CORD BLOOD TRANSPLANTS HELP ADULTS WITH LEUKEMIA

Umbilical cord blood is an acceptable source of hematopoietic stem cells for transplant in adult leukemia patients when a matched bone marrow donor is unavailable, according to two recent studies.

The findings, reported by US and European research groups in the New England Journal of Medicine (2004;351:2265–2275 and 2276–2285), offer a promising alternative to thousands of leukemia patients in need of treatment.

“As many as 16,000 leukemia patients diagnosed each year require a bone marrow transplant but have no matched relative or can’t find a match in the national bone marrow registry,” Mary J. Laughlin, MD, Associate Professor of Medicine at Case Western Reserve University School of Medicine and lead researcher of one of the studies, said in a statement. “Umbilical cords that are normally discarded after birth could provide real hope for these patients.”

Laughlin and colleagues compared outcomes in 600 patients aged 16 to 60 with acute lymphoblastic leukemia, acute myeloid leukemia, chronic myeloid leukemia, or myelodysplastic syndrome. Thirty-four patients received transplants of cord blood mismatched for 1 human leukocyte antigen (HLA); 116 patients received cord blood mismatched for 2 HLA antigens; 83 patients received bone marrow with 1 HLA mismatch; and 367 patients received HLA-matched bone marrow.

Disease-free survival was highest—at 3 years—among patients who received a matched bone marrow transplant. But the rates were similar for patients who received mismatched marrow or cord blood (19% vs. 23% at 3 years; \( P = .69 \)). Rates of treatment-related mortality were also similar for the mismatched marrow group and the cord blood group (\( P = 0.96 \)), as was overall mortality (\( P = 0.92 \)). These similarities were all the more remarkable, the researchers noted, because 77% of the cord blood transplants were mismatched for 2 HLA antigens, while the mismatched bone marrow grafts were only mismatched in 1 HLA antigen.

The European study, led by Vanderson Rocha, MD, PhD, of the Hôpital Saint-Louis in Paris, compared 682 adults with acute myeloid or lymphoblastic leukemia who received either a matched bone mar-
row transplant or a mismatched cord blood transplant (43% with more than 1 HLA mismatch). The researchers found no significant differences in transplant-related mortality, relapse, or disease-free survival between the two groups.

Cord blood transplants have been used successfully in children with leukemia, but the technique has some limitations when used in adults. One of the greatest obstacles, said Ralph Vogler, MD, Scientific Program Director at the American Cancer Society (ACS), is retrieving sufficient numbers of stem cells from the cord blood to populate the bone marrow of an adult. Typically, cord blood produces about one-tenth the number of usable cells compared with bone marrow.

One consequence of these numbers is the time it takes for neutrophil and platelet counts to return to normal after grafting. In Laughlin’s study, median neutrophil recovery occurred after 18 days in patients who received matched bone marrow, compared with 20 days in those receiving mismatched bone marrow and 27 days in those receiving cord blood. Infection-related deaths in the first 100 days following transplant were significantly higher in the cord blood group (45%) than in either of the bone marrow groups (21% for matched marrow, 24% for mismatched marrow). Neutrophil recovery in cord blood recipients was also significantly delayed in Rocha’s study.

But progress has been made in that arena, Vogler said. “Now what’s being done is after the transplant they’re giving growth factors to stimulate white cell production, and there is a growth factor that can stimulate platelet production,” he said. Platelets can also be transfused, he added.

There are also some advantages to cord blood transplants. There is no danger to the donor, because the blood is collected after birth before the placenta and umbilical cord are discarded. Once a suitable donor is identified, the cord blood can be made available more rapidly than bone marrow.

In addition, stem cells from cord blood are less immunogenic than those from adult blood, so grafts tend to be better accepted with less graft-versus-host disease (GVHD), Vogler said.

In Laughlin’s study, rates of acute GVHD were similar in patients who received cord blood and matched bone marrow, while patients who received mismatched bone marrow had higher rates of this complication. The European researchers, however, found lower risk of acute GVHD among cord blood recipients compared with recipients of matched bone marrow.

