to treat the ascending aortic and arch pathology in the standard open surgical fashion and follow the progression of the descending thoracic aorta. As Dobrilovic and Elefteriades¹ expertly point out, expansion of the descending thoracic aorta after acute type A dissection may be a slow process. There may, however, be additional reasons to consider simultaneous hybrid repair in this situation.

Total arch replacement involves the use of deep hypothermic circulatory arrest (DHCA). The increased risks associated with this technique have been well documented, and eliminating DHCA for the treatment of acute Type A aortic dissections would potentially make this a safer and better tolerated procedure. Another alternative hybrid approach would be to repair the entry point tear in the ascending aorta with standard open surgical techniques (interposition graft or ascending conduit) and simultaneously bypass the great vessels with grafts off the newly completed ascending aortic graft. Simultaneous deployment of an endoluminal graft in an antegrade fashion through the ascending graft, across the aortic arch, and into the proximal descending thoracic aorta would accomplish a total arch reconstruction without the need for DHCA.³ This approach maximizes the advantages of endovascular technologies by making a complex procedure less invasive while stabilizing the true lumen of the descending thoracic aorta. We have shown that stabilizing the true lumen in the descending thoracic aorta is an active process that in time leads to progressive expansion of the true lumen and continued thrombosis of the false lumen.⁴ In addition to potentially preventing future complications and need for reoperation, stabilization of the true lumen and continued active true lumen expansion after thoracic endografting can potentially improve distal organ perfusion.

Hybrid approaches to complex aortic pathologies may allow us to offer surgical repair to patients with acute type A aortic dissection who might not otherwise tolerate DHCA. The less invasive advantages of simultaneous arch exclusion with an endoluminal graft after great vessel transposition could accelerate patient recovery and provide the added potential advantage of distal true lumen stabilization. I therefore believe that the surgical paradigm may be shifting toward hybrid approaches, not away from them.

Grayson H. Wheatley III, MD
Arizona Heart Institute
Phoenix, Ariz

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Reply to the Editor:

We appreciate the thoughtful commentary from Dr Wheatley. We are aware of the imaginative work being done in catheter-based treatment of aortic diseases at the Arizona Heart Institute.

There are certainly many clever ways to "manipulate" the anatomy of the aortic arch to make stent therapy feasible, and we applaud the exploration of these techniques. We disagree, however, with the undercurrent of fear of deep hypothermic circulatory arrest (DHCA) manifest in Dr Wheatley's letter.

DHCA is a proven modality in aortic surgery, with a vast clinical experience demonstrating its clinical utility and safety.¹⁻⁴ At our own institution, Dr Arjet Gega has just completed (for upcoming submission) a review of 400 patients operated on under "straight" DHCA, without any adjunctive retrograde or antegrade cerebral perfusion. This experience included all comers: ascending, arch, descending, and thoracoabdominal; elective and emergency; and ruptured and nonruptured. Overall mortality was 6.5%, stroke rate was 4.9%, and reexploration for bleeding was 3.9%. Cerebral protection was excellent, with most strokes embolic in origin. The supposed bleeding diathesis of DHCA is simply not a problem. It is not uncommon for us to find the morning's DHCA patient extubated, vi-

brantly conversant, and having a light supper by the time of evening rounds. DHCA need not be feared. At our institution we marvel at the protective abilities of this technique, and we are pleased to call upon them at every opportunity.

Current results for surgery under DHCA at many expert centers worldwide sets a standard that will be hard to exceed with clever extra-anatomic and catheter based modalities. In fact, it remains to be shown in careful analysis of large clinical series that the alternative modalities can even come close to meeting the excellent results of traditional, direct arch surgery under DHCA.

John A. Elefteriades, MD

Nikola Dobrilovic, MD

Arjet Gega, MD

Department of Cardiothoracic Surgery

Yale University School of Medicine

New Haven, Conn

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When less is more: Go slowly when repopulating a decellularized valve in vivo!

To the Editor:

We read with interest the recent article by Juthier and colleagues¹ describing the effects of granulocyte colony-stimulating factor (G-CSF) on decellularized xenogenic heart valves implanted in systemic circulation in sheep. The hypothesis was tested

Figure 1. A, Decellularized porcine heart valve impregnated with biodegradable poly-(hydroxy)butyrate to reduce xenoreactivity and improve hemocompatibility and mechanical performance for a limited time. B, Note that polymer impregnation process preserves porosity of decellularized ECM scaffold, so that repopulation with host cells is not disturbed.

that bone marrow cell mobilization by GCSF would facilitate *in vivo* repopulation with endothelial and smooth muscle progenitor cells; however, it was found that the valves actually deteriorated sooner than the same scaffolds in untreated animals. Juthier and colleagues¹ concluded quite appropriately that GCSF accelerated valve deterioration through increased inflammatory reaction, and they suggested searching for alternative strategies to improve scaffold recolonization. Our group has been tackling this very problem in the past, and we believe we have found a promising solution. In 2004, we reported on the biologic

and mechanical properties of biomatrix/polymer composite material for heart valve tissue engineering.² In essence, porcine aortic valves were enzymatically decellularized and coated or penetrated with a slowly biodegradable polymer with known favorable biocompatibility and hemocompatibility. By doing so, we produced valve scaffold tissue that induces less coagulation and complement activation *in vitro*, displayed favorable behavior in a rabbit aorta *in vivo* model, and, most importantly, gave superior results in terms of endothelialization and clot deposition on implantation in both pulmonary and aortic positions in

sheep. Moreover, polymer impregnation can also help improve the mechanical properties of the valve leaflet, which may be particularly important when enzymatic processes are used for decellularization.³ The polymer impregnation process does not involve glutaraldehyde- or formaldehyde-based fixation steps, so both the biologic and structural properties of the extracellular matrix (ECM) components are left intact, and repopulation with host cells is not hampered (Figure 1). It also masks platelet-activating moieties on ECM components, thereby reducing the risk of collagen-induced platelet aggregation during the early postimplantation phase.

