Pregnancy in Patients with Prosthetic Heart Valves*

Asher Buxbaum, M.D.; Maurice M. Aygen, M.D.; Wehbi Shahin, M.D.;
Morris J. Levy, M.D., F.C.C.P.; and Benjamen Ekerling, M.D.

Five pregnancies in two patients with prosthetic mitral valves resulted in three spontaneous abortions, one missed abortion and one live baby. The incidence of fetal mortality in 50 pregnancies in 43 patients with prosthetic valves reported in the literature was 28 percent. One mother whose pregnancy was complicated by thromboembolism, died following cesarean section. The use of oral anticoagulants augmented considerably the risk to the fetus. Omission of the treatment on the other hand, increased the danger of systemic embolization to the mother.

Women with prosthetic heart valves can tolerate pregnancy and delivery. However, there is an increased risk to the mother and the child. Among various factors, anticoagulants appear to play an important role in determining the outcome of pregnancy. In this presentation we add the outcome of five pregnancies in two patients with prosthetic mitral valves to those reported in the literature and correlate the incidence of fetal and maternal morbidity and mortality to the use or omission of anticoagulants.

CLINICAL MATERIAL

CASE 1

The patient was a 23-year-old married woman without any history of rheumatic fever. At the age of 19 heart disease was discovered and she began to receive a digitalis preparation and diuretics because of shortness of breath on moderate exertion. One year later she was referred to Beilinson Medical Center for evaluation of her hemodynamic state. Clinical catheterization and angiographic studies established the presence of severe mitral regurgitation, moderate mitral stenosis, mild aortic regurgitation and pulmonary hypertension (Table 1). On July 10, 1966, her mitral valve was replaced by a No. 3 Starr-Edwards prosthetic valve. The operation and the postoperative period were uneventful. She was discharged on digoxin, 0.25 mg daily, warfarin sodium and monthly injections of benzathin penicillin. Six months after her discharge from the hospital, the patient became pregnant, but spontaneous abortion occurred in the third month. During the following year the patient felt well with almost no limitation of her activity and digoxin was discontinued. During the same year, a second spontaneous abortion occurred in the second month of pregnancy. In November 1967 postoperative right heart catheterization showed an increase in cardiac output and reduction in pulmonary capillary and pulmonary artery pressures from the preoperative levels (Table 1). In 1968 her third pregnancy terminated with spontaneous abortion in the first trimester. When she was seen in our clinic in January 1969, the patient was in the second month of her fourth pregnancy. The patient again desired to continue with the pregnancy, even though the dangers involved were fully explained to her. Because of previous episodes of spontaneous abortion in the first trimester, she was hospitalized for evaluation and possible change of her medication. Initially, warfarin sodium (Coumadin) was discontinued and she was given injections of heparin. This regimen, however, seemed to be too difficult to be followed for the whole period of her pregnancy and a week later phenindione was started and the heparin injections discontinued. Following her discharge and throughout her pregnancy the prothrombin time was maintained within the range of 20 percent to 30 percent of normal. No complications occurred during the pregnancy and her general and cardiac status remained good during the whole period. Two weeks before term the patient was hospitalized in the obstetrical ward. Phenindione was then discontinued and the clotting time was maintained at two to three times the normal level with intramuscular heparin injections. On September 23, 1969, the patient spontaneously delivered a normal baby boy. The baby's birth weight was 3,320 gm. Bleeding and coagulation times of the infant were normal. The patient had an increased blood loss during delivery and for a few days afterwards, and it was necessary to administer three units of whole blood to keep the hemoglobin concentration around 10 gm percent. Warfarin sodium was started on the fifth postpartum day and heparin was discontinued on the seventh day after delivery when the prothrombin time had reached 25 percent. The infant was circumcised when he was eight days old, with no untoward effects. Mother and child have been doing well during the 12 months since delivery.

*From the Cardiopulmonary, Thoracic-Cardiovascular Surgery and Obstetrics departments, Beilinson Medical Center, Petah-Tiqva, and Tel-Aviv University School of Medicine.
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...cardiac symptoms until the age of 30, when following a normal delivery, aided by low forceps, she began to complain of progressive exercise intolerance. In spite of intensive medical therapy, she developed chronic congestive heart failure with ascites, and she was severely incapacitated. The physical examination and hemodynamic studies revealed severe combined mitral valve disease and markedly elevated pulmonary artery pressure (Table 1). In January 1964 she underwent open heart surgery and the mitral valve was replaced by a Starr-Edwards valve. After the operation the signs of pulmonary hypertension disappeared, the liver regressed and her exercise tolerance improved markedly. Digitalis and diuretic therapy were gradually discontinued and she was maintained on treatment with warfarin sodium (Coumadin). Her menstrual periods, which had been absent for more than two years prior to the operation, reappeared. Postoperative right heart catheterization showed remarkable improvement in hemodynamics (Table 1).

In April 1968 she reported to our clinic in the third month of pregnancy. In accord with the desire of the patient, it was decided to continue the pregnancy without stopping the anticoagulants. In addition, two children died a few hours after birth. Autopsy in a stillborn and in a postpartum death showed multiple hemorrhages in the lungs, brain, cerebellum, liver and thymus. In 19 patients received oral anticoagulants of the coumarin and indandione group throughout the pregnancy and in the perinatal period. There were five spontaneous abortions and five stillbirths in this group. In addition, two children died a few hours after birth. Autopsy in a stillborn and in a postpartum death showed multiple hemorrhages in the lungs, brain, cerebellum, liver and thymus.