Risk of chronic GVHD was not significantly different between the two groups in the European study. In the US study, however, the rate of chronic GVHD was higher among cord blood recipients than among matched marrow recipients and similar to the rate among mismatched marrow recipients. Nevertheless, the US study found significant differences in the proportion of cases of extensive GVHD among all their patients with chronic GVHD: 33% of cord blood recipients, 52% of HLA-matched marrow recipients, and 71% of mismatched marrow recipients ($P = 0.03$).

Overall transplant results are still best when a matched bone marrow donor is available, and neither group of researchers recommends cord blood as a substitute for a matched marrow donor.

Although use of cord blood for transplantation is increasing, the optimal organization and regulation of cord blood banks remain topics of debate, according to Robert Steinbrook, MD, a correspondent with the New England Journal of Medicine. In a perspective article in the same issue of the Journal, Steinbrook noted the differences between public and private cord blood banks.

According to Steinbrook, public banks around the world currently store between 175,000 and 200,000 units of cord blood.
banks do not charge the donor for collection or storage, but do charge $15,000 to $25,000 when a unit is provided for transplantation. The fee is usually covered by health insurance, Steinbrook wrote. However, expansion of these public banks has been limited by a shortage of stored cord blood and a lack of funding for storage and collection, he added.

In contrast, private cord blood banks offer parents the opportunity to store their own child’s cord blood for subsequent use by the child or a sibling. Fees generally are about $1,000 to $1,500 for collection and $100 a year for storage. Blood from private banks has been used in only a handful of transplants, Steinbrook notes. One issue: “As medicine is currently practiced, a child’s own cord blood cannot be used if the child is born with a genetic disease or develops leukemia.”

Steinbrook concludes, “A person’s own cord blood is very unlikely to be needed for personal or family use, so patients and society are better served when matches from unrelated persons can be found in a public bank.”

DOES FRUIT AND VEGETABLE INTAKE PROTECT AGAINST CANCER?

A recent study questions whether the long-standing recommendation to eat an abundance of fruits and vegetables to reduce cancer risk may be overstated. In a report published in the Journal of the National Cancer Institute (2004;96:1577–1584), Walter Willett, MD, DrPH, and colleagues at the Harvard School of Public Health found that eating at least five servings of fruits and vegetables daily had an impact on cardiovascular disease risk but not overall cancer incidence.

Using data from the Nurses’ Health Study and the Health Professionals’ Follow-Up Study, Willett and colleagues examined the eating patterns of 71,910 women and 37,725 men as determined by food-frequency questionnaires. They compared fruit and vegetable intake with incidence of myocardial infarction, stroke, and all cancers combined (except non-melanoma skin cancer, in situ breast cancer in women, and organ-confined prostate cancer).

Study participants who ate greater amounts of fruits and vegetables showed statistically significant reductions in cardiovascular disease risk, with a relative risk of 0.88 for those who ate 5 servings of these foods each day. Overall cancer incidence, however, was not affected by the amount of fruits and vegetables in the diet.

“Our study means that everyone should still try to eat five or more servings of fruit and vegetables per day, but that the benefit will be mainly for cardiovascular disease,” said Willett, the study’s senior author and Professor of Epidemiology and Nutrition at the Harvard School of Public Health.

“It is still possible that there may be a small benefit for cancer,” he continued, “but it is very unlikely that there will be the 30% to 50% reduction in cancer risk that has been suggested. Not smoking, avoiding becoming overweight, and staying physically active will be more effective in preventing cancer.”

Other cancer experts, however, questioned the methodology of the study and reiterated the soundness of recommending fruit and vegetable consumption for cancer prevention, as the ACS, the National Cancer Institute, and other groups do.

“The existing evidence supporting a reduced risk for cardiovascular disease is definitely stronger than for all cancers combined, but that doesn’t really mean there is no protective effect of fruits and vegetables for cancer,” said Jeannne Calle, PhD, Director of Analytic Epidemiology for the ACS.

“When you eat fruits and vegetables, you’re meeting your calorie needs with healthy food, as opposed to meeting them with sugar, fat, or low-nutrient foods,” she said. “Making good food choices is going to directly protect you from heart disease, but it’s also going to protect