main conclusions seem to be that (1) performance of the Björk-Shiley valve is similar to that of other mechanical valves, (2) modifications in valve design (i.e., the introduction of the convexo-concave disc) have not reduced the threat of valve thrombosis, and (3) elective explantation of any of these valves (for risk of outlet strut fracture) is not warranted.

Inasmuch as my colleagues and I²⁻⁷ have published a number of papers on the long-term results with the Björk-Shiley valve based on the experience with more than 3000 valves, with a 99% follow-up covering more than 17,000 patient-years and with postmortem examinations in 75% of all fatalities, I would like to add some perspective to two of their conclusions:

I found that in 809 mitral valve replacements the actuarial incidence of valve thrombosis was almost sixfold lower among 451 patients with convexo-concave valves than among 358 patients with spherical disc valves ($p < 0.0005$). This reduction in valve thrombosis was achieved without any change in the incidences of embolism or anticoagulant-related bleeding, probably reflecting an unchanged level of the anticoagulant treatment over the years.² In our experience with 1758 aortic valve replacements³ there were no differences in thromboembolism with different valve models. The findings in the Mayo clinic series¹ seem similar to ours; *all* valve thromboses in mitral valves occurred in spherical disc valves whereas 20% of aortic valve thromboses occurred in convexo-concave valves. The convexo-concave prostheses constituted approximately 30% of all aortic prostheses in the Mayo series, but with a much shorter follow-up. In conclusion, and in contrast with the authors' statement, I believe that the findings by Orszulak and associates corroborate our findings that the convexo-concave design in fact dramatically reduced the risk of valve thrombosis in *mitral* valves. Inasmuch as the complication was mainly a mitral valve problem, the importance of this finding should not be underestimated.

Even though the convexo-concave design probably reduced the risk of valve thrombosis among mitral valves, it introduced a new problem—strut fractures.^{5,6} Despite this, Orszulak and coauthors could not document any case of strut fracture among their 356 fatalities. As they pointed out, a modest number of autopsies (32%) and a large number of sudden unexplained deaths (17%) "leaves doubt as to the true prevalence of valve-related problems." Furthermore, it is important to note that strut fracture of Björk-Shiley valves is mainly a problem with the 70-degree convexo-concave valve, which was never used in the United States.⁵ In fact, we found the actuarial incidence of strut fracture among early produced, large (i.e., 29 to 33 mm), 70-degree convexo-concave valves to be as high as 12.5% at 7 years, representing a linearized incidence of 2.0%/patient-year.⁶ For this particular group of 70-degree prostheses, we^{6,7} and others⁸ have recommended elective explantation although Blackstone and Kirklin⁹ have advised against such reoperations. We⁷ have performed a small series of prophylactic replacements. It should be noted that the risk of strut fracture among the valves referred to as "high-risk valves" by Orszulak and associates (i.e., 29 to 33 mm 60-degree convexo-concave valves) is much less than the corresponding risk among large 70-degree valves, and I agree that these 60-degree valves need not to be explanted as a pure prophylactic measure. In the case of need for reoperation for other reasons (periprosthetic leakage or valve thrombosis), I would suggest valve replacement (as opposed to

local repair) for any welded convexo-concave Björk-Shiley valve.⁷

The Monostrut valve (without any welds), which combines the advantage of the convexo-concave disc with improved durability, has now been available outside the United States for 11 years. We¹⁰ have not observed any case of strut fracture or valve thrombosis in patients with this valve who are receiving anticoagulants, and no strut fractures have been reported elsewhere.