**Case 2**

The patient was a 38-year-old woman who had had rheumatic fever at the age of 16. She had had no significant cardiac symptoms until the age of 30, when following a normal delivery, aided by low forceps, she began to complain of progressive exercise intolerance. In spite of intensive medical therapy, she developed chronic congestive heart failure with ascites, and she was severely incapacitated. The physical examination and hemodynamic studies revealed severe combined mitral valve disease and markedly elevated pulmonary artery pressure (Table 1). In January 1964 she underwent open heart surgery and the mitral valve was replaced by a Starr-Edwards valve. After the operation the signs of pulmonary hypertension disappeared, the liver regressed and her exercise tolerance improved markedly. Digitalis and diuretic therapy were gradually discontinued and she was maintained on treatment with warfarin sodium (Coumadin). Her menstrual periods, which had been absent for more than two years prior to the operation, reappeared. Postoperative right heart catheterization showed remarkable improvement in hemodynamics (Table 1).

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**Discussion**

In a series of 17,128 pregnancies, reported by Gilbert and co-workers, the fetal mortality among noncardiac pregnant women was 1.6 percent, among cardiac patients it was 3.2 percent and among cardiac patients with failure it was 10.5 percent. In 50 pregnancies in 43 patients with prosthetic valves reported in the literature, including those in our two patients, the fetal mortality was 28 percent. In these patients the degree of hemodynamic disorder and the functional incapacity, as well as the anticoagulants per se, may have a cumulative effect on the outcome of the pregnancy.

Quick and Kraus and associates administered large doses of coumarins to pregnant animals and observed very high incidence of fetal hemorrhage and death. On the other hand Hirsh and colleagues found no fetal hemorrhage in rabbits, when they stopped the warfarin a few days before term or when the delivery was performed by cesarean section. On the basis of these experiments and from clinical observations they concluded that oral anticoagulants may not increase the risk of fetal hemorrhage unless continued until term. Considering that the teratogenic effect of drugs passing the placental membranes are highest in the early period of fetal development, the same author also advised substitution of heparin for oral anticoagulants in the first 12 weeks of gestation.
The outcome of eight pregnancies in patients in whom the anticoagulant treatment was interrupted during pregnancy, was live babies. Similarly, no fetal morbidity or mortality was encountered in six pregnant women who received none of the anticoagulants throughout pregnancy.

In six pregnancies reported in the literature it was not possible to determine whether or not they received anticoagulants.

The fetal morbidity and mortality was confined to the pregnancies in patients with prosthetic mitral valves. The difference may be due to the fact that few patients with prosthetic aortic valves received anticoagulants. However, a hemodynamic factor cannot be excluded. In postoperative hemodynamic studies in patients with prosthetic mitral valves, Hultgreen and associates \(^27\) and others \(^28\) found low resting cardiac output and a subnormal output response to exercise. In contrast, patients with prosthetic aortic valves had normal output at rest and on exercise. \(^28\)-\(^30\) Failure to augment the cardiac output to satisfy the increased metabolic demands of the fetus may be a factor in causing fetal death in advanced months of pregnancy, but it is unlikely to be a cause for the abortions in the early months. Six of the fetal deaths occurred in the first trimester.

The maternal morbidity and mortality in 50 pregnancies are summarized in Table 3.

Maternal bleeding requiring transfusion in the postpartum period was reported in three patients receiving heparin, including our case. \(^31\)-\(^32\) One patient on oral anticoagulants was hospitalized twice during pregnancy for vaginal bleeding. \(^33\)

Systemic embolization occurred in three out of 30 pregnancies while the patients were receiving anticoagulants. From the literature it is impossible to determine whether or not they received adequate therapy. The highest incidence of thromboembolic phenomena occurred in patients in whom the anticoagulant therapy was interrupted during pregnancy.

The only case of maternal death in a patient with a prosthetic valve was reported by Bennett and Oakley. \(^17\) Their patient had episodes of cerebral embolization in the first month of pregnancy and developed severe congestive circulatory failure and oliguria requiring peritoneal dialysis in the eighth month. She died after cesarean section and subtotal hysterectomy. A large thrombus, which immobilized the mitral valve, was found at autopsy. This patient received oral anticoagulants in the first eight weeks of pregnancy and heparin until term.

The data demonstrated that oral anticoagulants augmented considerably the fetal mortality. Substitution of heparin in the perinatal period reduced the risk. The effectiveness of heparin in modifying the incidence of fetal morbidity and mortality,
when given to the mother in the first trimester of pregnancy remains to be determined.

Anticoagulants were not effective or adequate to eliminate completely the risk of thromboembolism. However the patients who stopped the treatment during pregnancy carried a higher risk than those who continued and than those who never received anticoagulants.

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Erratum
In the article "Advantages of the Beall Valve Prosthesis" by Vogel et al (Chest 89:249, 1971) figures 1 and 5 were reversed.

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