reconstruction. In our particular cases, little normal tissue was available to perform leaflet repair because of the numbers of procedures previously performed. Likewise, Zaidi and colleagues¹ reported the majority of failures in patients with multiple previous procedures. Could the inflammatory infiltration of the ECM be a result of adjacent damaged tissues, or perhaps a response to a proinflammatory state (ie, concomitant left ventricular assist device)? In contrast to all other patch materials, an ECM bioscaffold is intended to be replaced by the body over time. The local and systemic milieu in which the bioscaffold is implanted could thus be more important than simply its use for repairing one heart structure or another.

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Reply to the Editor:

We thank McConnell and Hibino for their interest in our article and for contributing more information about the behavior of CorMatrix used for valve repair in congenital heart defects.

Similar to our experience, neither of the cases shows histologic evidence

of remodeling to any structure resembling native valve tissue. The hematoxylin and eosin histologic staining from the case of reoperation at 158 days (Figure 1, A, in the letter of McConnell and Hibino) shows residual CorMatrix surrounded by a mild chronic inflammatory response composed of predominantly macrophages, a compact fibrin or proteinaceous layer, and thin pannus overgrowth. The compact surface fibrin and pannus is the likely anatomic explanation for the slightly thicker than normal valve cusps. The hematoxylin and eosin histologic staining from the case of reoperation at 339 days (Figure 1, B, in the letter of McConnell and Hibino) shows only unmodified CorMatrix with few or no cells and surrounded by loosely organized fibrin. McConnell and Hibino have expressed some ambiguity regarding the nature of the tissue (residual CorMatrix extracellular matrix vs tissue remodeled to collagen); however, the tissue does not contain any viable cells (as a remodeled tissue would) and does have the histologic appearance of CorMatrix that we have observed after only a few weeks in situ (before it could possibly have been remodeled to native collagen). The appearance is also in keeping with our clinical and experimental experience of the histology of unimplanted CorMatrix. These figures reinforce the fact that CorMatrix in the distal leaflet remains intact, with minimal infiltration by host cells, as long as 1 year after implantation.

As we and others have noted, inflammatory cells predominantly enter the prosthetic leaflet from its basal end, which is in contact with native tissue. Because McConnell and Hibino have described the implantation of an extracellular matrix cylinder valve after nearly total removal of diseased native valve tissue rather than surgical valvuloplasty, we would not expect to see the same degree of inflammation in the part of the leaflets shown in the figures as a result of the fact that these may have

been quite distant from native tissue. In fact, most of the inflammation that we observed was centered in the native tissue adjacent to the CorMatrix, with extension as a wave into the CorMatrix over various distances. In the time since our article was accepted, we have seen 4 additional cases in our clinical and consultation practices with similar histologic findings at the material-tissue interface. It would be interesting to see histologic sections from the surgical anastomosis between the native tissue and the CorMatrix in the cases described by McConnell and Hibino, because this may show inflammation that is more characteristic of our experience. Specifically, McConnell and Hibino have described the valve failures at the neocommissural attachments to the aorta and at least partially attributed the failures to technical reasons; it is also possible that inflammation at these attachment sites may have led to weakening of the tissues in these areas and contributed to the failures.

Although there is increasing evidence for the importance of endothelial-to-mesenchymal transformation for maintaining the interstitial cell population in native valves, it is unclear whether this transformation occurs in prosthetic leaflets. The neoendothelialization or pannus formation that we described, and which is shown in Figure 1, A, of the letter of McConnell and Hibino, seems more consistent with encasement of foreign material such as one sees in pannus overgrowth onto the cusps of a stented surgical bioprosthetic valve than with remodeling toward a functional leaflet.

We did not observe any significant inflammatory response after the use of autologous pericardium in our patients, strongly suggesting that the inflammation was related more to the presence of CorMatrix than to damaged native tissue, which would be present in both cases. Although we did not investigate this specifically, none of our patients seemed more predisposed toward an inflammatory state than any other patient

exposed to cardiopulmonary bypass (eg, no patient was supported with extracorporeal membrane oxygenation or a ventricular assist device).

As McConnell and Hibino point out, CorMatrix is a bioscaffold and the hope is that it will be remodeled and replaced by native tissue. That we saw minimal evidence for this was most concerning. Figure 1, B, in the report of McConnell and Hibino extends these observations out past 1 year. We would strongly encourage clinicopathologic studies of explanted CorMatrix material from additional centers where the material is in clinical use for valve repair in congenital heart disease.

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INSUFFICIENCIES OF DOWNSIZING RING ANNULOPLASTY IN TREATMENT OF FUNCTIONAL ISCHEMIC MITRAL REGURGITATION To the Editor:

The recent publication by Rabbah and colleagues¹ directs attention to functional ischemic mitral regurgitation (MR; Figure 1, A) and underlying mechanisms that have not as yet been definitely addressed. The desired criterion standard surgical treatment has not yet been documented, and this issue requires further research. We appreciate Rabbah and colleagues¹ for their efforts and would like to make some contributions.

The downsizing mitral annuloplasty (DSMA; Figure 1, B) is a surgical technique preferred by many surgeons that is effective in correcting annular dilatation. It is not effective, however, for left ventricular (LV) equatorial dilatations. We would like to discuss the DSMA, because it may

be a reason for the poor long-term outcomes. This hypothesis has been supported by Magne and associates,² who advocate that persistence of MR early after DSMA is related to the increased posterior leaflet tethering potentially caused by prosthetic ring implantation, which anteriorly displaces the posterior leaflet and reduces its mobility. From a different point of view, we think that there are two mechanisms causing poor outcomes. The first and initial deleterious effect of DSMA is in the isovolumetric contraction phase (IVCP) of the cardiac cycle, when both aortic and mitral valves are in the closed position (Figure 1, A). Ventricular pressure is sharply raised up to diastolic tension according to the volume–pressure relationship of the LV. In this period, the intraventricular volume is constant; DSMA, however, reduces the inflow cavity of the LV, which also results in further dilatation in the equatorial axis (Figure 1, B). The dilatation further increases the tethering forces on the chordae of mitral leaflet because there is no ejection in the IVCP yet. This is the triggering vicious circle, which continues until the surgically created coaptation line is broken down. Once the coaptation line has disappeared by means of spherical dilatation caused by DSMA in adverse ventricular remodeling, there is recurrent MR, and after this stage the second phase (never ending vicious circle) is engaged and gains autonomy. In each cardiac cycle, recurrent MR further causes LV dilatation, which in turn results in increased LV sphericity.

Rabbah and colleagues¹ reported, “The large patch procedure with true-size annuloplasty resulted in the best improvement in coaptation length, and decreased tethering forces on the chords of posterior papillary muscle when compared with the functional ischemic MR group.” In another study by Magne and associates,³ it was demonstrated in a “non-persistent MR group” that the

coaptation depth was smaller than that in a “persistent MR group” (8.1 ± 2 mm vs 11.7 ± 2 mm; $P < .01$). Moreover, the angle between the annular plane and leaflets was smaller than in the persistent MR group ($36^\circ \pm 7.5^\circ$ vs $53^\circ \pm 6^\circ$; $P < .01$). In other words, deeper coaptation depth and larger angle in the persistent MR group mean more downsizing, which explains the greater tethering in the IVCP. This result proves that the increased tethering in IVCP is the result of increased equatorial axis of the LV.

We believe that the never ending vicious circle can be broken by breaking the triggering vicious cycle with true sizing and patch augmentation, which may result in better outcomes. This point of view may be helpful for surgeons to improve the poor outcomes of functional ischemic MR in long-term follow-up.

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