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New bone marrow transplant method eases risk

Experimental technique just tamps down, not destroys, immune system

By LAURAN NEERGAARDAP Medical Writer

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WASHINGTON - Bone marrow transplants are undergoing a quiet revolution: No longer just for cancer, research is under way to ease the risks so they can target more people with diseases from sickle cell to deadly metabolic disorders.

The old way: High doses of radiation and chemotherapy wipe out a patient's own bone marrow before someone else's is infused to replace it, hopefully before infection strikes.

The new way: Rather than destroying the patient's bone marrow, just tamp it down enough to make space for the donated marrow to squeeze in alongside and a sort of twin immune system takes root. It's what doctors taking a page from mythology call "mixed-cell chimerism" — patient and donor blood and immune cells living together to improve health.

To find the best methods for these less intense transplants, different mixes of low-dose radiation and immune-suppressing drugs are under study at hospitals around the country.

But the ultimate quest is to allow transplants even when donors aren't a good genetic match, says Dr. Suzanne Ildstad of the University of Louisville — whose technique involves an experimental tweaking of donated cells to help them grow better.

"It makes it possible for anyone who has a mom or dad willing to donate marrow to them to have a transplant," says Ildstad, who has families with sickle cell and other childhood genetic illnesses lining up to try.

Separately, several hospitals are testing how to combine kidney transplants with bone marrow transplants from the same donor, in hopes that a hybrid immune system lessens the need for lifelong anti-rejection drugs.

"People are watching with eager expectation," says Dr. Lakshmanan Krishnamurti of Children's Hospital of Pittsburgh, who is helping to plan a multi-hospital study of some of the new methods for hard-to-treat adults with sickle cell disease.

Doctors have long known that a traditional bone marrow transplant can cure young children of sickle cell — if they have a well-matched donor. New marrow produces healthy red blood cells to replace the sickle-shaped ones that can't squeeze through small blood vessels, the cause of the disease's pain, infections and life-threatening organ damage.

But only about 17 percent of children have a suitable donor, usually a healthy sibling. Attempts to

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transplant adults have failed, their bodies too ravaged from years of the disease. Another hurdle: Certain immune cells in donated marrow sometimes become too aggressive and attack the recipient, called graft-versus-host disease or GVHD.

Enter the new research.

First came a tantalizing success in severely ill adults. Nine of 10 patients who underwent a less intense transplant — using low-dose radiation and two drugs to inhibit problem immune reactions — had their sickle cell apparently eliminated, Dr. John Tisdale and colleagues at the National Institutes of Health reported in December. They developed a hybrid immunity that produces normal red blood cells with no GVHD.

But those people had perfectly matched donor cells provided by healthy siblings. Few patients do.

Back in Louisville, Ildstad gives donated marrow a boost to try to overcome that problem while avoiding GVHD, a risk that worsens with mismatched donors. She removes troublesome immune cells from the donated infusion, leaving concentrated amounts of the blood-producing stem cells patients need plus "facilitating cells" that she discovered seem to help them take root.

In an NIH-funded experiment at Louisville and Duke University, the method so far worked in two children with sickle cell who had well-matched donors and one of four with a half-match.

Dr. Joseph Leventhal of Northwestern University gave an Ildstad-treated stem cell infusion to a handful of kidney transplant recipients who developed hybrid immune systems that seem to be holding nearly a year later. The first three treated are using one anti-rejection drug instead of the usual cocktail, and one soon will attempt full weaning.

"We're doing this in patients where it could have potentially the biggest impact," those with unrelated donors, says Leventhal, who anticipates giving one patient a month the dual transplant as the study continues at Northwestern Memorial Hospital.

The attraction to families: "You don't die from the new way," is how Bob Evanosky of Aurora, Ill., puts it.

His three sons have a devastating metabolic disease called metachromatic leukodystrophy, or MLD. Last summer, son John got an experimental outpatient transplant at Duke — a far cry from the months his brother Jack had to spend in intensive care after a well-matched transplant the old-fashioned way.

Dad was John's donor even though he's only a half-match — and the new cells are making the enzyme his body had lacked, too late to reverse the brain damage that has paralyzed the 8-year-old but perhaps able to ease some complications, says Evanosky, who plans to donate to his John's twin Christopher this fall.

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