

## ATTEMPTED SPLEEN TRANSPLANT IN CLASSICAL HEMOPHILIA<sup>1</sup>

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Recent evidence has indicated that the spleen may be partly responsible for synthesis or storage of antihemophilic factor (factor VIII) in dogs (8) and in man (2). Transplantation of the spleen into dogs with congenital deficiency of factor VIII has been shown to result in increased circulating levels of this clotting factor for prolonged periods (3). Spleen transplantation in man has been done without significant morbidity because of the procedure itself or graft-versus-host reaction (1, 5). Therefore, it seemed reasonable to attempt allogeneic grafting of a spleen into a patient with severe factor VIII deficiency.

### CASE REPORT

Q. N., a 16-year-old boy with hemophilia A (factor VIII, antihemophilic factor deficiency), had been followed at the University of Colorado Medical Center from the age of 17 months. The diagnosis of severe hemophilia A had been confirmed many times. His factor VIII level was 0%, and bleeding times were normal. No antibody against factor VIII had ever been demonstrated. The patient's mother was shown to be a hemophiliac carrier with repeated factor VIII assays that ranged from 26%–38% of normal.

During the 14-year period that the patient was followed at this institution he required 41 hospital admissions for treatment of hemarthroses involving almost all of the major joints, recurrent hemorrhages

into major muscle groups, bleeding from open lacerations, and retroperitoneal hemorrhages.

On January 31, 1968, the patient was admitted to Colorado General Hospital for an elective splenic homotransplantation with the father as the donor. The only donor-recipient mismatch in the HLA (7) antigen system was in the Terasaki Group 3.

Two days prior to surgery the patient was given a "test" infusion of 1911 units of glycine-precipitated AHF (Hyland), and serial factor VIII assays were done. All factor VIII assays were done in duplicate by the method of Pool (4). The initial level of 27% factor VIII fell to 2% in 30 hr. During the same period administration of heterologous antilymphocyte globulin (ALG) and azathioprine (Imuran) was begun (6).

Based on the results of the previously determined decay rate of exogenously administered AHF the patient was given 3782 units of glycine-precipitated AHF 2 hr prior to operation on February 3, 1968. Splenic transplantation was completed in 5 hr. The donor spleen was transplanted to the right extraperitoneal space of the recipient by a previously described technique (5). The ischemic time from donor removal to revascularization by the recipient was 60 min. After completion of the anastomoses it was necessary to readjust the position of the spleen many times because of kinking of either the anastomosed splenic artery or vein. An additional 1800 units of glycine-precipitated AHF were infused 2 hr after surgery was begun. The

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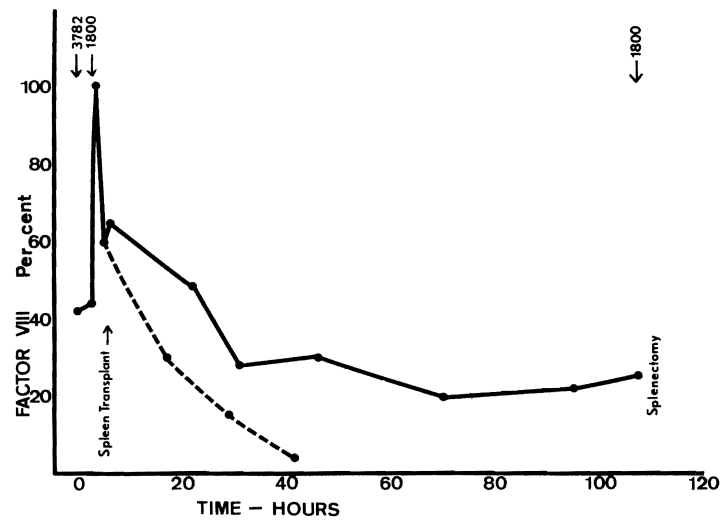


FIGURE 1. The numbers at the top of the graph refer to units of Factor VIII given to the patient. A unit of factor VIII is that activity contained in the equivalent of 1 ml of fresh normal plasma. The dotted line represents an estimate of decay of exogenous factor VIII.

patient tolerated the operation well. Blood loss was estimated to be 50 ml.

The recipient was followed by routine laboratory studies plus daily factor VIII assays (Fig. 1). Medications were limited to i.v. fluids, antibiotics, ALG, azathioprine, and Prednisone (McKesson Laboratories, Bridgeport, Connecticut). No further factor VIII was administered. Ambulation was begun on the 4th postoperative day. In the evening of February 7, 1968, the patient began to complain of exquisite pain over the right iliac fossa in the area of the incision. Because we were concerned with possible bleeding, the patient was given 1800 units of AHF cryoprecipitate. Symptoms persisted, and the patient was taken to the operating room for exploration. At surgery approximately 2 liters of fresh blood were found in the iliac fossa along with several large clots. The transplanted spleen was markedly swollen with three lacerations. Postoperatively the patient was kept continuously corrected with glycine-precipitated AHF or AHF cryoprecipitate i.v. every 12 hr for 14 days. Factor VIII levels were maintained between 25–60%. No additional problems were encountered, and he was

discharged on February 27, 1968, with complete healing of the incision. Since that time he had had four additional hospital admissions for treatment of hemarthroses of his shoulder.

Spleen scans with technetium sulfide done on February 4, 1968 (1 day postoperative) and on February 7, 1968 (2 hr prior to second laparotomy) showed good uptake over the patient's own spleen and the donor spleen.

Pathological examination of the ruptured donor spleen revealed prominent lymphoid nodules containing increased numbers of lymphocytes, histiocytes, and reticulum cells.

#### COMMENTS

As shown in Figure 1, our patient maintained levels of at least 20% factor VIII for 4 days, long after the effects of intraoperative therapy should have been dissipated. It is impossible to say whether the factor VIII was newly synthesized or slowly released from storage in the donor spleen; however, if this level could have been maintained it would have transformed the patient into a very mild hemophilic.

The reasons for the rupture of the donor spleen and subsequent termination of this investigation remain unclear. Mechanical factors from the abnormal position of the organ, swelling or increased friability because of rejection, or trauma from too early ambulation of the patient could each have played a part.

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