


Discussion

Dr John E. Mayer, Jr (Boston, Mass). First let me congratulate Hawkins and colleagues on a clear presentation of important work. The finding that decellularized homografts do not elicit the same antibody response as cellular grafts is of significant interest, particularly for patients who ultimately may require transplantation. I have found it interesting from a historical and scientific standpoint how our pendulum has swung from the concept years ago, when we were told that preserving the viability of cells on homografts was critical to their long-term function, to the other end of the spectrum. Now we’re being told that decellularization will actually be a better process.

I have no specific comments about the antigenicity. And in some ways I think that the findings are almost what one would predict. But if one disregards those immunologic considerations, I wondered about a few things.

First, Dr Hawkins, you have shown that the explanted graft of homograft material was cellularized, but we don’t really know what kind of cells they are. In particular, I wondered whether you had any notions about what the cells on the luminal surface were like. Have you done any studies on whether they’re true endothelial cells? One of the fundamental differences between human beings and most experimental animals is that the ability to reendothelialize seems to be much less, growing in a few millimeters from either end of the anastomosis between the artificial material and the true native vessel. I wondered if you had any information about that.

Second, on the basis of your clinical experience with this material, could you comment on the effects of the decellularization process on the structural and hemodynamic performance of the implanted material?

Dr Hawkins. Actually, we did do some special stains in this case. I hesitate to make too many conclusions on the basis of a single patient, but that happens to be all that I have. We did do stains for endothelial cells and could not find any when we looked at multiple areas with multiple stains. There is no doubt that there are cells present. I could conjecture that they’re probably fibroblasts. But are they fibroblasts that function? Not only do we need, at least theoretically, a graft that has normal cells that have grown into it, we need those normal cells to function to the point that they participate in protein and collagen turnover. So we don’t really know the answer to the question of whether these cells are functional. My guess is that they’re probably fibroblasts, and at least in this case they were not endothelialized at 4 months.

Your second question has to do with my clinical experience with the hemodynamic function of these decellularized grafts. I think that a conclusion from the data that I presented today would be premature. There is no way to know at this point what the hemodynamic data are of these valved allografts versus standard. They appear to be equivalent. But are they biomechanically identical to the human valve? I don’t know. I think that’s the claim, but I don’t think we really know yet. My own personal opinion is that the tissue seems—and I stress that this is an anecdotal observation—to stretch more and to be a bit more elastic than standard allograft material; however, I believe that the experimental data from the company and animal data indicate that it’s biomechanically the same.

Dr W. Steves Ring (Dallas, Tex). Do you have any data on what might be an appropriate third control group? That would be patients who undergo bypass surgery. Even though you’ve filtered your blood, what’s the elevation in the flow PRA in that particular group of patients where you don’t have a homograft?

Dr Hawkins. When we did our original studies back in 1996, we did a control group of about 14 or 15 children who underwent a variety of cardiac procedures that did not include implantation of a homograft but did include bypass with Leukopore-filtered irradiated blood. Their PRA at 1 month and 3 months was 0. We did not do the 12-month time point, because we considered that it was probably not ethical to put them through yet another blood sampling for to check a level that was 0 at 3 months. So we have done such a control group. I did not include it in this report for the sake of time.

Dr Marshall L. Jacobs (Philadelphia, Pa). Earlier today Dr Zahid Amin, in discussing acute homograft conduit failure, identified persistent postoperative fever as a marker or predictive factor with an odds ratio of 9.1, or something that seemed rather compelling. It’s a simple observation to make. Was there any difference in the incidence of persistent postoperative fevers in your decellularized patient group as compared with your historical control group?
Dr Hawkins. We did not look at that specifically, Dr Jacobs, but I think that’s a good question. I’ve always regarded fever in patients with an allograft as somewhat mysterious. There are many causes for this. The central question that I think we’re all asking is about the role of immunologic factors in valve failure. We know that there’s an immune response, with 100% of the patients having HLA antibodies; however, not 100% of the valves fail acutely. Thank goodness. And so the exact role of immunology in this is difficult to sort out. Perhaps a valve that is nonimmunogenic will allow us to sort out exactly whether failure is due to immunology or to all these other factors that Dr Amin discussed.