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SUCCESSFUL ORTHOTOPIC TRANSPLANTATION OF LIVER HOMOGRAFTS AFTER EIGHT TO TWENTY-FIVE HOURS PRESERVATION

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Dog liver homografts were preserved with varying techniques and tested by orthotopic homotransplantation to unrelated mongrel dog recipients. The latter were treated with azathioprine, antilymphocyte globulin, and a short course of prednisone. There were 6 groups of experiments:

Group I—Controls

Twelve homografts were removed from cooled donors, infused through the portal vein with chilled electrolyte solution, and transplanted within an hour. Only 1 recipient died in less than a week. Imposing an arbitrary limit of 70 days survival for individual animals, the mean survival was $38.7 \pm 29(\text{SD})$ days. Evidence of acute ischemic injury of these organs was minimal.

Group II—Hyperbaric oxygenation and perfusion at 3 ml./gm. tissue/hr. with diluted blood

The perfusate consisted of a balanced salt solution with a pH of 7.45. Oncotic pressure was controlled by adding low molecular weight dextran. This solution was mixed with an equal volume of blood. The organs were flushed as in Group I, and placed into a cold (4° C.) hyperbaric chamber which contained a simple oxygenator. The livers were connected by their vessels to perfusion lines which passed through externally located pumps. The flow rates were 2.4 and 0.6 ml./gm. tissue/hr. to the portal vein and hepatic artery, respectively. The oxygen compression was 40 pounds per square inch per gram.

In 7 experiments the homografts were stored in the chamber for 10 to 14.5 hr. Before their removal, decompression was completed in 25 to 35 min. Gas emboli developed in the organs and the perfusion lines. Gains in liver weight were common (average 16%). After homotransplantation 6 of the 7 recipient animals survived operation but they all died 2 to 9 days later (mean 6.2). Convulsions, observed in 2 animals immediately after graft revascularization may have been due to air emboli. Early postoperative rises in serum glutamic pyruvic transaminase (SGPT) (average 975 units) and serum glutamic oxalopyruvic transaminase (SGOT) (634 units) were attributed to ischemic injury. Serious coagulation defects were invariable. Later, the dogs became hypoproteinemic and had a high (67%) incidence of acute gastrointestinal ulceration.

In 10 more trials, homografts were preserved for 8 to 15.5 hr. under conditions which were the same except for chamber decompression over 3 to 4 hr. The gas emboli were greatly reduced and weight gain of the grafts did not occur. Nine of the 10 recipients of these livers survived operation but 7 died within 2 weeks (average 8.4 days) of the same syndrome described above of early ischemic necrosis and later subnormal liver function. The other 2 animals are alive after 102 and 80 days.

Group III—Hyperbaric oxygenation and perfusion at 6 ml./gm. tissue/hr. with diluted blood

The conditions were the same as for the slowly decompressed organs of Group II except for the increased flow which was divided as before in a 4:1 portal/arterial ratio. Homografts stored for 8 to 9.5 hr. lost 42% weight. The 5 dogs which received these livers survived operation and lived for 9, 19, 34, 46, and 80 days. The mean survival as statistically defined for Group I was 35.6 ± 24 (SD) days, essentially the same as with the controls. Acute ischemic injury was minimal.

Five additional homografts, which were preserved in this way for 24.75 to 25.17 hr., gained an average of 4.3% weight. Two of the recipients of these livers died of an uncontrollable hemorrhagic diathesis a few hours later. Another died after 8 days. The other 2 are still alive after 19 and 55 days. Serum glutamic oxalopyruvic transaminase and serum glutamic pyruvic transaminase values were initially elevated in the chronic survivors. However, the acute injury was highly reversible and good long-term function was obtained.

Group IV—Oxygenation at atmospheric pressure and perfusion with diluted blood

Three homografts, preserved with the same conditions as in Group III except for exposure to 100% O₂ at ambient pressure, gained an average weight of 27.1% during storage for 20.25 to 25.25 hr. After transplantation, all 3 livers developed outflow block and the recipients died in 6 to 28 hr.

Group V—Hyperbaric oxygenation and perfusion with noncellular fluid

Five homografts were preserved as in Group III except that blood was not added to the perfusate. After preservation for 21.25 to 24.5 hr., the organs lost a 1.9% average of their weight. Four of the recipients of these livers died just after operation of hemorrhage and hepatic insufficiency; the other survived for 9 days despite persistently poor function.

Group VI—Hyperbaric oxygenation without perfusion

The recipients of 3 homografts preserved for 22.5 to 25 hr. died after 12 hr., 18 hr., and 3.5 days. The last dog never awakened completely from anesthesia.

CONCLUSIONS

The combined use of hypothermia, hyperbaric oxygenation, and perfusion with diluted blood at the rate of 6 ml./gm. tissue/hr. permitted successful storage of hepatic homografts for 8 hr. and with less consistency for more than a day (Group III). When used as orthotopic transplants these livers supported life both immediately and chronically. The deterioration of results with reduction (Group II) or elimination (Group VI) of perfusion, omission of blood from the perfusate (Group V), or elimination of high pressure oxygen (Group IV) suggests that each of these preservation components may have played a significant beneficial role.