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REFERENCES

1. Orszulak TA, Schaff HV, DeSmet J-M, Danielson GK, Pluth JR, Puga FJ. Late results of valve replacement with the Björk-Shiley valve (1973 to 1982). *J THORAC CARDIOVASC SURG* 1993;105:302-12.
2. Lindblom D. Long-term clinical results after mitral valve replacement with the Björk-Shiley prosthesis. *J THORAC CARDIOVASC SURG* 1988;95:321-33.
3. Lindblom D. Long-term clinical results after aortic valve replacement with the Björk-Shiley prosthesis. *J THORAC CARDIOVASC SURG* 1988;95:658-67.
4. Lindblom D, Lindblom U, Åberg B. Long-term clinical results after combined aortic and mitral valve replacement. *Eur J Cardiothorac Surg* 1988;2:347-54.
5. Lindblom D, Björk VO, Semb BK. Mechanical failure of the Björk-Shiley valve: incidence, clinical presentation, and management. *J THORAC CARDIOVASC SURG* 1986;92:894-907.
6. Lindblom D, Rodriguez L, Björk VO. Mechanical failure of the Björk-Shiley valve: updated follow-up and considerations on prophylactic rereplacement. *J THORAC CARDIOVASC SURG* 1989;97:95-7.
7. Ericsson A, Lindblom D, Semb G, et al. Strut fracture with Björk-Shiley 70 degrees convexo-concave valve: an international multi-institutional follow-up study. *Eur J Cardiothorac Surg* 1992;6:339-46.
8. Birkmeyer JD, Marrin CAS, O'Connor GT. Should patients with Björk-Shiley valves undergo prophylactic replacement? *Lancet* 1992;340:520-23.
9. Blackstone E, Kirklin JW. Recommendations for prophylactic removal of heart valve prostheses. *J Heart Valve Dis* 1992;1:3-14.
10. Lindblom D, Lindblom U, Henze A, Björk VO, Semb BK. Three-year clinical results with the Monostrut Björk-Shiley prosthesis. *J THORAC CARDIOVASC SURG* 1987;94:34-43.

Reply to the Editor:

Dr. Lindblom's comments are appreciated, and we compliment his efforts and accomplishments with the Björk-Shiley

prosthesis. Although the results of the original paper from our institution may be viewed from a different perspective and appear to satisfy different results, the fact remains that the altered design of the Björk-Shiley valve did not reduce or eliminate the risk of valve thrombosis. More spherical than convexo-concave discs were affected by thrombosis; however, the mean time to valve thrombosis was 3.7 years. The follow-up of the convexo-concave cohort was not sufficiently long to state that the risk was absent. The presence of two of ten aortic thromboses confirms the possibility. The development of thrombosis in any location would be cause for concern. Our data demonstrated that thrombosis did occur and appears time related. The absence of a mitral occurrence in our review with the convexo-concave prosthesis is not a valid testimony to correction of this complication of thrombosis, as time will verify or negate its occurrence.

We do not recommend elective replacement of the convexo-concave prosthesis alone. If the need for repeat cardiac surgery for other cardiac disease arises, elective replacement should be *considered*, and if the combined procedure does not increase the operative risk significantly, we would support the explantation of the convexo-concave prosthesis.

There is no U.S. experience with the Monostrut valve, but I would surmise from Dr. Lindblom's comments that strut fracture and thrombosis have been avoided in his experience. We are attentive to any improvements that will minimize or eliminate risks to our patients. It is difficult to predict when or whether this prosthesis will reach the U.S. market.

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Cellular kinetics of posttransfusion graft-versus-host disease after heart operations

To the Editor:

Postoperative erythroderma evidenced by high fever, erythroderma, liver dysfunction, diarrhea, and pancytopenia has been understood as a graft-versus-host disease (GVHD) caused by blood transfusion.¹⁻³ This devastating disease typically occurs when the donor's human leukocyte antigen (HLA) haplotypes are homozygous for one of the patient's HLA haplotypes, because graft-versus-host reaction against the patient's major (and minor) histocompatibility antigens is much stronger than host-versus-graft reaction against the donor's minor histocompatibility antigens in this case.^{4,5} In practice, the fresher and more closely related the transfused blood is, the greater is the risk of GVHD.⁶⁻⁸ Moreover, not only immunocompromised hosts but also postcardiotomy patients seem to be vulnerable to this disease.⁹ Its prevalence after heart operations in Japan has been reported to be 0.15%. The mortality rate is as high as 90%.⁹

We present here three cases of GVHD occurring after heart operations and the transfusion of fresh or preserved blood. In one of these cases, extensive analysis of the cellular kinetics of post-transfusion GVHD after a heart operation (including HLA typing of the patient, his family and the blood donors) was performed.

