Erythrocyte Destruction in Different Types of Starr-Edwards Aortic Ball Valves

By Erik Myhre, M.D., Jon Dale, M.D., and Knut Rasmussen, M.D.

SUMMARY
Increased destruction of red blood cells follows the insertion of ball valves into the heart in most cases. Usually, hemolysis is slight, but in some patients uncompensated hemolytic anemia develops. To study the influence on hemolysis of the mechanical properties of the prostheses, the degree of erythrocyte destruction was evaluated in patients with Starr-Edwards aortic prostheses of different types and size.

Fifty-six patients with Starr-Edwards aortic ball valves were examined; 13 had prostheses of the 1200 series with silastic rubber balls, and 43 had valves of the 2300 series with hollow Stellite (metallic) balls. Thirty-one patients had valves with an orifice area of 1.8 cm² or less; the others had larger-sized valves.

The degree of hemolysis was predicted from the serum lactic dehydrogenase activity, which has previously been shown to correlate well with the red blood cell survival. The half-life of ⁵¹Cr-labelled red cells was also determined in 16 cases.

Hemolysis was significantly higher in patients with Stellite ball valves than in those with silastic rubber ball valves, and red blood cell destruction was more pronounced in patients with small prostheses than in patients with larger valves. Hemolysis was not higher in three patients with paravalvular leakage than in patients with competent prostheses. Valve type and size seem to be the most important factors in producing hemolysis.

Additional Indexing Words: Intravascular hemolysis Serum lactic dehydrogenase

INCREASED destruction of red blood cells is the most common side effect following insertion of ball valve prostheses. Usually, it is slight and compensated by increased erythrocyte production, but in a few patients severe hemolytic anemia develops.¹ Paravalvular leakage²,³ and ball variance⁴-⁶ might explain the hemolysis in some cases, but in others no faults of the prosthesis or its insertion could be demonstrated.⁵,⁸

Valve prostheses of different construction may have different traumatic effects in the red blood cells.⁹ This study shows that the hemolytic effect may be changed considerably even by modifications of the same valve type.

Methods
Fifty-six none selected patients with Starr-Edwards aortic ball valve prosthesis admitted to Medical Department B of the University Hospital during 1969 were studied. The time since operation varied from 3 weeks to several years; most patients were reexamined 3 and 6 mo postoperatively.

The size of the ball valve prosthesis was recorded in all cases. Thirty-two patients had prostheses of number 10A or less (orifice area 1.8 cm² or less), arbitrarily classified as small valves. Larger prostheses (11A to 14A) had been inserted in 24 patients.

Thirteen patients had prostheses of the 1200 series and 43 had valves of the 2300 series. The main differences between these two series are that the ball is made of silastic rubber and the cage of noncovered metal in the 1200 valves, whereas the 2300 valves have hollow Stellite balls (metallic)
and Teflon-covered cages. Furthermore, the cage height and the orifice area are somewhat larger in the 1200 valves.

A close correlation has been shown to exist between serum lactic dehydrogenase activity (LDH) and the half-life of $^{51}$Cr-labelled erythrocytes. Therefore, red blood cell destruction was predicted from the LDH values. Serum LDH was determined according to Wroblewski and La Due, the upper normal limit in our laboratory being 200 U/L ($\mu$M/min/L). LDH levels of 200 U/L or less indicated a normal red blood cell survival, 500 U/L corresponded roughly to twice a normal red cell destruction, 750 U/L to three times and 1,000 to four times the normal destruction rate.

As 16 of the 56 patients in this series also did enter a previous study, the half life (T/2) of their $^{51}$Cr-labelled erythrocytes was known. These patients were unselected from the viewpoint of valve type and size.

Statistical analyses were performed by the use of the $t$-test.

**Figure 1**

LDH values and predicted erythrocyte destruction related to valve size and type. Prostheses with Stellite balls (Starr-Edwards 2300) are indicated by black circles, and silastic rubber balls (Starr-Edwards 1200) by open circles. The mean values in each group are indicated by a broken line.

**Results**

Hemolysis as determined by the LDH increment in different valve sizes and types is shown in figure 1. The size of the prostheses is indicated by the valve number given by the manufacturer. The mean LDH in cases with hollow Stellite balls was 501 U/L compared to 281 U/L in those with silastic rubber balls, the difference being highly significant ($P<0.01$).

In patients with prostheses of smaller sizes the mean LDH was 518 U/L, whereas it was 359 U/L in patients with larger valves ($P<0.05$). Considering the metallic balls, the mean LDH was 553 U/L in small sizes and 412 U/L in the larger ones ($P<0.05$). The difference of LDH in the group with small-sized valves of Stellite and silastic rubber balls was highly significant ($P<0.01$), the mean values being 553 and 327 U/L, respectively. In the group
with valves of larger sizes, the mean LDH in metallic balls was 412 U/L and 252 U/L in silastic rubber balls \( (P < 0.01) \). In patients with silastic rubber ball valves the mean LDH was 327 U/L for the small sizes and 252 U/L in the larger ones; the difference was not statistically significant.

