICS AND HOW MUCH WILL SHIPPING COST?**

If your delivery hospital is located in the Greater Toronto Area (GTA), it is complimentary to have your baby's cord blood picked up at the bedside.

For locations outside the GTA, Progenics will pay a portion of the courier fees in order to make it more affordable for our clients to choose the highest level of courier service (next flight out) provided by the designated medical courier.

- **HOW DO I KNOW IF THE CORD BLOOD HAS BEEN RECEIVED BY PROGENICS?**  
You will be notified by our office as soon as the cord blood is received and processed.

### Cord Blood Collection

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- **WHAT IS CORD BLOOD?**

After a baby is delivered, the umbilical cord is clamped and cut close to the baby's "belly button". Fetal blood, also known as "cord blood", is left in the remaining umbilical cord that is still attached to the placenta. This "leftover" blood was traditionally discarded with the placenta as biomedical waste. However, scientists have discovered that cord blood is very rich in special kinds of cells called Hematopoietic (blood-forming) Stem Cells (HSCs). It also contains unrestricted somatic stem cells (USSC), mesenchymal stem cells (MSC) and endothelial progenitor cells (EP), which are important stem cells that can differentiate into almost all types of specialized, mature cells.

- **WHAT ARE HEMATOPOIETIC STEM CELLS (HSC)?**

HSCs are multipotent cells that have the ability to replicate and differentiate into the components of the blood and immune system. Every day, HSCs produce billions of red blood cells, white blood cells, and platelets that are essential for our health. The three sources of hematopoietic (blood-forming) stem cells that are routinely used for medical treatments are:

- Bone marrow
- Peripheral (circulating) blood
- Umbilical cord blood

- **WHAT TESTS WILL BE PERFORMED TO ASSESS THE SUITABILITY OF MY BABY'S CORD BLOOD FOR BANKING?**

Suitability of a cord blood donor is assessed based on Health Canada regulatory requirements and other accredited standards. Suitability of cord blood donors is screened by our trained clinical staff. Testing for infectious disease markers in maternal blood strictly adheres to Health Canada regulations, so the cord blood stored at Progenics is safe and can be used anywhere in the world. The tests include:

- Hepatitis B surface antigen (HBsAg)
- Hepatitis B core antibody (anti-HBc)
- Hepatitis C virus antibody (anti-HCV)
- HIV-1 and HIV-2 antibody (anti-HIV-1 and anti-HIV-2)
- HTLV-I and HTLV-II antibody (anti-HTLV-I and anti-HTLV-II)
- Serologic test for syphilis
- Nucleic acid amplification testing (NAT) for HIV-1 and HCV
- NAT for West Nile Virus (WNV)
- Cytomegalovirus (CMV)

- **WHEN SHOULD CORD BLOOD BE PROCESSED AFTER COLLECTION?**

Cord blood should be processed within 43 hours after collection. However, the faster processing begins, the higher the quality of the cord blood.

**Note:**

Acceptable time frames between collection and processing are defined differently depending on the bank. Usually, 43 hours after collection is the limit for most cord blood banks but a shorter transit time of  $\leq 24 - 36$  hours before processing is preferred.

At Progenics, the average time between collection and processing is 17 hours, which could be the shortest time frame in this field. If a cord blood unit is received after 48 hours from the time of collection, then the viability will be assessed to determine whether the cord blood is still eligible for processing and storage.

- **HOW IS CORD BLOOD PROCESSED?**

Volume reduction is often used as the routine processing depletion approach for cord blood. Cord blood volume is reduced by depleting the volume of red blood cells (RBCs) and plasma to obtain a final product that contained the remaining nucleated cells which include the stem cells that will be cryopreserved and stored in the liquid nitrogen vapour phase.

It is important for you to know the percentage of total nucleated cells after processing the cord blood unit collected by your healthcare provider.