A 67-year-old Japanese man (patient 1) with rheumatic mitral stenosis and regurgitation was referred to Matsuyama Red Cross Hospital. Blood test results were all within the normal limits. Mitral valve replacement was performed in September

1991. For priming of the cardiopulmonary bypass (CPB) circuit, 260 gm 5-day preserved concentrated red blood cells (CRBCs) from donor 1 and 130 gm 15-day preserved CRBCs from donor 2 were used. Soon after the operation, an additional 260 gm 5-day preserved CRBCs from donor 3 was given. All three blood donors were unrelated to the patient. The patient's postoperative course was uneventful until spiking fever started on postoperative day (POD) 10. On POD 14, a mild elevation of liver enzyme activities (such as aspartate aminotransferase, alanine aminotransferase, and lactic dehydrogenase) and a rash on the face and neck were observed. The rash gradually spread over the entire body surface, culminating in an appearance similar to that of a second-degree burn by POD 19. On POD 17, watery (later bloody) diarrhea associated with redness, swelling, and erosion in the lips and anus began. Delirium was observed from POD 16 through POD 19. The patient entered into a state of shock on POD 19 and died on POD 20. Permission for autopsy was refused, but the histologic appearance of the skin at death was fully compatible with GVHD.¹⁰ The bone marrow was not examined.

The hemoglobin level and red blood cell count were relatively constant throughout the postoperative course (Fig. 1). The decreased platelet count caused by CPB had returned to its normal level by POD 10 but decreased again after POD 14. The white blood cell count, which increased after the operation, appeared to have returned to normal by POD 10; thereafter, however, it continuously decreased, to 3100 cells/mm³ on POD 18 and to 500 cells/mm³ on PODs 19 and 20. The differential count of the white blood cells was dramatically and suddenly changed from granulocyte dominance (>80%) to lymphocyte dominance (>96%) on POD 18. The absolute number of lymphocytes decreased from 1403 cells/mm³ before operation to 411 cells/mm³ immediately after operation; it then showed a plateau at about 1000 cells/mm³ from PODs 7 through 14, followed by a further rapid drop to 93 cells/mm³ on POD 17. The lymphocyte count did, however, increase again to about 500 cells/mm³ after POD 18.

Shortly before the patient's death, blood was drawn to examine the HLA phenotypes and lymphocyte subpopulations. Moreover, the patient's wife, his three children, and the three unrelated blood donors were tested for their HLA phenotypes. Although the expected HLA haplotypes of the patient were A24, Bw52, C-, DR2, DQw1/A-, B35, Cw9, DR4.1, DQw4 (a/b, Table I), his HLA haplotypes just before his death were found to be a/a—exactly the same as the HLA haplotype of donor 3 (a 23-year-old man). The frequency of haplotype a in Ehime Prefecture, Japan, has been reported to be 0.0593.¹¹ If the patient had been a mixed chimera, the patient's original lymphocytes, bearing haplotype b-encoded antigens, would have been detected. From a quantitative analysis of the HLA-typing scores (Table I), however, Cw9, DR4.1, and DQw4 were scored into 1 and B35 was scored into 2, suggesting that the existence of host-type lymphocytes was negligible (Table I). From a flow-cytometric analysis of the patient's blood, T cells (CD3⁺) accounted for 84% of the mononuclear cells, whereas B cells (CD19⁺) represented 0%. Among the donor-originated T cells, 10% were CD4⁺ and 79% were CD8⁺ (Fig. 1). This patient was the first to have posttransfusion GVHD among 400 heart operations at Matsuyama Red Cross Hospital from 1983 through 1991.