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Kidney Allotransplantation in Miniature Pigs*

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Summary. Kidney allotransplantation was performed in 15 fully grown miniature pigs, mainly females, and 2 female piglets. In fully grown animals the donor organ was transplanted in the iliac fossa. A different technique was employed in young dwarf pigs; the donor kidney was removed en bloc with a segment of the abdominal aorta and vena cava and was transplanted isotopically in the recipient. Blood group incompatibility is discussed as a cause of failure of pig kidney allotransplants from non-related animals. Between sister animals with similar blood groups kidney transplants could be performed successfully, but transplants between sisters of proven different blood groups did not function. In dwarf pigs hyperacute early rejection must be distinguished from late rejection. Hyperacute early rejection which occurs only a few hours after transplantation in cases of blood group incompatibility between donor and recipient, is due to immunological damage to vascular endothelium, leading to widespread arterial thromboses. Later rejection between sister animals of identical blood group occurs between the 14th and 40th day after transplantation. It is characterised by a large, oedematous kidney with petechial haemorrhages in the parenchyma and microscopically demonstrable changes in the arterial tree.

Key words: Renal transplantation, allotransplants, hyperacute rejection, delayed rejection, azathioprine, prednisone, miniature pigs.

Until now almost all experimental kidney allotransplantation has been performed in dogs and renal transplantation in other mammals has been little studied. Transplantation has been reported in baboons (39), rhesus monkeys (15, 16, 17), rats (10, 12, 14, 20) and rabbits (1, 26). Pigs have been used as experimental animals only for transplantation of skin (2, 29) and liver, (4, 6, 11, 22, 38) and for ex vivo perfusion studies (8, 9, 21, 23, 28). Although the morphological structure and functional performance of the porcine kidney resembles that of man rather than the dog (18, 34), kidney transplants in pigs have been reported only in connection with homologous liver transplantation, kidney xenotransplantation (4, 31) and autotransplantation in studies of kidney preservation. (19, 27).

The present experiments were undertaken in order to answer the following questions: - Can kidney allotransplantation be performed in pigs without undue technical difficulties and is this species suitable as a model for allogenic kidney transplantation? Besides differences in the technique of transplantation special consideration has been given to the different blood group systems of pigs.

Material and Method

16 fully grown miniature pigs, mostly females, were used in the experiments. In 4 cases the donor and recipient were not related, 8 animals were of the same litter, including 2 each with similar blood groups. 2 out of 4 sister animals had different blood groups[1]. In 2 female piglets the transplants

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1 The blood group determinations were performed by the Institut für Tierzucht und Haustiergenetic, Göttingen (Dir.: Prof. Dr. F. Haring).

were done isotopically, donor and recipient coming from the same litter. At the time of operation, the fully grown animals weighed 12 to 30 kg, the piglets used in the experiment weighed 5 kg. After premedication with dehydrobenzperidol and atropine, the operations were performed under intubation anaesthesia with halothane and nitrous oxide.

a) Fully grown animals. In 15 fully grown animals the donor organ was removed with as much renal vein and artery and ureter as possible, and it was cooled immediately and the blood washed out by gravity perfusion through the arterial system. Ringer-lactate solution was used for perfusion, adjusted to pH 7.3 to 7.5 with sodium bicarbonate, at a temperature of 3 to 5° C. Heparin 1 000 U was added to each litre of perfusion fluid. The kidney was weighed before and after perfusion. After gravity perfusion the donor kidney was transplanted to the contralateral iliac fossa of the recipient. The renal vein was anastomosed end-to-side with the common iliac vein and the renal artery end-to-end with the common iliac artery. As the pig's bladder lies intraperitoneally, the ureterocystostomy was done extraperitoneally by forming a submucous tunnel about 1 cm long (Fig. 1). All operations were done without drainage, ureteric splinting or insertion of an indwelling catheter. After completion of the vascular and ureteric anastomoses the operation was finished by removing the recipient's own kidney or kidneys. In only 2 cases were animals left with one of their own kidneys in addition to transplant (Experiments 1 and 2).