Juthier and colleagues¹ convincingly showed that removal of all xenogenic cells without altering the biologic characteristics of the ECM components reduces the inflammatory response in sheep and improves *in vivo* repopulation with host cells. However, as they themselves pointed out, some immunogenicity of xenogenic ECM inevitably persists.⁴⁻⁶ Even the smallest amount of residual cell detritus can trigger cellular immune response, with macrophage invasion and subsequent blood vessel ingrowth, and the various ECM components possess an inherent immunogenic potential when exposed in a xenogenic setting. We were therefore not surprised to read that massive inflammatory stimulation by GCSF accelerated inflammatory valve matrix infiltration and structural deterioration. After all, the mobilization of (theoretically) beneficial bone marrow stem cells and endothelial progenitor cells by GCSF is secondary to the release of mature leukocytes, and Juthier and colleagues¹ elegantly demonstrated the substantial increase in white blood cell count even in the sheep model. Taken together, we believe that any proinflammatory action should be avoided soon after *in vivo* implantation of decellularized ECM conduits. The rapid failure of Synergrafts in children (with their pronounced inflammatory response to extracorporeal circulation) adds to the evidence.⁷ On the contrary, measures that help reduce the susceptibility of decellularized ECM conduits to cellular and humoral inflammatory are needed. Coating with biodegradable polymer is one such approach, masking proinflammatory components during the early postimplantation phase and thus buying time for vascular host cell re-

population with re-endothelialization and matrix turnover.

Christof Stamm, MD^a

Gustav Steinhoff, MD^b

Dept. of Cardiothoracic and Vascular Surgery
Deutsches Herzzentrum Berlin
Berlin, Germany^a

Dept. of Cardiac Surgery
Universität Rostock
Rostock, Germany^b

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Reply to the Editor:

We thank Drs Stamm and Steinhoff for their comments. In the field of tissue-engineered heart valves, the choice between synthetic and biologic (either allogeneic or xenogenic) scaffolds is a major concern. As have many others, we hypothesized that the best valve replacement remains a heart valve. Porcine heart valves have been used for decades in cardiac surgery with good clinical results, especially in terms of durability in elderly patients. In particular, hemodynamic behavior of the latest gener-

ation of porcine bioprostheses, the stentless porcine valves, was found to be similar to that of native aortic valves.

These scaffolds, however, need preimplantation treatment to avoid acute xenogenic rejection. Decellularization seems a promising choice, because it both induces a decrease of cell-induced acute rejection and may allow autologous cell recolonization. Our study suggests that nonenzymatic decellularization may be used without inducing mechanical failure of the matrix in vivo. Previous decellularization procedures, such as deep osmotic shock (with distilled water)¹ or use of trypsin and ribonuclease,² have resulted in graft failure.³ Adverse immune reaction was advocated; however, we observed that a less aggressive decellularization procedure did not induce mechanical failure after 4-month exposure in the systemic arterial strain, suggesting that the decellularization procedure was critical for the in vivo outcome.

Stamm and coworkers⁴ used an enzymatic decellularization procedure, but they reinforced the scaffold with a biodegradable polymer coating. Short-term results were satisfactory, but little is known about the long-term behavior of these polymers. Previous long-term studies on biodegradable scaffolds as heart valve substitutes have reported fibrosis, retraction, and graft dysfunction.⁵

As noted by Stamm and Steinhoff, coagulation and complement activation, with the risk of collagen-induced platelet aggregation early after implantation, are a major concern with decellularized matrices. We found no evidence of thrombus formation on implanted decellularized scaffolds, and thrombosis occurred only in a nondecellularized xenograft. However, it should be underlined that in our study all animals received aspirin therapy (500 mg daily), as in usual clinical practice with biologic valves.

Finally, our study suggests that xenogenic scaffolds decellularized through a nonenzymatic procedure do not induce matrix failure in a sheep model, and interestingly allow partial recellularization in vivo. Longer implantation studies are mandatory to confirm these mechanical results. Moreover, because autologous cell recolonization of these decellularized scaffolds remains only partial, other strategies to induce complete recolonization by proper autologous cells are needed.

André Vincentelli, MD, PhD

Francis Juthier, MD

Brigitte Jude, MD, PhD

Institut National de la Santé et de la
Recherche Médicale (Inserm) ERI-9,
Faculté de Médecine

and

Clinique de Chirurgie Cardio-vasculaire
Cardiologic Hospital
Lille, France

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Lung transplantation in a patient with Mounier-Kuhn syndrome

To the Editor:

We previously reported the first case of successful lung transplantation in a patient with Mounier-Kuhn syndrome.¹ The patient was a 59-year-old woman with a history of bronchiectasis of unknown etiology since childhood. The patient developed very severe obstructive lung disease and multiple episodes of pneumonia due to *Pseudomonas aeruginosa* that necessitated hospitalization. Computed chest tomography and bronchoscopy were diagnostic of Mounier-Kuhn syndrome. The patient underwent bilateral lung transplantation, and the degree of bronchomegaly was not as pronounced as the tracheomegaly and posed little difficulty during transplantation. The patient had a difficult postoperative course, with multiple failed extubations, *P aeruginosa* pneumonia, and prolonged respiratory failure necessitating tracheostomy. The pa-