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## USE OF EXTRACORPOREAL CADAVER PERFUSION FOR PREPARATION OF ORGAN HOMOGRAFTS

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A practical solution to the problem of cadaver organ procurement and preservation requires provision for immediate cooling and/or perfusion of the potential homograft. In the present study, a simple method is described by which both these objectives are met.

### METHODS

Thirty-two dogs were used, weighing 9 to 20 kg. The animals were killed with an overdose of pentobarbital after arterial and venous catheters had been placed in the inferior vena cava and aorta via the femoral vessels. Respiratory failure invariably preceded disappearance of pulses by 5 to 15 min. During this time, 3 mg./kg. heparin was given intravenously. Four to 12 min. after cessation of the animals' circulation, extracorporeal perfusion was instituted. The apparatus employed gravity drainage with a disposable bubble oxygenator, a DeBaakey pump, and a heat exchanger. The extracorporeal circuit was usually primed with lactated Ringer's solution, pre-cooled by recirculation to 15° C. In 2 of the experiments on liver transplantation, 5% glucose in water was used for the priming fluid. In all experiments, 1 gm. procaine chloride per liter was added to the perfusate.

Studies were first performed to determine suitable perfusion and cooling rates. After standardization of the technique, cadaver perfusions were carried out for 1 to 14 hr. At the end of this time, either the liver or kidney, or both, were removed and transplanted to suitable recipients, after recipient hepatectomy or bilateral nephrectomy had been performed. Postoperative anti-rejection therapy was provided with azathioprine. The state of preservation of the homografts was judged by their function, and by subsequent histologic studies.

### RESULTS

*Flow rates and blood pressure requirements.* Six dogs were studied to determine if existing data on extracorporeal perfusion in living subjects would be transferable to the cadaver. First, flow rates were adjusted to provide an arterial pressure of 70 mm. Hg. As much as

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600 cc./kg./min. were required to maintain the blood pressure at this level. The kidneys and liver became swollen and edematous in a few minutes, with transudation of large amounts of surface fluid. Ultimately, it was concluded that flow rates should be arbitrarily limited to 40 to 60 cc./kg./min. and then reduced to 20 to 30 cc./kg./min. as the cadaver temperature dropped below 20° C. The appearance of the organs was satisfactory with the use of the reduced flow rates, although arterial pressures never exceeded 20 mm. Hg, and were usually undetectable.

*Degree of cooling.* Five dogs were cooled to 2° to 10° C. with the low flow perfusion. This invariably required less than 60 min. Transplantation was carried out immediately thereafter. Upon revascularization, the kidneys temporarily assumed a mottled appearance, with islands of cyanotic tissue surrounded by normal parenchyma. Within an hour, these areas disappeared and the kidneys seemed normal. Nevertheless, the dogs were anuric until death. These events were not observed with temperatures of 15° C. or above. It was concluded that cooling to less than 10° C. was harmful, and, in the definitive series, the ultimate temperatures were controlled at 15° C.

*Renal homografts.* Eleven kidneys were grafted after perfusion for 1 to 14 hr. Perfusion time for 5 of the 11 cadavers was 11 or more hours. Mean perfusion time was 7 hr., 33 min. All animals produced urine within the first 48 hr. Postoperative survival averaged 20 days with a range of 7 to 47 days. Survival time was influenced more adversely by pneumonia than by rejection. Seven dogs died of pneumonitis. Only 5 of the 11 animals were uremic at the time of death. With perfusion for 6 or more hours, sharp rises in BUN were observed immediately after operation, with subsequent return toward normal. With perfusions of 6 hr. or less, early azotemia was not prominent. Histologic sections of the renal grafts showed varying degrees of mononuclear infiltrate compatible with minimal rejection. No other pattern of parenchymal injury ascribable to perfusion was detectable.

*Hepatic homografts.* Ten livers were transplanted after perfusion for 71 to 416 min. Consistent clotting deficiencies were detected in every animal after the homografting, with increases in fibrinolysins and decreases in fibrinogen. Five of the animals died of hemorrhage on the operating table or in the immediate postoperative period. The other 5 animals lived for 1 to 5 days, although autopsy revealed hemoperitoneum in 3 of these. Hepatic function was inferred from the facts that the animals awoke from nembutal anesthesia and that they survived without glucose therapy. Nevertheless, acute rises in SGOT and bilirubin indicated that severe hepatic injury had occurred. Histologic sections showed varying degrees of parenchymal

injury which could not be ascribed to rejection. The changes consisted of centrilobular congestion and necrosis.

*Clinical application.* Two cadaveric renal and 2 cadaveric hepatic homografts, prepared with this technique, have been used clinically. One liver graft provided satisfactory function for 22 days until death from pulmonary embolus. Histologic structure was essentially normal at autopsy. One renal graft functioned for 2 weeks and then become anuric. The other 2 organ grafts had no evidence of function.

Problems of perfusion were encountered with human cadavers, which had not been seen in dogs. In the first 3 clinical cases, poor venous return resulted in less than optimal perfusion. In the last case, in which a satisfactory liver was obtained, this was avoided by acutely expanding the blood volume immediately after death with transfusion of whole blood and plasma.

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#### SUCCESSFUL STORAGE OF KIDNEYS AT SUB-ZERO TEMPERATURES

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Previous attempts in this laboratory to preserve the function of kidneys stored in a frozen state outside the body and subsequently autotransplanted have been unsuccessful. We are currently evaluating the effects of sub-zero cooling with the hope of prolonging the period of safe renal ischemia prior to transplantation. In this technique, the freezing point is depressed to between  $-5^{\circ}$  to  $-6^{\circ}$  C. and the kidney stored at that temperature.

#### METHOD

Fifteen experiments have been carried out on dogs. In these, the right kidney was mobilized transperitoneally and prior to its removal surface cooled to  $15^{\circ}$  C. over a 15 min. period. The renal artery was tied and the pedicle injected with 1 cc. of 2% procaine and 10 mg. of

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