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EDITORIAL COMMENTARY

Responsible innovation

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See related article on pages 2216-25.

Innovation in both operative techniques and devices has been a hallmark of thoracic surgery since its inception. Included has been the search for the optimal prosthetic patch, a quest that has been ongoing since the earliest years of congenital heart repairs. A biologic scaffold that allows recipient cellular ingrowth and remodeling with subsequent appropriate native tissue function and growth potential would be the ultimate solution to the patch dilemma. When animal studies suggested that an extracellular matrix made from the submucosa of porcine small intestine (CorMatrix; CorMatrix Cardiovascular, Inc, Roswell, Ga) provided a bioscaffold that allowed ingrowth of “organized and healthy tissue,” optimism, perhaps out of proportion to the evidence base, ensued. Written information provided by the manufacturer¹ further suggested that their acellular biomaterial could be expected to regulate cell adhesion, cell differentiation, cell division, and cell migration.

CorMatrix was initially recommended for pericardial reconstruction and, again according to the company's brochure, “Clinical data suggest complete reformation of the pericardial space, including an intact mesothelial lining.” Interestingly, a recent publication, “Histology of CorMatrix Bioscaffold 5 Years After Pericardial Closure,”

reported that with regard to the histologic analysis of the explanted pericardial patch “no evidence was found of an endothelial lining on the putative visceral face of the sample.”² This suggested that further investigation into the behavior of CorMatrix, even when used in its most fundamental application, was warranted.

It seems fair to say that evidence showing that CorMatrix remodels and restores function when used for cardiac valve reconstruction is at best scanty and is based primarily on animal studies (where in many cases the bioscaffold was allogeneic) and clinical reports with relatively small numbers of patients and short follow-up describing echocardiographic findings of repaired valves.³ This reinforces the importance of this article by Zaidi and colleagues⁴ from Boston Children's Hospital, which gives us histologic information on the status of cardiac valve patches explanted after failed valve repairs.

The study has several weaknesses recognized by its authors. The overall number of patients with CorMatrix valve repairs was small, and the number of explants available for histologic study was even smaller ($n = 9$). This small sample was also divided between mitral ($n = 6$) and aortic ($n = 3$) reconstructions. The duration of implantation was short in a number of patients, with only 5 of 9 patches in situ longer than 3 months (101-261 days). The study thus can't address favorable remodeling that might be occurring at a later point after implantation, because we have no data on the status of the CorMatrix in patients with a more durable valve repair.

With that said, this is the largest experience with human explants of CorMatrix used for valve repair, and the histologic findings are consistent. There was an intense inflammatory response to the patches that did not abate as late as 9 months. In some cases, this was associated with a fibrous peel of neointima that appeared to be encasing the CorMatrix. This mixed inflammatory infiltration is very concerning and in keeping with histologic findings in previously reported human cases.⁵ Only in the material with the

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longest duration in situ was any significant resorption of the bioscaffold seen. This is unexpected. Most disturbing was the finding that there was little to no remodeling to form tissue resembling a 3-layered native valve as late as 9 months after implant. In fairness, there is no well-established evidence base describing the expected time interval to remodeling, although animal data (of uncertain applicability) would suggest an interval as short as 3 to 4 months.

So what are we to think? According to written materials provided by the manufacturer, CorMatrix Cardiovascular,¹ CorMatrix ECM Bioscaffold has Food and Drug Administration clearance and a European CE Mark to be sold for pericardial patch repair and reconstruction, cardiac tissue repair, and carotid repair. They state, “It is an acellular biomaterial that does not encapsulate when surgically implanted, but is gradually remodeled, leaving behind organized healthy tissue.”¹ Is this really true? One wonders what evidence the Food and Drug Administration considered in approving CorMatrix to be used for the wide range of potential applications that might be included under the descriptor “cardiac tissue repair.”

This report by Zaidi and associates⁴ brings into question a number of issues regarding the performance of

CorMatrix and reminds us that with innovation comes a responsibility to examine and document outcomes carefully to be sure that what we are doing is at least as good if not better for our patients than alternatives. It is to be hoped that others who use CorMatrix will be as diligent as the group at Boston Children’s and will document their results when the opportunity arises. Innovation, yes—as long as it is introspective, carefully studied, and reasonably cautious.

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