

Letter to the Editor

In response to

Wilhelmi MH, Bara C, Kofidis T, Wilhelmi M, Pichlmaier M, Haverich A. Long-term cardiac allograft valves after heart transplant are functionally and structurally preserved, in contrast to homografts and bioprostheses. *J Heart Valve Dis* 2006;6:777-782

It was with great interest that I read the thought-provoking article by Wilhelmi MH, et al. (1) in the November 2006 issue of the *Journal of Heart Valve Disease*. The study addresses the curious phenomenon that, while homograft aortic valves are likely to undergo degenerative changes and eventually functional deterioration over time, those in transplanted hearts retain long-term normal morphology and function.

Although this phenomenon is indeed worth calling attention to, I disagree with the authors' hypothesis that the reason for these findings is that, while the valves in transplanted hearts are protected from rejection by pharmacological means routinely received by patients, implanted homograft aortic valves are not; *ergo propter*, immunosuppressive therapy may be the solitary reason for preservation of the integrity of aortic valves. This hypothesis is highly dubious for several reasons:

First, we do not know of any study proving conclusively that degenerative changes in allograft valves could be prevented by immunosuppressive therapy. Second, the authors disregard the process which is an important - if not the most important - factor in the deterioration, namely *stress*. The aortic valve is a delicate structure which is subjected to significant stresses of folding, pressure and shear, and these are mitigated by complex stress-releasing mechanisms inherent to the functional integrity of the valve's anatomically and biologically perfect native aortic root and left ventricular outflow tract (2). Indeed, an imbalance between the stress exerted and the degree of this protection has been identified as the principal cause of degenerative aortic valve disease (3).

The aortic valve which has been transferred within the transplanted heart does indeed carry with it this inherent protection. The solitary implanted valve does *not*. The latter also lacks connection to the vasa vasorum and to the lymph microcirculation, which may be another less important reason for the limited 'survival' of transplanted, solitary allograft valves.

It is as simple as that.

References

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Reply

We are grateful to Dr. Robicsek for the interest in our article entitled, 'Long-term cardiac allograft valves after heart transplant are functionally and structurally preserved, in contrast to homografts and bioprostheses'.

In his recent letter, Dr. Robicsek raised some interesting questions regarding the manuscript, to which I would like to respond and, hopefully, answer. First, he asked for an evaluation of hemodynamic parameters during the process of allograft deterioration which, as he wrote, are not evaluated in broader extension in our present article. It is correct that we did not evaluate this in any form of in-vitro model. However, previously we have performed studies on tissue-engineered heart valves, as well as immunological investigations on explanted deteriorated allografts. In these studies we were able to show that inflammatory reactions play a pivotal role in the process of tissue/valve deterioration (1-3). Furthermore, we implanted tissue-engineered heart valves in infants and observed these valves for more than 3.5 years. All of these latter-mentioned valves showed a good preserved function over time, and gave no hint of any valvular/functional deterioration. Just the opposite, in fact - at the time of implantation in infants we were able to show that these valves grew within, and in parallel to, the host organism (4). For that, the only difference between these tissue-engineered valves and allograft valves is the process of preservation and tissue origin, and we

surmise that the hypothesis of immunological reasons for deterioration, and in turn that the possible administration of anti-inflammatory medication might have a positive influence on the fate of these valves, is justified.

Dr. Robicsek also commented about the formation of a neovasculature within allograft valves. In all of our previously published studies, we sought - and identified - a vascularization process over time. What we found was that: (i) neovessels begin to grow within these grafts very soon after implantation; and (ii) as in every inflammatory process, a form of pathological vessel ingrowth ('overvascularization') could be observed in parallel to the formation of inflammatory relevant adhesion molecules expression and leukocytic cellular infiltrates (1-3,5,6).

References

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