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CHAPTER II — *Tissue Transplantation*

STUDIES ON ORTHOTOPIC HOMOTRANSPLANTATION OF THE CANINE HEART *

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A technique has been developed for replacement of the canine heart with a homologous heart. The recipient animal can be expected to survive for several days, during which time the denervated, transplanted heart appears to function normally.

Experiments were performed on healthy, adult mongrel dogs weighing 17 to 25 kg., and, although donor and recipient animals were of comparable size, in no instance did they resemble each other with regard to breed. No attempt was made to alter the immunologic status of the animals.

METHOD

The donor animal is first prepared by exposing the heart and great vessels under pentobarbital anesthesia. Intravenous heparin, 2 reg. /kg., is given, and the body temperature is lowered to 30° C. by surface cooling.

The recipient is heparinized and prepared for circulatory bypass with a rotating disc oxygenator. The heart is exposed through a left thoracotomy and longitudinal pericardiotomy. Catheters are inserted into the vena cavae through the jugular and femoral veins for diversion of venous blood to the oxygenator; the femoral artery is similarly cannulated. After bypass is instituted, a noncrushing clamp is placed through the transverse sinus for occlusion of the pulmonary artery and aorta. The heart is excised, and there is left only the common posterior atrial wall containing the ostia of the vena cavae, the pulmonary veins, and a ridge of atrial septum. The aorta and pulmonary artery are divided about a centimeter distal to the commissures.

The donor heart is then quickly excised in the same manner and is immersed in normal saline at 4° C. for approximately 5 minutes, during which time the myocardial temperature drops to 12° to 15° C. The heart is implanted in the recipient animal by joining the atrial walls and atrial septum to the posterior atrial wall of the recipient with a continuous suture. The aortic and pulmonary artery anasto-

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moses complete the transplantation. Prior to completion of the aortic anastomosis, bronchial blood is allowed to fill the left side of the heart, which displaces the air. Coronary flow is re-established by disocclusion of the aorta, and, when the myocardium is adequately rewarmed, the heart is electrically defibrillate. After a further brief period of support by the pump-oxygenator, bypass is discontinued and the incisions are closed. The total duration of cardiac anoxia is approximately 1 hour.

RESULTS

In a series of 8 consecutive transplantations, 5 of the recipient animals lived for 6 to 21 days. The recovery from anesthesia was uneventful. During convalescence the dogs ate and exercised normally. The pulse rate was variable and increased moderately with exercise.

Electrocardiograms occasionally demonstrated ST-T wave changes compatible with postoperative pericarditis, and P waves in some instances were abnormal. Tracings taken a few hours prior to death in 3 instances showed no evidence of arrhythmia or conduction defects. The electrocardiogram taken 5 hours prior to death on the twenty-first postoperative day of the longest survivor was normal except for T wave inversions primarily in leads II, III, and AVF.

The terminal course was usually rapid, occurring over the span of about 24 hours, during which time the animal became lethargic and progressively tachypneic. Postmortem examination of the heart revealed it to be ecchymotic and edematous, with a fibrinoid pericarditis and generalized dilatation. Microscopic examination of sections demonstrated severe myocarditis, with massive round cell infiltration, patchy necrosis, interstitial hemorrhage, and edema. The regional lymph nodes were large, but microscopic examination showed a non-specific increase in plasma cells and histiocytes.

DISCUSSION

During convalescence, function of the transplanted, denervated heart appears to be completely normal. The reason for the difference in survival time is not clear. This difference probably represents an individual variation in immunologic response, despite the implication, from work with other tissues, that homograft rejection occurs on a more rigid timetable. The exact mode of death remains obscure, and electrocardiographic studies suggest that it is not related to disturbances in rhythm or conduction. Apparently the massive infiltration of round cells and interstitial hemorrhage produces rapid myocardial failure. Observations on these animals suggest that, if the immunologic mechanisms of the host were prevented from destroying the graft, in all likelihood it would continue to function adequately for the normal life span of the animal.