

7TH INTERNATIONAL UMBILICAL CORD BLOOD TRANSPLANTATION SYMPOSIUM

Reflections on the 2009 Cord Blood Symposium

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A colleague suggested that as a first-timer at the 2009 Cord Blood Symposium in Los Angeles this year, I write about the meeting from the point of view of someone that has not been personally active in the stem cell field for a good many years. Having been involved early in the HLA field and tissue banking, I felt a bit like Rip Van Winkle awakening from a long slumber. Lots of things had changed; but surprisingly, some things are as much a mystery today as then.

First, there were several items that were news to me and which are based on actual use of cord blood stem cells (CBSC) in many transplants since 1995. Research is ongoing in many of these areas, but progress is clearly being made.

- Increased cell dose leads to increased engraftment, graft survival, even to the point of overcoming HLA mismatch. How the cell dose should be counted is still far from uniform, but transplant physicians use the Total Nucleated Cell (TNC) count, while others use other measures including enumeration of CD34+ cells.
- The rising use of double cord transplants. Although the initial dose is increased, only one unit of the two survives, probably through a competitive mechanism not yet completely understood. Still graft survival and patient survival are both improved, especially in adults, and not just because of the additional cells, it seems. Cord blood is slower to engraft than bone marrow derived stem cells, and some argued that further work was needed to determine the relative roles of myelosuppression vs. immunosuppression by the CBSC and preparative regimens.
- There appears to be a slight advantage to infusing CBSC directly in the marrow space rather than infusing them intravenously.
- Good HLA matches (e.g.: 6 of 6 or 5 of 6) suggest engraftment and improved patient mortality, but was not a particularly good marker for relapse. There was a suggestion that an HLA crossmatch or mixed lymphocyte culture could detect incompatibility not seen by matching only.
- Patient preparation for CBSC transplantation is important, but varied widely, depending on the patient's underlying disease process. There were also significant differences even within the same illness.

- Measures of the quality of the final product are still undecided, though there was consistent agreement on a few points: The number and % recovery of CD34+ cells is a good guide, as are colony forming units (CFUs) in the final product—but the value of this is limited because it takes 12 to 14 days for the colonies to grow. TNC, a measure long used by clinicians, and Total Mononuclear Cells (TMC) are a helpful but not absolute index of the number of CBSCs in the final product. A number of newer measures, such as ALDH "bright" cells are promising, but need more work before widespread acceptance.
- There is markedly less GVHD in CBSC recipients, but double CBSC infusion seems to nullify this to some degree. Other factors which influence GVHD are the age of the patient, cell dose as measured by TNC, and the degree of HLA mismatch.
- CBSC transplants have a lower relapse, increased time to engraftment, and lower patient mortality, despite the fact that they take longer to engraft
- There are extensive trials of CBSC in patients who do not have hematologic malignancies. I was particularly impressed with the Spinal Cord Injury trial in China and their use in anoxic brain disorders; but CBSC infusion seems to be of help in a very broad variety of disorders, some common, some rare. Their use in correcting Sickle Cell Disease is a huge step forward for that very difficult and common illness.
- Automation of CBSC processing appeared to be a time saver, and perhaps produce more consistent products; but with little if any improvement in CBSC concentration in the final product.

I was surprised by the fact that some arguments of 10, 15, and even 25 years ago remain incompletely resolved.

- Arguments over the importance of the HLA system are nearly the same as 25 years ago, with our expanded knowledge of the system presenting new complexities for the analysts. As predicted way back then, HLA-A, -B, and DR1 seem to be most important but there was data suggesting that HLA-C and others are important as well.
- The slow adoption of CBSC transplantation is puzzling, as is the widespread failure to recognize how vital all those frozen units would be should we have to mobilize for a nuclear accident or terrorist act.
- Finally, after all these years, the quality of CBSC products is still monitored primarily by TNC and CD34+ counts. Some kind of breakthrough is needed which can give better information about the viability and number of CBSCs in the final product.