Laboratory-grown urethras implanted in patients, scientists report

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Researchers at the Institute for Regenerative Medicine at Wake Forest University Baptist Medical Center and colleagues reported today on a new advance in tissue engineering. The team is the first in the world to use patients' own cells to build tailor-made urinary tubes and successfully replace damaged tissue.

In an article published Online First by The *Lancet*, the research team reports replacing damaged segments of urinary tubes (urethras) in five boys. Tests to measure urine flow and tube diameter showed that the engineered tissue remained functional throughout the six-year (median) follow-up period.

"These findings suggest that engineered urethras can be used successfully in patients and may be an alternative to the current treatment, which has a high failure rate," said Anthony Atala, M.D., senior author, director of the Wake Forest Institute for Regenerative Medicine and a pediatric urologic surgeon. "This is an example of how the strategies of tissue engineering can be applied to multiple tissues and organs."

Atala's team used a similar approach to engineer replacement bladders that were implanted in nine children beginning in 1998, becoming the first in the world to implant laboratory-grown organs in humans. Researchers at the institute are currently working to engineer more than 30 different replacement tissues and organs.

Defective urethras can be the result of injury, disease or birth defects. While short defects in the tube are often easily repairable, larger defects can require a tissue graft, usually taken from skin or from the lining of the cheek.

"These grafts, which can have failure rates of more than 50 percent, often become narrowed, leading to infections, difficulty urinating, pain and bleeding," said Atlantida-Raya Rivera, lead author and director of the HIMFG Tissue Engineering Laboratory at the Metropolitan Autonomous University in Mexico City.

Between March 2004 and July 2007, the research team built engineered urethras for five boys, ages 10 to 14, using the patients' own cells. Three patients had widespread injury due to pelvic trauma and two patients had previous urethra repairs that had failed. The engineered tubes were used to replace entire segments of damaged urethra in the section that runs between the penis and the prostate (posterior section) -- considered the most difficult to repair.

The first step in engineering the replacement urethral segments was taking a small (one-half inch by one-half inch) bladder biopsy from each patient. From each sample, scientists isolated smooth muscle cells and endothelial cells, the cells that line blood vessels and other tubular structures. These cells were multiplied in the lab for three to six weeks and were then placed on a three-dimensional scaffold shaped like a urethral tube. Smooth muscle cells were placed on the outside of the scaffold and endothelial cells on the inside. The scaffolds, which were sized for each individual patient, were made of a biodegradable mesh material. After cell placement, the scaffolds were incubated for seven days – with the total time for construction ranging from four to seven weeks. By day six, all surface areas were completely covered with cells.

After incubation, the tubes were surgically implanted by removing the

defective segment of the urethra and scar tissue and sewing the replacement tubes in place. Once in the body, the cells continued to expand and tissue formation began. Biopsies showed that the engineered urethras had normal layers of epithelial and smooth muscle within three months after implantation. Flow measurements, urine tests and patient questionnaires confirmed patient satisfaction as measured by lack of nighttime leaking, straining to urinate, and urinary tract infections – common symptoms when urethral tubes become narrowed.

Provided by Wake Forest University Baptist Medical Center