

were given to our patient; one was given at 2 a.m. on June 15, one at 10 a.m. on June 15, and one at 10 a.m. on June 16. After the first transfusion, the patient's viral load was reduced by a factor of approximately 12 (from 1.68×10^5 to 1.42×10^4 copies per milliliter) during the first 8 hours (from 2 a.m. to 10 a.m. on June 15) and was undetectable within 32 hours. A radiograph obtained on June 15 showed reduced density of the pulmonary lesions in the left lobe; however, consolidation in the right lower lobe had progressed. Oseltamivir treatment was stopped at 10 a.m. on June 16 because of persistently negative results on RT-PCR. The patient recovered and was discharged on August 4.

We performed tests of neutralizing antibodies against A/chicken/Hong Kong/282/2006, a virus closely related to A/Shenzhen/406H/2006. The neutralizing-antibody titer was negative on June 14 and 15, then it rose steadily and was between 1:40 and 1:80 by June 20. This increase may have been the result of both the treatment with convalescent plasma and the patient's own humoral immune response, since the neutralization antibodies were maintained at this level thereafter. H5N1 viruses were successfully isolated from tracheal aspirates from both this patient and the plasma donor. A subsequent analysis revealed that the virus from the plasma donor and the current patient were closely related genetically, with greater than 99% homology in their hemagglutinin genes. Both viruses were Fujian-like H5N1 variants that have been predominant in poultry and have caused

other human infections in southern China since 2005 (e.g., A/Guangxi/1/2005, A/Zhejiang/16/2006, and A/chicken/Hong Kong/282/2006).² Our results indicate that passive immunotherapy may be a viable option for the treatment of influenza A (H5N1) infection. Therefore, the development of passive immunotherapy with humanized monoclonal or polyclonal antibodies warrants further consideration.³⁻⁵

Boping Zhou, M.D., Ph.D.

Shenzhen Donghu Hospital
Shenzhen 518020, China

Nanshan Zhong, M.D.

Guangzhou Institute of Respiratory Disease
Guangzhou 510120, China

Yi Guan, M.D., Ph.D.

University of Hong Kong
Hong Kong SAR, China
yguan@hkucc.hku.hk

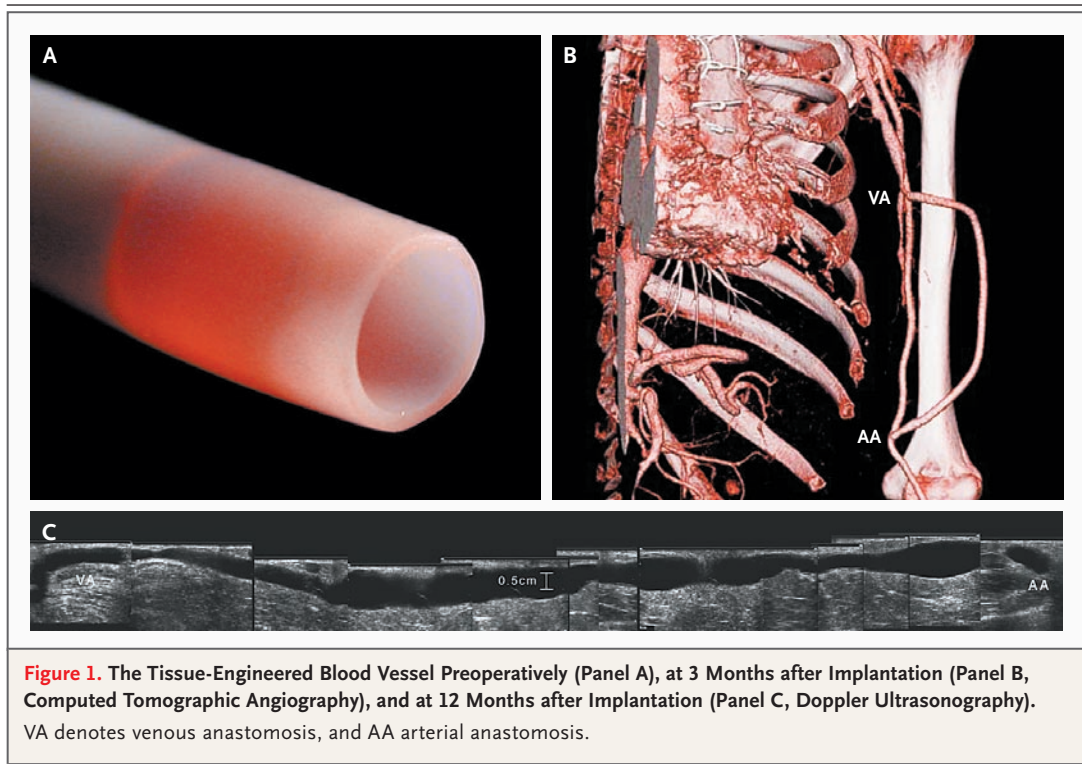
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Tissue-Engineered Blood Vessel for Adult Arterial Revascularization