Patients were included in the study irrespective of their cardiac or hematologic state. However, no patients with acute myocardial or pulmonary infarction, severely impaired liver function, or elevated levels of serum glutamic-oxalacetic and glutamic-pyruvic transaminases were included. Increased red blood cell destruction was the only probable explanation of the LDH increment in the patients studied. Hemolysis as predicted from the LDH levels\(^{11}\) was increased to 1.5 times of the normal in patients with large metallic ball valves and twice the normal in those with metallic ball valves of smaller sizes. The predicted red blood cell destruction in the group with silastic rubber ball valves was only slightly above normal.

Figure 2 shows the half-life of \(^{51}\text{Cr}\)-labelled erythrocytes in 16 patients. The half-life of \(^{51}\text{Cr}\)-labelled erythrocytes was on average 23.4 days in six cases with silastic rubber balls, whereas it was 16.8 days in 10 cases with Stellite ball valves. In this last group two patients had valve incompetence, and two had frank hemolytic anemia. When these four patients were excluded, the average half-life of \(^{51}\text{Cr}\)-labelled erythrocytes in this group was 20.2 days, that is, significantly shortened as compared with patients with silastic rubber
ball valves. Even in this small series, the red blood cell survival was considerably shorter in the patients with small valves than in those with larger valves.

Figure 3A shows that the observation period after operation varied from less than 2 mo to more than 9 mo; many of the patients have been observed for several years. The apparent decrease of LDH after 9 mo is false because of over-representation of patients with silastic rubber ball valves in the group observed for a longer period. The length of the observation period seemed to be less important than the type of prostheses as shown in figure 3B; the LDH levels did not change significantly with time in any of the groups.

The postoperative LDH values were not related to the preoperative levels (fig. 4). For convenience, only data on the group with metallic ball valves were plotted in this figure; the results, however, were similar in the smaller group of patients with silastic rubber ball valves.

The preoperative and postoperative hemoglobin concentrations are shown in figure 5. In patients with silastic rubber balls the hemoglobin concentration remained unchanged after operation, whereas the average value decreased considerably in the group with Stellite ball valves. Two patients in this series

Figure 3
LDH values before and after insertion of Starr-Edwards aortic ball valves. The black circles indicate Stellite balls and the open circles silastic rubber balls. The broken lines indicate the mean value in each group. Two patients developing severe hemolysis are marked by asterisks (*) in figure 2A.

Figure 4
LDH values before and after insertion of Stellite ball valves (Starr-Edwards 2300). Cases with small size balls are marked by black circles, those with large size balls by x. The upper normal limit of LDH is indicated by broken line.
ERYSIROKE DESTRUCTION

Figure 5

Hemoglobin concentration before and after operation in patients with Stellite and silastic rubber ball valve prostheses. The mean value in each group is indicated by broken lines.

dveloped severe hemolytic anemia, and serum LDH increased from 960 to 3850 U/L and 660 to 1870 U/L, respectively. Paravalvular leakage or prosthesis malfunction was not found in these two patients; both had small valves of the 2300 series. In three other cases paravalvular leakage was diagnosed; the LDH values, however, did not differ significantly from the average in cases with competent prostheses.

Discussion

Hemolysis varies greatly from patient to patient following insertion of prosthetic heart valves, and it is surprisingly constant in the individual patient from time to time after operation. Factors such as physical activity and iron deficiency are of some importance for the development of hemolysis, but can only in part explain the great variation between individuals.

Our results strongly suggest that the new Starr-Edwards aortic valves of the 2300 series provoke significantly more hemolysis than the preceding 1200 valves. This is in contrast to reports of others and information given by the manufacturer. Furthermore, we could not confirm the generally accepted view that both paravalvular leakage and valve malfunction were important determinants of increased red blood cell destruction. Prediction of the erythrocyte destruction from the LDH levels was adopted to permit study of a sufficiently large series of patients. Other sources of LDH than erythrocytes were excluded as far as possible. Although the method gives a somewhat rough estimate of hemolysis, its general appropriateness has been stated earlier. This was reconfirmed in the present study by the fact that similar results were obtained by determination of the erythrocyte survival time in a limited number of patients and estimation of hemolysis from the LDH levels in the whole material. The LDH levels did not change during the first years of observation in either patient group. Therefore, reliable information about hemolysis might be obtained by LDH determination 1 to 2 mo after the operation.

Starr-Edwards valves of the 1200 and 2300 series have several differences; the most important one probably is the material of the ball. The 2300 model was introduced to reduce ball variance and thromboembolism. Ball variance, however, is also a rare event in the 1200 valves. The general view is that a reduction in thromboembolism has been achieved, but conclusive evidence has to our knowledge not been presented. Evaluating the 2300 series of Starr-Edwards prosthesis, the possible reduction in thromboembolism must be weighed against the definite increase of hemolysis provoked by this valve.

Our findings call in question the generally accepted theory that intravascular hemolysis is caused by turbulence of the blood stream. The differing ball material and cage covering of the two types of valves most probably have

Circulation, Volume XLII, September 1970
little important effect on turbulence, but the impact on the red blood cells of metallic balls must be more damaging than that of silastic rubber balls. The Teflon covering may, if not properly endothelialized, keep the cells within its network and prevent their escape when the ball closes toward the valve ring. Therefore, we believe that the direct traumatic effect on the erythrocytes is more important to hemolysis than turbulent blood stream.

Our conclusion is that the 2300 series of Starr-Edwards aortic valves provokes considerably more hemolysis than older models. The material of the ball and the size of the prosthesis seem to be major determinants of hemolysis following insertion of aortic ball valves.

References