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WHY RED BLOOD CELLS SHOULD BE REMOVED BEFORE CORD BLOOD STORAGE

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Very early in the field of cord blood banking, laboratories that process cord blood for storage began removing most of the plasma (plasma depletion) and the red blood cells (RBC depletion) before cryopreserving the remaining component of the blood that holds the stem cells.

The main reason for removing the plasma is to reduce the volume of the final unit so that it is easier to cryogenically freeze. Plasma contains proteins, but no stem cells, so it is not needed for transplant therapy.

Similarly, red cells are not believed to help during transplant, so they are not needed either. In fact, having red cells present during transplant can be dangerous for a couple of reasons. First, even when a patient and donor are perfectly "matched" for transplant, which is to say they have the same HLA type, they may still have completely different blood types. Hence if any of the donor's red blood cells are infused into the patient they may trigger an "adverse reaction". This can be minimized by giving hydration to the patient.

The most important reason that red blood cells are dangerous to patients is that they tend not to survive the freezing and thawing process. Red blood cells undergo "lysis" during cryopreservation, a rupture of the cell membrane that spills the cell's contents, which include the hemoglobin and empty membrane sacks called red cell "ghosts". This can also make patients very sick by affecting their kidney function, and can potentially be fatal.

For all of the above reasons it has become standard practice among both public and private cord blood banks to remove red blood cells before storage.

Currently, most of the automated processing systems used in cord blood laboratories around the world perform partial RBC depletion and plasma depletion that result in good recoveries of the stem and progenitor cells needed for engraftment (the mononuclear cells and CD34+ cells). Partial RBC depletion results in a much lower number of RBCs than the fresh cord blood collection, so that the color of the final product is light red or pink, but not dark red like the original blood collection.

The only argument for not performing RBC depletion before cord blood storage is that some blood cells may be lost during the centrifugation step that is necessary in order to separate the different blood components. However, most of these cells are granulocytes, not progenitor cells, and they are not needed for engraftment. On the other hand, if cord blood units have not undergone RBC depletion before storage, then they will have to be "washed" after storage and thawing to remove the RBC. The washing stage is another opportunity for cell loss.

Cord blood units that have not had their red cells removed are more difficult to use for patients. When the frozen unit is thawed, the red cells undergo lysis and break apart. The medical literature reports serious and life-threatening reactions when these products are infused without any dilution or wash. The current recommendation from the National Marrow Donor Program (Be The Match) is NOT to infuse units holding red cells as they are, but to wash or at least dilute them.

Washing cord blood units that hold red cells after they have been thawed is technically challenging. The free hemoglobin and the cellular debris released from the lysed (broken) red cells makes it difficult for laboratory scientists to see the demarcation between the nucleated stem cells that they want to keep versus the residual "supernatant" to be removed. The separation of different cell types becomes more difficult than it was in the pre-freezing cord blood unit, leading to some loss of desirable cells. In addition, post-thaw tests of cord blood potency with the Colony-Forming-Unit (CFU) assay may be difficult to interpret.

In summary, given the problems with handling cord blood units that hold red cells, both in the laboratory and in the patient care setting, the current industry standard is for most cord blood banks to perform partial depletion of RBC and removal of plasma before cryopreservation. In addition, those public cord blood banks that have been licensed by the FDA all use a system to deplete RBCs and plasma.

References

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