follow surgical oncologic principles and should be regarded as a bailout procedure and used judiciously.

Raja M. Flores, MD
Division of Thoracic Surgery
Mount Sinai School of Medicine
New York, NY

Reference

1. Flores RM, Ihekweazu U, Dycocco J, Rizk NP, Rusch VW, Bains MS, et al. Video-assisted thoracoscopic surgery (VATS) lobectomy: catastrophic intraoperative complication. *J Thorac Cardiovasc Surg.* 2011;142:1412-7.

doi:10.1016/j.jtcvs.2012.03.045

WILL THE REAL CULPRIT OF HETEROGRAFT VALVE CALCIFICATION PLEASE STAND UP?

To the Editor:

Sinha and colleagues¹ are not the first to implicate glutaraldehyde as a culprit for tissue valve calcification. Although they are to be commended for their careful methods and the suggestion that glutaraldehyde concentration and exposure times appear to correlate with the degree of calcification, they unfortunately failed to reach far enough back into the literature to recognize that most of their questions had already been answered by others.² A closer look at the literature might also have led these researchers to arrive at a different conclusion; that is, calcific degeneration of heterograft tissues is primarily an immunologic phenomenon.

Alain Carpentier and his wife Sophie, a biochemist, are given credit for the introduction of aldehyde chemistry to the modern manufacture of heterograft tissue valves.³ At the time, they did not advance an argument that aldehyde preservation rendered heterograft tissues nonimmunogenic. That perception belongs to perspicacious marketing departments within the tissue valve industry. The observation that calcific degeneration of heterograft valves is an age-related

phenomenon was an early and important clue to the problem of tissue valve durability.⁴ These issues notwithstanding, the Carpentiers' discovery had already spawned the multibillion dollar industry of heterograft tissue heart valves.

More than 30 years ago, Salgaller and Bajpai⁵ detected both cellular and humoral immune responses to glutaraldehyde-treated and untreated bovine pericardium. Their data provided the first real proof that glutaraldehyde-preserved heterograft tissues are not biologically inert and remain antigenic. The association between a smoldering immune response and tissue valve durability was never widely recognized, however, and glutaraldehyde continued to be the presumed cause of heterograft calcification, leading researchers and companies to search for new tissue treatments designed to retard calcification.

Love and associates⁶ first described the successful use of autologous pericardium briefly treated in 0.6% glutaraldehyde for use as a stent-mounted valve replacement. Since this introduction, multiple investigators have reported wide success with the use of autologous pericardium briefly treated in 0.6% glutaraldehyde for the replacement of semilunar heart valves⁷ and the repair of damaged and shortened mitral valve leaflets.⁸ All these techniques have proved durable, and in none of the published experiences, including those with pediatric or very young patients, has calcific degeneration been considered a limitation.

The more than 20-year clinical experience with autologous pericardium briefly immersed in glutaraldehyde and used for valve reconstruction should finally dispel any perception that aldehydes are directly responsible for calcific degeneration of tissue valves.

Charles S. Love, BA
Spot On Medical, LLC
Santa Barbara, Calif

References

1. Sinha P, Zurakowski D, Kumar TK, He D, Rossi C, Jonas RA. Effects of glutaraldehyde concentration, pretreatment time, and type of tissue (porcine versus bovine) on postimplantation calcification. *J Thorac Cardiovasc Surg.* 2012;143:224-7.
2. Fishbein MC, Levy RJ, Ferrans VJ, Dearden LC, Nashef A, Goodman AP, et al. Calcifications of cardiac valve bioprostheses. Biochemical, histologic, and ultrastructural observations in a subcutaneous implantation model system. *J Thorac Cardiovasc Surg.* 1982;83:602-9.
3. Carpentier A. From valvular xenograft to valvular bioprosthesis (1965-1977). *Med Instrum.* 1977;11:98-101.
4. Dunn JM. Porcine valve durability in children. *Ann Thorac Surg.* 1981;32:357-68.
5. Salgaller ML, Bajpai PK. Immunogenicity of glutaraldehyde-treated bovine pericardial tissue xenografts in rabbits. *J Biomed Mater Res.* 1985;19:1-12.
6. Love JW, Calvin JH, Phelan RF, Love CS. Rapid intraoperative fabrication of an autologous tissue heart valve: a new technique. In: Bodnar E, Yacoub M, eds. Proceedings of the Third International Symposium on Cardiac Bioprostheses. New York: Yorke Medical; 1986:691-8.
7. Chan KM, Rahman-Haley S, Mittal TK, Gavino JA, Dreyfus GD. Truly stentless autologous pericardial aortic valve replacement: an alternative to standard aortic valve replacement. *J Thorac Cardiovasc Surg.* 2011;141:276-83.
8. Chauvaud S, Jebara V, Chachques JC, el Asmar B, Mihaileanu S, Perier P, et al. Valve extension with glutaraldehyde-preserved autologous pericardium. Results in mitral valve repair. *J Thorac Cardiovasc Surg.* 1991;102:171-8.

doi:10.1016/j.jtcvs.2012.01.085

Reply to the Editor:

We thank Mr Love for responding to our article¹ and for emphasizing the importance of immune mechanisms in heterograft calcification. We are in agreement that aldehyde treatment is just one of several factors that can exacerbate calcification of implanted tissues. In the clinical setting of pediatric cardiac surgery, where autologous pericardium is often used and immune mechanisms are presumably not so important, however, it is the factor that can be most readily modified. Unfortunately, our animal model was not suited to autologous pericardium implantation.

We strongly disagree with Mr Love's assertion that calcific degeneration never occurs in the pediatric setting when glutaraldehyde-treated autologous pericardium is used for