TO THE EDITOR: A material that will approach the efficacy of native vein has been widely sought.¹ Using autologous cells and a technique termed sheet-based tissue engineering, we were able to produce autologous tissue-engineered blood vessels with physiologic mechanical properties.² No synthetic or exogenous materials were used; instead, the vessels were created with the use of autologous fibroblasts and endothelial cells harvested

from a small biopsy specimen of skin and superficial vein. Here we report on the preliminary use of these tissue-engineered blood vessels in an adult arterial model.

Ten patients receiving hemodialysis whose arteriovenous shunts were failing were enrolled in this study. The subjects had typical risk factors for end-stage renal disease, including previously failed dialysis-access grafts, diabetes, controlled hyper-



tension, and obesity. Patients ranged in age from 29 to 89 years (mean \pm SD, 68 ± 17). Vessel patency was evaluated by means of Doppler and angiographic imaging. Mechanically viable vessels were created with autologous cells for each patient. The average burst pressure among 54 vessels was 3340 ± 849 mm Hg, which compares favorably with native veins.³

The primary objective of this study was to demonstrate that a tissue-engineered blood vessel produced in vitro could withstand the challenges of arterial pressure produced by an arteriovenous fistula for at least 3 months. After this observation period, grafts were punctured for hemodialysis access. To date, the first six patients have had vessels implanted and have been followed for up to 13 months.

The tissue-engineered blood vessel in Patient 1 (Fig. 1) was used for more than 13 months, until the patient underwent successful kidney transplantation. At 11.5 months, an aneurysm was noted near an area that had many punctures. A small portion of the vessel wall was resected, and the tissue-engineered blood vessel continued to func-

tion until the kidney transplantation. In total, the 14-cm-long graft was punctured more than 200 times.

Patient 2 died at day 39 of unrelated causes with a functioning tissue-engineered blood vessel. The vessel in Patient 3 had a thrombotic failure at 12 weeks, attributed to a low postoperative flow rate (<500 ml per minute) and a moderate, diffuse dilatation that further reduced flow velocity. At up to 5 months after implantation, Patients 4, 5, and 6 have functioning grafts without complications.

Compliance measurements derived by ultrasonography at 5 months show a 4.8-fold increase for Patient 1 (3.1 to 15.0% per 100 mm Hg) and a 2.7-fold increase for Patient 4 (2.3 to 6.2% per 100 mm Hg) in compliance relative to preoperative values, without concomitant dilatation or evidence of mechanical degradation. This may indicate the formation of an elastic component, which would be consistent with our preclinical results.

Although these are clearly early results, we have demonstrated in 24 patient-months of use that this new approach may be feasible. This transition to

human use represents an important milestone for cardiovascular engineering.⁴

Nicolas L'Heureux, Ph.D.

Todd N. McAllister, Ph.D.

Cytograft Tissue Engineering
Novato, CA 94949
nico@cytograft.com

Luis M. de la Fuente, M.D.

Instituto Argentina de Diagnostico y Tratamiento
1122 Buenos Aires, Argentina

Drs. L'Heureux and McAllister report holding stock in Cytograft Tissue Engineering.

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