### **WHAT IS THE YIELD OF TOTAL NUCLEATED CELLS?**

The percentage yield of TNC indicates the processing quality for each sample and the yield of the number of TNC per millilitre represents the processing quality of a cord blood bank. Therefore, the accuracy of percentage yield must be supported by the yield per millilitre. At Progenics, the average yield (%) and the yield per millilitre are determined on all cord blood units that are banked at our facility. This distinguishes Progenics' results from claims made by most other cord blood banks. In addition, our quality has been published in a peer-reviewed journal (Yang H et al, Transfusion (2011) 51;284-292).

$$\text{Yield (\%)} = \frac{\text{Number of TNC extracted from processing for banking}}{\text{Total number of TNC before processing}} \times 100$$

This formula can be applied to indicate processing quality regardless of processing methods! Simply put, higher yield equals higher quality. However, it should also be supported by the yield of cells per milliliter are determined from processing.

- **WHY IS THE YIELD OF TOTAL NUCLEATED CELLS FROM PROCESSING IMPORTANT BUT NOT THE YIELD OF STEM CELLS?**

***Feasibility and Accuracy!***

Almost no private cord blood bank (banks that store cord blood for families) are able to provide the recovery rate (yield) of CD34<sup>+</sup> cells (CD34<sup>+</sup> is a stem cell marker) to each family, since it is not practical to perform a CD34<sup>+</sup> cell count both before and after processing due to higher cost and the waste of valuable cells for the test (reduction in the number of cells available for transplantation). Progenics performs a CD34<sup>+</sup> count and viability assessment on all cord blood samples after they are processed.

**Note:** The number of total nucleated cells (TNC) is the most reliable indicator for a successful transplant (Moroff G et al. Transplantation and Cellular Engineering (46) 507-515, 2006).

- **DOES DOUBLE STEM CELL EXTRACTION PROCESSING INJURE MORE CELLS THAN THE CONVENTIONAL PROCESSING TECHNIQUE?**

Absolutely not. In fact, the viability of nucleated cells after processing is slightly higher (5% higher). The following published scientific and medical articles are available for your reference on the matter:

- (Solves et al., Cytotherapy (2009) Vol. 11, No 8, 1101-1107)
- (Yang H et al. Factors affecting banking quality of umbilical cord blood for transplantation. Transfusion (2011) Vol.51, 284-292)
- (Pope B. et al Transfusion (2012) Nearly all Stem cells (CD34<sup>+</sup> cells) survive processing (99.43%).

- **HOW DO I KNOW IF THE CORD BLOOD HAS BEEN SUCCESSFULLY PROCESSED?**

At Progenics, the success of processing cord blood is based on the yield of TNC, which is  $\geq 85\%$ .

Progenics will send you a “Certificate of Cryopreservation” which reports the processing date, volume collected yield (recovery rate) of total nucleated cells (%) and the number of total nucleated cells.

If the cord blood volume is  $\geq 10\text{mL}$  (minimum processing volume), you will receive the Certificate of Cryopreservation after Progenics has obtained all of the results for both the maternal viral marker blood tests and the cord blood microbiological tests. If the cord blood volume is below 10 mL, as per your request in the consent and agreement you completed at registration, we will either proceed with processing regardless of the volume of contact you and provide you with information about the cord blood prior to processing it. A 50% discount on the annual storage fee for 20 years is honored for all cord blood units that are  $< 20\text{mL}$ .

The certificate with processing results and the quality guarantee confirms the successful processing and storage of your child’s cord blood.

- **HOW IS CORD BLOOD CRYOPRESERVED?**

Basically, the cryopreservation procedure includes the addition of a 10% Dimethyl Sulfoxide (DMSO) solution with an optimal cooling rate using a controlled-rate freezer.

Almost no cells can survive freezing without an optimal cryopreservation process. The cryopreservation of cord blood started out as a purely empirical approach that was initially successful in the cryopreservation of bone marrow. It was gradually adapted for the cryopreservation of cord blood. Basically, the cryopreservation procedure includes the addition of a 10% Dimethyl Sulfoxide (DMSO) solution with freezing at a rate of around  $1^\circ\text{C}/\text{min}$  using a controlled-rate freezer. The controlled-rate freezer is a proven

and commonly used piece of equipment for cryopreserving cord blood. Most, if not all, transplanted cord blood samples are cryopreserved using this cryopreservation technique.

## Storage of Cord Blood

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- **HOW IS CORD BLOOD STORED?**

At Progenics, processed cord blood is stored in the vapor phase in a liquid nitrogen freezer, where the temperature is  $\leq -150$  °C.

