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MEDICINE

Discovery Spurs Heart to Grow Blood Vessels

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In a significant advance for the treatment of heart disease. German researchers successfully used genetic engineering to grow new vessels around clogged coronary arteries.

Heart experts said the accomplishment represents an important milestone in an international effort to replace or at least complement coronary-bypass surgery, a widely used treatment for blocked arteries, which are the major cause of heart attacks.

In the first controlled study of the new method, doctors spurred the growth of new blood-carrying vessels in patients' hearts by injecting the patients' heart muscles with a genetically engineered version of a substance the body uses to grow vessels naturally.

The new study is expected to give a boost to several research collaborations between academic scientists and startup companies that are racing to develop techniques to stimulate the growth of new blood vessels. If larger and longer trials are equally successful, doctors believe they will be close to creating a major new medical procedure easily worth hundreds of millions of dollars a year.

Researchers at Fulda Medical Center Fulda, Germany, injected a human protein called fibroblast growth factor, or FGF-1, directly into the heart near the obstructed vessels of 20 patients suffering from coronary heart disease.

Within four days, a network of tiny new blood vessels sprouted around the diseased arteries of all 20 patients, eventually leading to a new channel that rerouted blood flow around the blockages. Twenty other patients, who were given an inactive form of the growth factor, didn't develop any new vessels.

"With this growth factor we are able to build new vessels," said Thomas-Joseph Stegmann, head of thoracic and cardiovascular surgery at the German facility "That is the important thing we have shown."

Dr. Stegmann heads the research group whose study in today's issue of Circulation, a journal published by the American Heart Association, is the first published report suggesting that stimulating coronary blood vessel growth through genetic-engineering techniques can work in humans.

"At the moment, we have to say that this procedure isn't replacing bypass surgery, " said Dr. Stegmann. "But it could be an additional procedure for vessels that can't be bypassed in the conventional manner.

That alone would be a significant advance for patients, said' Stephen Ellis, director of the cardiac-catheterization laboratory at the Cleveland Clinic. About 800,000 patients worldwide undergo bypass surgery each year. Another 800,000 have a less invasive procedure called balloon angioplasty.

"But another 150,000 have severe [chest pain] and aren't candidates for either" procedure, Dr. Ellis said.

"It's an important piece of the puzzle," said Elizabeth Nabel. a gene-therapy researcher and the chief of cardiology at the University of Michigan, Ann Arbor. She noted that several research groups have similar studies under way, most of them focused either on one of several varieties of fibroblast growth factor or on another family of such proteins called vascular endothelial growth factor, or VEGF.

For instance, Genentech Inc., South San Francisco, Calif., is conducting a human trial in which it is injecting bioengineered versions of the VEGF protein into heart patients with the hope of inducing blood vessel growth. Human Genome Sciences Inc., Rockville. Md., is working with Jeff Isner, a gene-therapy researcher at Tufts University School of Medicine, Boston, to develop a therapy that will cause the body's cells to produce VEGF to spur vessel growth. Ronald Crystal, a researcher at New York Hospital Cornell Medical Center and founder of GenVec Inc., RockvWe. Md. began a human trial last month using a VEGF? producing gene. In addition Collateral Therapeutics. San Diego, filed an application to begin a gene-based treatment involving a version of fibroblast growth factor. It is backed in the venture by Schering AG of Germany.

Dr. Stegmann said his group isn't currently backed by corporate financing.

His approach, like the technique Genentech is using with VEGF, isn't gene therapy because it doesn't involve injecting the genes that make the growth factors into the patient where it then works in the cells to produce growth factor proteins. Instead, Dr. Stegmann's group uses biotechnology techniques to produce the growth factor outside the body and then injects the substance directly into the heart. The German group injected the proteins during bypass surgery, but it is expected such, proteins could be administered in the future without open-heart surgery, researchers said. '

All of the patients in the study underwent traditional double or triple bypass surgery to reroute blood flow around blockages in major arteries, but they also had obstructions in other vessels that couldn't be reached easily with bypass, Dr. Stegmann explained. It was at those sites that the researchers injected the protein.

After 12 weeks, images taken of the heart showed substantial growth of new vessels in patients given the treatment and the new network of vessels was seen sprouting from a section of artery above the blockage and rejoining the artery below it, thus circumventing the obstruction, he said.