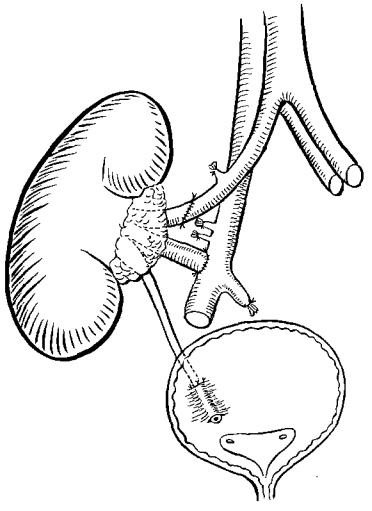

Fig. 1. Heterotopic renal allotransplantation in the miniature pig. The renal vein is anastomosed end-to-side with the common iliac vein, the renal artery end-to-side with the common iliac artery and ureterocystostomy is done by forming a submucous tunnel

b) Young animals. In fully grown miniature pigs heterotopic transplantation of the kidney into the pelvis of the recipient animals was possible, but this technique could not be used in young animals because their renal and pelvic vessels are too small for anastomosis. Instead, the kidney intended for transplantation was taken from the donor animal with a segment of aorta and vena cava. The entire ureter was included in the kidney transplant, together with a bladder flap the size of a shilling with the ureteric ostium in its centre. After ligation of the proximal ends of the aorta and vena cava of the kidney transplant, the organ was perfused via the aorta with the solution described above. Both of the recipient's kidneys were removed. The V. cava and aorta of the transplant were anastomosed end-to-side with the corresponding vessels of the recipient and the posterior peritoneum closed. A 3 cm sized patch was excised from the bladder of the recipient and the piece of donor bladder with the ureteric ostium in its centre sutured tightly into the opening (Fig. 2).

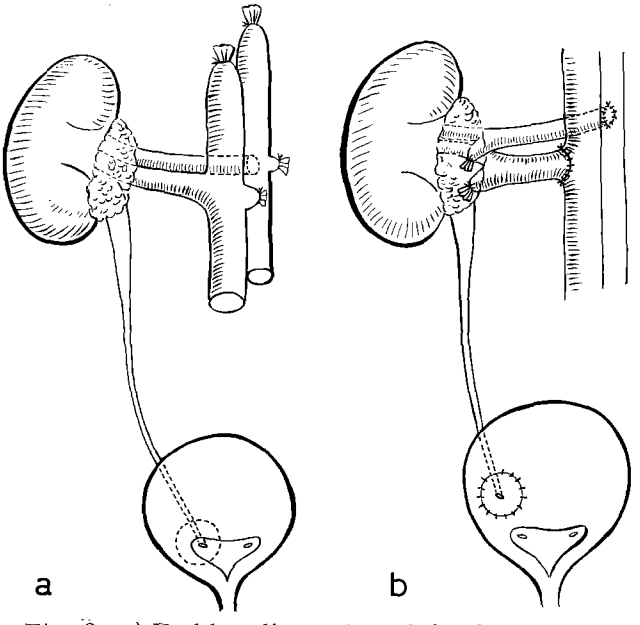

Fig. 2. a) En bloc dissection of the donor kidney with a segment of the aorta and v. cava; the entire ureter with a bladder flap and the ureteric ostium is included in the kidney transplant. b) Isotopic transplantation, v. cava and aorta of the transplant are anastomosed end-to-side with the corresponding vessels of the recipient.

Intra- and postoperative treatment. During the operation glucose-Ringer solution was infused in all animals through a foreleg vein according to the volume of blood lost. After opening the vascular anastomoses the animal

Table 1. Results of Renal Allotransplantation in Miniature Pigs

Group	Recipient Pig Nr.	Renal Weight (g) Pre- and Postperfusion		Cold Ischemia (min)	Immunsuppressive Treatment after Transplantation (mg/kg)		Death Days Post-transplant	Cause	Comment and/or Autopsy
I[a]	1	85	105	40	3A	2.5 MP	13	sacrificed	Ischemic small transplant, intact anastomoses
	2	73	91	46	3A	2.5 MP	13	sacrificed	Ischemic small transplant, intact anastomoses
	3	66	81	42	3A	2.5 MP	1	Postoperative shock	Transplant of normal size
	4	86	121	55	3A	2.5 MP	5	Hyperacute rejection Uraemia	Small ischemic Transplant
II[b]	5	76	95	40	7A	3.5 MP	3	Uraemia	Intact anastomoses, transplant of normal size (75 g)
	6	78	95	35	7A	3.5 MP	14	Rejection Uraemia	Oedematous transplant, petechial interstitial haemorrhages (300 g)
	7	92	128	55	5A	3.5 MP	6	Uraemia	One of two renal veins had been ligated intraoperatively, haemorrhagic infarction of the transplant (300 g)
	8	96	125	85	5A	3.5 MP	48	Rejection Uraemia	Oedematous transplant, petechial interstitial haemorrhages (200 g)
	9	56	79	60	ø	ø	5	Uraemia	One of two venae renales had been ligated, ischaemic transplant, renal arterial thrombosis
	10	Renal donor for pig No. 9, not suitable for recipient							
	11	67	89	40	3A	2.5 MP	5	Rejection Uraemia	Ischaemic transplant, renal arterial thrombosis
	12	67	89	80	3A	2.5 MP	6	Rejection Uraemia	Ischaemic transplant, renal arterial thrombosis
III[c]	13	62	65	35	3A	2.5 MP	3	hyperacute rejection	Transplant of normal size, intact anastomoses
	14	58	73	70	ø	ø	1	Postoperative shock (hyperacute rejection)	Ischaemic transplant arterial thrombosis
	15	66	93	50	ø	ø	1	Postoperative shock (hyperacute rejection)	Arterial thrombosis
IV[d]	16	51	71	100	3A	2.5 MP	5	Rejection Uraemia	Arterial thrombosis
	17	ø	ø	60	7A	6 MP	5	Rejection	Intact anastomoses
	18	52	71	50	7A	6 MP	20	Rejection	Intact anastomoses

