

5 babies born to save ill siblings, doctors say

Peter Gorner, Tribune science reporter. Chicago Tribune. Chicago, Ill.: May 5, 2004.

Genetic testing of embryos outside the womb has led to the births of five babies selected to produce umbilical cord blood or bone marrow to save the lives of seriously ill siblings, Chicago doctors reported Tuesday.

Infusion of cord blood, a procedure similar to a bone marrow transplant, has so far put one sibling's leukemia into remission, the scientists reported in the *Journal of the American Medical Association*.

The controversial procedure, which employs cutting edge genetic tests during in-vitro fertilization, expands the possibilities of the creation of so-called "savior babies" to provide stem cells for older children who lack compatible donors for bone marrow transplants.

The procedure raises questions among ethicists, but is backed by public opinion. In the largest survey about preimplantation genetic testing so far, researchers at Johns Hopkins University found 61 percent of the public embraces the idea of using the tests to select an embryo that could benefit an ailing sibling.

Scientists at the Reproductive Genetics Institute, 2825 N. Halsted St., reported the first use of the technique to test tissue compatibility in embryos.

After eggs are removed from women and fertilized with the husband's sperm, they are tested for genes that make antigens, which tell the body whether transplanted tissue is "self" or "non-self" and should be rejected. These antigens--known as HLA--are proteins on the surface of body cells that give the immune system a way to determine what belongs in the body and what does not. Matching antigens will permit the body to accept a transplant and not reject it.

Compatible embryos are then transferred back into the womb in the hopes that at least one will implant in the uterus and a pregnancy will develop. At the time of publication, the Chicago scientists were able to create babies for five of nine couples whose other children already suffered from bone marrow failure.

The affected youngsters have acute lymphoid leukemia, acute myeloid leukemia or the rare blood disorder Diamond-Blackfan anemia, diseases that require antigen-matched stem cell transplantation.

Umbilical cord blood from one of the babies already has saved a sibling, another transplant is pending, and three of the affected children were in remission and may need the stem cell transplants later, the scientists said.

Thousands of children die each year because matching donors for bone marrow transplants can't be found. Genetic testing of embryos may offer the last resort for couples who want to have another child who is healthy and can perhaps also save the life of a sibling.

"Screening embryos for compatibility is still highly controversial and even not allowed in some countries, but it appears to be a reasonable option for couples," said the institute's director, Yury Verlinsky, who has pioneered the field of preimplantation genetic diagnosis, or PGD.

"Desperate people are getting pregnant and terminating pregnancies because the baby would have the wrong [antigen] type. With this technique they can create a baby that's compatible and save the stem cells for the victim."

Past successes

In the past, Verlinsky gained worldwide publicity for doing genetic testing that led to the birth of Adam Nash, who saved his sister, Molly, from dying of the lethal genetic blood disease Fanconi anemia.

The institute also gained considerable publicity for creating the first baby to be born free of a severe and often lethal birth defect and a healthy baby girl who was born without the gene that is causing early-onset Alzheimer's disease in her mother, as well as children who escaped inherited predispositions to many forms of cancer that may not show up until adulthood.

In an editorial accompanying the report Tuesday, Dr. Norman C. Fost, a pediatrics professor and the director of the bioethics program at the University of Wisconsin, favored the use of the technology to test compatibility for transplantation.

"In all other cases, PGD was used to make sure a baby did not have some serious genetic disorder that runs in the family. What's new here is that the older children have diseases, like leukemia, with no known genetic causes. So the point of PGD is to select embryos of the same tissue type.

"In some of these PGD families, cord blood may work, but months or years later the bone marrow supply may slowly die out and another transplant would be needed. So there's some chance these children could be bone marrow donors."

Ethical objections about bone marrow donation are not sufficient to prohibit families from getting this kind of assistance, Fost said.

"It offers the opportunity to save the life of an existing child with an otherwise untreatable disorder and allows couples to avoid confronting the difficulties of prenatal diagnosis for [antigen] typing in mid-pregnancy, with selective abortion of fetuses who are poorly matched with the affected child," he wrote in JAMA.

Another expert, Arthur L. Caplan, director of the Center for Bioethics at the University of Pennsylvania, has followed the work of Verlinsky and other PGD innovators with interest.

2 possible problems

"The two key issues I see are the possible health risks of embryo biopsy and testing to any children made via PGD--that is unknown at this time and it's not clear what follow-up is going on with PGD babies by Yury [Verlinsky] or anyone else.

"The second problem is the presumption that you must donate tissue if you are made to be a match."

Stem cells from cord blood are no problem, Caplan said, but the matching sibling could face pressures later in life that are not consistent with donor ethics of organs and tissues.

"That said, I don't think this practice should be banned. I am more concerned about proper counseling for parents who are thinking about going this route by someone other than the purveyor of the technology."

Verlinsky wrote that he assembled a large and diverse board of volunteers, independent of his institute, who studied the ethics and approved of the procedure before he attempted it.

To test the embryos, DNA was removed following in-vitro fertilization and analyzed for antigen genes to determine if the embryo's genes matched those of the sibling.

The testing required a total of 199 eight-celled embryos, many of which lost the luck of the draw merely because they weren't compatible. Verlinsky said the loss was preferable to aborting fetuses for the same reason. "I don't think many of our clients are creating a second baby just for treatment," he said.

"They want to have another baby. A healthy one. But on top of that, they now have a way of saving the child who's sick."

The public apparently agrees, but still has concerns, according to the survey announced Tuesday.

"There is strong support for using these technologies when there is a health benefit, even when that benefit is for another person," said Kathy Hudson, founder and director of the Johns Hopkins University Genetics and Public Policy Center.

"But this support coexists with deep-seated worries about where all these technologies may be taking us. For example, 80 percent of respondents were concerned that if not regulated, reproductive genetics technologies such as PGD could get 'out of control.'"

HOW THE GENETIC TESTING WORKS

- 1 The mother takes drugs to stimulate her ovaries to produce several mature eggs. The eggs are removed using a needle guided by ultrasound.
- 2 An average of eight eggs are retrieved and fertilized.
- 3 After three days, one cell from each formed embryo is removed and placed in a test tube for DNA analysis.
- 4 The embryos' HLA (human leukocyte antigens) genes are compared to the same genes of the sick child. HLA genes form a group of proteins involved in recognition of foreign cells and play an important role in rejection or survival of transplanted cells.
- 5 When there is a full match, the embryo is transferred into the mother's uterus to establish a pregnancy. About one in four embryos will have an HLA match with the sick sibling.