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Help for growing hearts: Researchers are using bone-marrow stem cells to make valves that will grow as a child ages

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Author: Delthia Ricks, Newsday, Melville, N.Y.

Sep. 14--Doctors say they are a significant step closer to producing stem-cell-generated heart valves for children, structures that can grow with the child, eliminating the need for repeat surgeries as now is the case when conventional methods are used.

Medical researchers at Children's Hospital Boston say they can create the valves from stem cells derived from the bone marrow and coax those cells in the lab to grow into a complete, functioning heart valve. The process is called tissue-engineering, an area of science in which investigators are attempting to develop replacement parts for structures damaged by disease and age.

Dr. John Mayer said the valves should be available for clinical trials within the next three years.

"These are stem cells derived from the bone marrow," Mayer said. "They are not embryonic stem cells."

Mayer and his collaborators report their work in this week's edition of *Circulation*, a journal of the American Heart Association. "We had published other work on this two years ago in the same journal where we actually implanted them in sheep for periods up to eight months," he said.

Tissue engineers at Wake Forest University in Winston-Salem, N.C., already have grown a functioning human bladder derived from stem cells. The new work involving heart valves, which provide one-way blood flow from the heart's right ventricle into the pulmonary artery, are more complex. They have three "leaflets" -- flaps -- that must open and close in synchrony.

Dr. David Martin, director of research and development at Tepha Inc., a Boston-area biotechnology company, has aided previous experiments at Children's Hospital, providing the complex material on which the valves are grown.

"The scaffold is biodegradable, but it mimics the shape and size of a heart valve," Martin said, adding that when stem cells are introduced to the scaffold, a lattice frame, in the laboratory "they invade it."

Growth is encouraged through a soup of cellular nutrients.

"We are fine-tuning the technique to make this whole process work better," Mayer said.

Surgeons have long been able to repair congenital heart defects in children by implanting artificial valves made of synthetic materials, or they have used valves from pigs. Either way, children grow and need replacements, which means at least two or three repeat surgeries.

Mayer, who is a pediatric heart surgeon, said there are several pediatric heart conditions that lend themselves to repair with a tissue-engineered valve. One such condition is called tetralogy of Fallot, a disorder marked by four significant defects, including a damaged pulmonary valve.

Dr. Alan Russell, director of the McGowan Institute for Regenerative Medicine at the University of Pittsburgh, called the experiments exciting -- and one of the most complicated developments to date.

"The concept is incredibly important," Russell said. "Dr. Mayer has been working on this for many, many years."

Scientists at McGowan are working on a bioengineered pediatric heart. Russell said new work involving valves is moving the field forward.

"This kind of work is very important and also very difficult because the valves have to be perfect," he said. By perfect, Russell means the valve has to function the moment it is secured in the heart.

Fewer surgeries for children

Tissue-engineered heart valves that grow as a patient grows could eliminate the need for repeat operations among child patients.

About the pulmonary valve

Allows blood to flow from the heart's right ventricle into the pulmonary artery. The pulmonary artery carries deoxygenated blood to the lungs.

Has three small flaps that open to allow blood to flow into the pulmonary artery.

Artificial valves made from synthetic materials and pig valves have been available for years.

Right atrium

Left atrium

Area of Pulmonary valve

Left ventricle

Right ventricle

'Engineered' valves

Using stem cells from the bone marrow, researchers are designing valves that can "grow" with children. They do not require replacement.

Currently, children in need of a heart valve must undergo repeat surgeries for replacements.

The engineered valves are grown on lattice frames fed with cellular nutrients to coax appropriate shape and development.

Tissue-engineered valves are not rejected by the body because they come from the patient's own cells.

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