Bioprosthetic Heart Valves: The Past, Present, and Future

David’s life was saved— and then taken— by medical techniques owed to our animal neighbors. A half century ago, the first successful xenotransplant, or a cross-species transplant, of an aortic valve in a human was performed. Although the procedure initially suffered a 45% one-year success rate, the advent of glutaraldehyde-fixed bioprosthetic heart valves vaulted that percentage to 89%, allowing for their commercialization. However, surgeons soon realized grave problems with calcification of these valves, and my uncle was among the indicative data points.

As a child, he was diagnosed with an aortic coarctation, or narrowing of a segment of the aorta, the artery carrying oxygenated blood for all of the body’s organs. Surgery was performed to replace this constricted area with a synthetic graft. This procedure allowed David to grow into a broad-shouldered young man, but due in part to such prosperity he outgrew this synthetic graft as the graft did not expand with the developing aorta. When subsequent surgery was performed, the heart was found to be hypertrophic or oversized, presumed to be the consequence of the increased difficulty the left ventricle faced in pumping blood through the again constricted aorta. The battery of following tests also revealed an insufficiency (regurgitation) of the aortic valve where the valve between the left ventricle of the heart and the aorta failed to properly close, causing a backflow of blood.

My young uncle was presented with two options for heart valve replacement: bioprosthetic or mechanical. Mechanical valves require continual anticoagulation treatment (due to their high risk of causing thromboembolism) and thus are less ideal for young candidates. Provided this information, my grandparents selected the bioprosthetic heart valve (BHV) for their child, built with porcine heart valves that were treated with glutaraldehyde. After a successful surgery, prospects seemed up from there; however, he soon suffered a catastrophic
stroke, undoubtedly the result of thromboembolism created by the valve. His death was likely preventable given further research with animals.

Young recipients of BHVs like David have been shown to exhibit excessive destruction of their new valves because of the increased immunity and metabolism of calcium in younger persons. A particular hurdle is the α1, 3 galactose (Gal) antigen common in pig tissues that is targeted by human IgM antibodies in an immune response, a connection evidenced by much greater calcification of tissue from wild pigs than GTKO pigs (McGregor et al., 2013). GTKO pigs have been genetically engineered to have the gene for α1, 3-galactosyltransferase “knocked out”. Yet despite the success of eliminating the Gal antigen hurdle, other barriers of unhindered xenotransplantation remain. Thus, for example, pigs have been engineered to be transgenic for human complement-regulatory proteins, anti-inflammatory proteins, and coagulation-regulatory proteins, edging nearer to porcine valves ideal for transplantation into humans. All of these methods owe their development to extensive animal testing, in particular the ultimate phase of xenotransplantation into non-human primates.

Although, the removal of the Gal antigen from porcine transplants is a major stride in the development of obstacle-free xenotransplantation, it is most significant in that it paves the endless road for similar techniques in the future. Developments like genetic engineering that rely heavily upon our animal neighbors have applications in medicine far beyond transplantation, far beyond saving just my uncle’s life.
References Cited