Normally cord blood stem cells are cooled down gradually to  $-80^{\circ}\text{C}$ , then transferred to a liquid nitrogen freezer for long-term storage. When cord blood is stored in a liquid nitrogen freezer, it is very stable in either the vapor phase or liquid phase. The critical temperature for storing cord blood is  $\leq -150$  °C. If a sample reaches a temperature warmer than  $-150$  °C during storage the cord blood can be damaged by intracellular recrystallization. Therefore, it is critical that the temperature of the storage freezers be monitored 24 hours a day and that the power supply be equipped with a backup generator. At Progenics, processed cord blood is cryopreserved using a controlled-rate freezer and is then stored in a liquid nitrogen freezer (in the vapor phase), where the temperature is continuously maintained. In addition, the storage facility and the temperature inside the freezers are monitored 24 hours daily by security, video surveillance, environmental monitoring and alarm systems. A backup liquid nitrogen freezer is available at all times in case of emergency.

- **HOW LONG CAN CORD BLOOD BE STORED?**

Cord blood stem cells have demonstrated the ability to be stored for over 20 years in liquid nitrogen without significant damage (Broxmeyer He et al. Proc Natl Acad Sci USA 2003; 100: 645-650, Blood online March 10, 2011). Theoretically the cells can be stored in liquid nitrogen indefinitely.

- **HOW DO I RETRIEVE THE CORD BLOOD WHEN I NEED IT FOR TREATMENT?**

If a member of your family becomes ill with a disease that can be treated with stem cell transplantation, the attending transplant physician, with your authorization, will contact us for information about the stored cord blood. If the physician decides to proceed with a transplant using that cord blood unit, he or she will send us a request along with your consent for the shipment of the unit to the transplant center.

- **SHOULD I TRANSFER MY BABY'S STORE CORD BLOOD IF I MOVE?**

No, it is best to keep your stored cord blood in the same storage facility since transferring it from one bank to another poses the risk of losing the sample to a variety

of potential accidents during transportation, including the risk of exposing the cord blood unit to potential warming events that may affect the TNC viability. Therefore, it is better to keep the cord blood unit at its initial storage facility and then have it transferred directly to the transplant facility when the stored cord blood is needed for treatment of a disease. The transportation will be arranged by Progenics and the transplant facility. The stored cord blood can be shipped nearly anywhere in the world.

## Cord Blood Transplants

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- **WHY TRANSPLANT STEM CELLS?**

Sometimes, the HSCs in the bone marrow may become diseased (malignant or non-malignant) or may be destroyed by cancer chemotherapy and/or radiotherapy. When this occurs, stem cell therapy is essential.

Traditionally, the source of HSCs has been the bone marrow, hence the term “bone marrow transplant.” However, umbilical cord blood is another very important source of these precious lifesaving stem cells. In fact, researchers have discovered that stem cells derived from cord blood have many advantages over bone marrow-derived stem cells and are preferred in transplants.

The concept of stem cell transplant is to replace dysfunctional stem cells of an ill patient suffering from diseases treatable by healthy stem cells.

Hematopoietic (blood-forming) Stem Cells are capable of developing into various types of mature cells in the blood and immune systems. For some diseases, a stem cell transplant is the standard treatment. For some diseases they are the only therapy, and in some cases, they are only employed when front-line therapies have failed or when the disease is very aggressive.

When a patient required a stem cell transplant, the attending physician will decide which source of stem cells to use. This will depend on several factors, including but not limited to: the degree of HLA match between donor and patient (sometimes the donor and patient are the same person), the expected speed of engraftment (number of available cells), and the amount of time available to search for a perfectly matching donor. Over 40,000 cord blood transplants have been performed worldwide. (Ballen K., F1000 Research, V1 referees: 2 approved, 2017). It has been recommended that transplanting cord blood stem cells with a close HLA match should be the first choice over bone marrow to treat malignant diseases (Smith A. and Wagner J. BJH147, 246-261, 2009).

- **WHAT IS THE DIFFERENCE BETWEEN CORD BLOOD AND BONE MARROW TRANSPLANTS?**

Transplantation using stem cells derived from cord blood rather than bone marrow has many advantages. These include immediate availability, a painless and non-invasive collection process, a lower risk of infectious complication, a superior capacity for proliferation and differentiation, a greater tolerance for HLA mismatch and most importantly, a reduced risk of fatal post-transplantation “graft-versus-host” disease. This is because cord blood stem cells are more immunologically primitive.

