Cord Blood’s Role in Cancer Therapy Awaits Answers

Within a year, medical researchers may have answers to some key questions about the role that placental cord blood will play in cancer treatment.

The answers will come from a $30 million study sponsored by the National Heart, Lung, and Blood Institute to determine whether placental cord blood (PCB) represents a safe and effective alternative to at least one type of bone marrow transplantation. Seven transplant centers will enroll a total of 300 patients with diseases amenable to treatment with marrow transplants. The exact breakdown of medical conditions remains undecided, but a large number of the patients will have leukemias.

In PCB transplant, 75 milliliters of blood harvested from umbilical cords is injected intravenously into a patient whose own bone marrow has been depleted by drug therapy or radiation. The stem cells are the seeds that will grow to direct the production of every kind of blood cell.

**Allogeneic Transplant**

The same type of re-seeding occurs during traditional allogeneic bone marrow transplantation, where the stem cells come from the bone marrow of another person. In an allogeneic transplant 1 to 2 pints (500 to 1,000 ml) of marrow is taken from the donor during surgery and given to the patient intravenously. The donor and patient must have similar human leukocyte-associated antigens, the proteins that allow the immune system to distinguish the body’s own cells from other people’s cells. Six HLA antigens are typed, and the more that match, the better the chance that the transplant will be successful.

In theory, PCB transplantation is better because there is no trauma to the donor and HLA antigen matching may be less important. However, the limited amount of placental cord blood available from a single donation may be problematic.

**Dr. JoAnne Kurtzberg**

The 5-year study is designed to answer two key questions about PCB transplantation: Does the size of the recipient affect the transplant? And how closely must the donor and recipient match up genetically? Smaller patients have been considered better candidates for cord blood transplants because of the limited number of stem cells found in cord blood as compared with bone marrow. But investigators now say patient size may not be a problem.

"There may be no limit as to the size of the recipient. There is already some data to suggest that cord blood transplants will work in large patients," said John Wagner, M.D., associate director of the bone marrow transplantation program at the University of Minnesota, Minneapolis, one of the participating centers.

Similarly, some evidence suggests that the degree of permissible genetic mismatch is comparable for PCB and bone marrow. With bone marrow, the chances for a successful transplant drop off dramatically when the donor and recipient share fewer than four of the six major HLA antigens.

In the past year, Wagner’s group and a team at Duke University Medical Center, Durham, N.C., have published results indicating that PCB transplants can be successful with two HLA mismatches, at least in children. Some investigators think even more mismatches may be acceptable with cord blood, but others are skeptical.

"Some people say you can do mismatches with impunity, but there is little data to support that position," said Paul McCurdy, M.D., director of the blood resources program at NHLBI’s Division of Blood Diseases and Resources. "We also don’t know whether recipient size affects HLA matching. For example, with larger recipients, a larger cell dose might be needed to accommodate a greater degree of HLA mismatch."

**Banking Centers**

NHLBI funds cord blood banking centers at Duke; the University of California, Los Angeles; and Children’s Hospital of Orange County, Calif. The
three banks will use DNA technology to determine the degree of match between donors and recipients. The technology should provide more accurate information about HLA typing.

“A lot of people can wear a size 42 suit, but when you look at the waist, how the shoulders fit, where the buttons are and so forth, a size 42 doesn’t fit everyone the same way,” McCurdy explained by way of analogy. “That’s why most of the better stores that sell suits have tailors. With DNA technology, we’re talking about a size 42 that’s at least partially tailored.”

Although time consuming and a potential source of delay in transplantation, detailed analysis of each cord blood donation will provide information that may improve transplantation specialists’ ability to predict the success of a procedure.

“We’re going to try to correlate outcomes with the specific composition of a cord blood graft,” said Wagner. “We want to be able to define what is an optimal graft for transplantation.”

Cancer patients enrolled in the program will include children and adults. In general, the patients will have one of three types of leukemia: acute lymphocytic leukemia, acute myelogenous leukemia, or chronic myelogenous leukemia. The first transplanted patients probably will be children, whose smaller body mass makes success more likely.

**Children First**

“I suspect that transplanters will want to see some results with children before they start transplanting adults,” said Wagner.

The timing of the first transplant depends on how long the three banking centers take to accumulate an adequate supply of donations, said JoAnne Kurtzberg, M.D., director of the pediatric bone marrow transplantation program at Duke, which will also perform some of the transplants. The NHLBI contract calls for the banks to accumulate a combined total of 15,000 PCB units. Collection should begin by April.

“I estimate that it will be 6 to 8 months after the start of banking before the centers have enough units on hand to allow for adequate matching,” said Kurtzberg. “That means the first transplants probably won’t begin until the end of the summer or early fall.”

Aside from Duke and Minnesota, participating transplant centers include UCLA, Children’s Hospital of Orange County, Dana-Farber Cancer Institute in Boston, Fred Hutchinson Cancer Research Center in Seattle, and Indiana University in Indianapolis.

— Charles Bankhead

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**Stat Bite**

**Cancer Survival in Children**

Survival rates for U.S. children with cancer have increased dramatically since the 1960s, largely as a result of advances in treatment. For all cancer sites combined, the 5-year relative survival rate (adjusting for non-cancer deaths) for children under age 15 has increased from less than 30% to more than 70%. Today, almost one of every 1,000 people who reach adulthood are cured survivors of childhood cancer. The table below shows trends in cancer survival for selected sites dating from the inception of NCI's Surveillance, Epidemiology, and End Results (SEER) Program in the 1970s.

<table>
<thead>
<tr>
<th>Site</th>
<th>Survival rate, percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Sites</td>
<td>55.5</td>
</tr>
<tr>
<td>Brain &amp; nervous system</td>
<td>54.4</td>
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<tr>
<td>Leukemia</td>
<td>44.9</td>
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<tr>
<td>Neuroblastoma</td>
<td>52.2</td>
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<tr>
<td>Non-Hodgkin’s lymphoma</td>
<td>44.5</td>
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<tr>
<td>Wilms’ tumor (kidney)</td>
<td>74.3</td>
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Source: Surveillance, Epidemiology, and End Results (SEER) Program.