branching technique for the stent graft placement still carries some morbidity and mortality risk. The optimal use of endovascular stent graft for mycotic aortic aneurysm needs to be clarified in further studies.

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Grey zone area for Glenn and future Fontan candidates

To the Editor:

We enjoyed the very good article by Scheurer and colleagues.¹ We have a few comments.

Inhaled nitric oxide produces significant reduction in Glenn pressures and improvement in systemic perfusion and pulmonary gas exchange in patients with marked increases of Glenn pressures after bidirectional Glenn anastomosis. Patients who do not respond should be investigated for an anatomic lesion.²

Glenn shunt mortality was higher with surgical intervention before age 120 days but was not affected by surgical intervention during the respiratory virus season. Operations in the youngest age groups might adversely affect mortality.³

There were no differences in morbidity and mortality outcomes after the bidirectional Glenn operation between the Norwood-Right ventricle to pulmonary artery and Norwood-Blalock Taussig Shunt groups. Despite younger age at presentation, the Norwood-Right ventricle to pulmonary artery patients had better growth rate, which might have contributed to the similar postoperative outcomes.⁴

Atrial septal defects should be left open for all patients with severe right heart hypoplasia and in patients with postbypass right atrial pressures of more than 12 mm Hg.⁵

The advantages of incorporating a hypoplastic ventricle to partly support the pulmonary circulation are the following: (1) ability to increase the cardiac output; (2) adaptation to exercise; (3) maintenance of pulsatile flow in the pulmonary circulation; (4) flexibility to increased pulmonary vascular resistance; (5) circulation at low venous pressure in the Inferior Vena Cava system; and (6) capability of a hypoplastic right heart to adequately handle the reduced preload.⁶

There is a major debate for the gray-zone high-risk patients who do not fulfill the Choussat commandments. The current protocol in those patients is first to review all the data in detail. Full consideration is given as to whether there are any surgically (or interventional) correctable lesions, such as atrioventricular valve regurgitation amenable to repair or isolated stenoses or hypoplasia within the central pulmonary arteries. Ventricular function, if impaired, might be optimized by altering medical management (vasodilators, diuretic therapy, and trial of oral enoximone, if appropriate). Evidence of increased pulmonary vascular resistance is treated with a course of pulmonary vasodilator therapy (sildenafil or bosentan). The patients are then reassessed for suitability for Fontan completion. The evidence would suggest that only 2 of the original 10 commandments of Choussat carry significant weight for both early and late outcome over the Fontan procedure and that they are preoperative ventricular function and preoperative pulmonary artery pressures of greater than 15 mm Hg.⁷

We found that right ventricular morphology; single ventricle; intact septum; semilunar valve abnormalities; diastolic dysfunction; myocardial hypertrophy, dilatation, or both; older age; bilateral superior vena cavae; pulmonary airway disease; and hypotonia all carry a worse prognosis and a tough postoperative course.

To be right ventricular morphology; single ventricle; intact septum; semilunar valve abnormalities; diastolic dysfunction; myocardial hypertrophy, dilatation, or both; older age; bilateral superior vena cavae; Interrupted IVC; pulmonary airway disease; and hypotonia all carry a worse prognosis and a tough postoperative course.

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Hypertension in coarctation

To the Editor:

I read with great interest the article by Hager and associates¹ on coarctation repair. The authors note that the majority of patients remained hypertensive in the long term, even after coarctation repair. This very interesting phenomena, however, has to be examined in the mirror of the little known fact that most patients are often hypertensive *below the level of the coarctation even before the coarctation is repaired!* While pressure measurements indeed show significantly higher pressures above the coarctation, the mean arterial pressure below the coarctation is also higher than that of an average normal subject. Thus, arterial hypertension

observed after coarctation repair is not a new phenomenon, but is simply the continuation of the neurosympathetic process that existed before the coarctation repair.

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Reply to the Editor:

Robicsek outlined in his letter to the Editor in response to our article¹ that arterial hypertension exists distal the coarctation even before coarctation repair. Hypertension in the long-term follow-up is simply the continuation of this neurosympathetic process.

Previously published data from our group² on blood pressure and aortic distensibility in neonates with coarctation before and after surgical repair did not show poststenotic hypertension before repair in general. However, we totally agree with Robicsek and other authors^{3,4} that inborn processes not touched by current modes of repair are also responsible for hypertension in the long-term follow-up after successful repair. We believe that the starting point of the pathophysiologic chain is the inborn alteration of the arterial wall with elastic fiber fragmentation, fibrosis, and cystic medial necrosis, which are later exaggerated by existing hypertension. This causes the increased stiffness most pronounced in the central elastic arteries, the blunted baroreceptor reflex, and the neurosympathetic activation. However, the novelty of our study was the extent of this phenomenon. Our relation to age showed that arterial hypertension has to be expected in almost all patients after coarctation repair in older ages. Close surveillance and aggressive treatment of arterial hypertension might prevent further cardiovascular disease.

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Heart valve tissue engineering: Research should proceed along validated routes

To the Editor:

In their article focusing on in vivo autologous recellularization of a tissue-engineered heart valve, Vincentelli and colleagues¹ raise 2 main questions: (1) Which are the best candidates for scaffold repopulation? (2) Does direct injection of cells into the scaffold guarantee adequate cellular recolonization?

According to the cell type chosen for scaffold seeding, the adoption of nonselected bone marrow-derived mononuclear cells was associated with early degeneration with thickening and retraction of the cusps, growth of fibrotic pannus along the suture lines, and thickening and calcification of the wall conduits. Histologically, a marked inflammatory response with extracellular matrix disarray and macrophage infiltration both in the adventitia and the media layers were observed, along with a loss of the proper collagen allocation between the

ventricularis, spongiosa, and fibrosa of the leaflets. Additionally, a significant increase of both transvalvular and distal gradients were recorded at 4-month follow-up echocardiographic analysis. On the contrary, scaffolds repopulated with mesenchymal stem cells did not evidence either degenerative notes or inflammatory reactions.

These findings might suggest “the onset of a structural deterioration of the scaffold in the [bone marrow–derived mononuclear cell] group and a protective effect of the injections of [mesenchymal stem cells].”¹ We are concerned that such conclusions seem audacious because the study suffers from a main limitation represented by the cell-seeding modality. In fact, the authors, looking for an answer to question number 2, choose to inject the cells directly into the decellularized scaffold (onto the conduit walls and valve annulus, excluding the leaflets), instead of adopting a biomimetic environment.

The adoption of this alternative technique, which has been derived from the myocardial setting,² represents an innovative concept for the valvular field and therefore requires a careful validation. Fluorescent cell tracking, which was performed on 4 of 14 animals in the first postoperative week, evidenced, on day 1, the cell persistence onto the injection site and, on day 7, a few scattered cells into the matrix, the arterial wall, and the leaflets. Moreover, nonlabeled cells of host origin were found.

Is this enough to say that “in situ injection of bone marrow cells into a porcine decellularized scaffold before implantation enhanced the in vivo recolonization and induced full re-endothelialization”?¹ First, endothelialization and scaffold repopulation do not coincide. Even bioprostheses undergo an endothelialization process of the inert components once implanted. Second, the process of repopulation implies an architectural and hierarchic cell-specific distribution along the leaflet’s ventricularis, spongiosa, and fibrosa,³ which was not observed in this experience.

In the article’s “Discussion” section, the authors themselves affirm that they had no direct evidence that cells would grow inside the matrix. According to the hypothesis that injected cells might enhance autologous recellularization, further evidence is needed to draw definite conclusions, and the provided results do not concretely support the initial hypothesis.