- **WHAT KINDS OF DISEASES CAN BE TREATED WITH CORD BLOOD STEM CELLS?**

Numerous types of diseases have been successfully treated with stem cells. These include cancers such as leukemia, lymphomas, and myelomas, blood disorders such as thalassemia, sickle cell anemia, Fanconi’s anemia, and immune deficiency diseases.

Recently, cord blood stem cells have been used in clinical trials to repair damaged tissues and organs (regenerative medicine), and the outcomes have been promising.

- **WHAT IS THE CHANCE OF USING CORD BLOOD?**

The chance of a child using his or her own stem cells over the course of his or her lifetime is 1/400 (0.25%) (Nietfeld J.J. and Verter F., 2008). The opportunities for using cord blood are expected to increase with advances in research and improvements in transplantation. With reference to the information published by Center for International Blood & Marrow Transplant Research (CIBMTR), the number of patients using their own stem cells (autologous treatment) for adult bone marrow or peripheral blood stem cell transplants, is about 3 times higher than those who received donated stem cells (allogeneic treatment). This suggests that there is a higher probability for individuals to use their own cord blood stem cells when they are older.

- **HOW MUCH CORD BLOOD IS NEEDED FOR A TRANSPLANT?**

The success of a transplant is closely related to the number of Total Viable Nucleated Cells in the cord blood unit. The optimal amount of cord blood for a transplant is defined as  $2 \times 10^7$  nucleated cells per kilogram of the recipient’s body weight (Tse and Laughlin, Hematology (Am Soc Hematol Educ Program) 2005; 377-383); so saving more cells by preventing cell loss during processing is critical to ensure that the cord blood will be suitable for transplantation as time passes and the child grows. Any volume of cord blood could be useful, a small volume of cord blood could be used in regenerative medicine or could be expanded in the future.

- **SHOULD I BANK CORD BLOOD FOR EACH OF MY CHILDREN?**

Since there is a high chance that a child will closely match a sibling, it is more beneficial to save cord blood stem cells from each child to increase the probability of matching a family member who may develop a disease requiring stem cell therapy. Moreover, the additional cord blood units can be used for patients whose treatments may require two cord blood units.

- **CAN A SUCCESSFUL TRANSPLANT OF CORD BLOOD BE GUARANTEED?**

No, the success of a transplant is determined not only by the quality of the cord blood cells but by the condition of the recipient as well. More importantly is whether the number of cells banked is sufficient for the transplant when needed.

The success of a transplant DOES correlate with the cell dose of total nucleated cells (TNC) infused into the patient. Because a small volume of cord blood and low cell count limit its application, obtaining a high yield (recovery rate) of TNC from processing (saving more cells by preventing cell loss during processing) plays a role in determining the success of a transplant. When comparing result from different cord blood banks (Moroff G et al. Transplantation and Cellular Engineering (2006) 46:507-515).

## Company Information

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- **WHAT DOES A CORD BLOOD BANK DO?**

There are basically 8 steps that all cord blood banks perform in order to bank cord blood stem cells, but only one of these steps is key to determining final banking quality. It is this particular step in processing which makes each cord blood bank different. For other steps, cord blood banks generally employ very similar techniques.

1. Screen mothers to ensure they meet the eligibility criteria for cord blood banking
2. Provide a cord blood or cord blood and cord tissue collection kit
3. Provide information on transportation of collected cord blood or cord blood and cord tissue samples.
4. Provide collection instructions to healthcare providers
5. Processing
6. Storage
7. Arrange shipping of cryopreserved (frozen) cord blood for transplant
8. Follow up after transportation

- **WHY IS ACCREDITATION IMPORTANT?**

It is essential for a cord blood bank to be accredited as accreditation provides assurance of meeting international quality standards such as AABB (American Association of Blood Banks) and FACT (Foundation for the Accreditation of Cellular Therapy).

Progenics has been AABB accredited since 2005, just one year after being in operation. Accreditation provides assurance of meeting international quality such as AABB and FACT.

- **CAN I MAKE PAYMENTS AND CHANGE MY INFORMATION ONLINE?**

Yes, visit our secure website and simply click on “My Account” and follow the instructions to make your payments or update your information.