received 20% Mannitol solution 250 ml and for immunosuppression 2-4 mg prednisolone per kg body weight and the same dose of azathioprin. Postoperatively these immunosuppressants were added to the food or drinking water (see Table 1).

Results

a) Kidney allotransplantations in fully grown miniature pigs. In 4 experiments the donor and recipient animals were not related, 8 were sister animals, including 2 each with similar blood groups. 4 other pigs were sisters but all with different blood groups (Tab. 1). In none of the first 4 animals which were unrelated did the transplant function. In the first 2 animals the left kidney was removed and the right kidney left behind. The organs transplanted in the iliac fossa showed no blood circulation 12 days after the operation and were greatly shrunken (Experiments 1 and 2). Bilateral nephrectomy was performed on 2 other animals after the transplantation. The first animal died the following day from operative shock; the transplanted kidney showed a good circulation and the vascular anastomoses were patent (Experiment 3). The second animal died of uraemia 5 days after transplantation. The transplanted kidney had had a moderate circulation but had produced no urine since the operation (Experiment 4). The period of cold ischaemia of the kidneys in these 4 experiments varied from 40 to 55 min. The weight of the kidneys after perfusion cooling had increased on average by 28%.

The next series of experiments consisted of 8 fully grown sister animals, 2 each with similar blood groups (Tab. 1). All the animals had a bilateral nephrectomy during the operation. The period of cold ischaemia of the allotransplants varied from 35 to 85 min. The weight of the kidneys after perfusion had increased on average by 32%. In 2 experiments in this series there were technical difficulties in constructing the anastomoses which must be held primarily responsible for the failure of the transplant (Experiments 7 and 9). In one animal the transplanted kidney had 2 large veins, one of which was ligated. The transplant showed a poor circulation and autopsy revealed thrombi in the renal artery, the larger intra-renal arterial vessels and in the renal vein (Experiment 9). In another transplant, the venous anastomosis was thrombosed and the kidney showed a haemorrhagic infarct. In this transplant, too, one of 2 renal veins had had to be ligated (Experiment 7). In 2 other animals the transplant developed livid discoloration even during the operation and the pigs died of uraemia on the 6th and 7th days after operation. In both cases autopsy showed thrombus in the renal artery which had caused failure of the transplant. Histologically, both these cases showed anaemic infarction in the cortical region and the tubules were necrotic (Experiments 11 and 12). In 2 animals the transplant functioned for a longer period; the periods of survival were 14 days and 48 days (Experiments 6 and 8 respectively). Both animals died of uraemia. The transplants showed massive oedema indicating a rejection crisis (kidney weights 300 and 200 g), and innumerable petechial haemorrhages in the cortex and medulla. The renal interstitium in both cases showed large areas of fibrosis and areas of varying sizes infiltrated by lymphocytes and plasma cells. The arterioles and vasa afferentia showed multiple obstructions of the lumen due to intimal proliferation. Lymphocytes and plasma cells were also demonstrated around the vessels.[2]

4 sister animals, 2 each with dissimilar blood groups, died of renal failure 5 to 7 days after transplantation. The animals had had both kidneys removed during the operation. The period of cold ischaemia of the transplants varied from 35 to 100 min., and the average weight increase of the kidneys after perfusion was 27% (Experiments 13, 14, 15 and 16). Despite massive immunosuppressive treatment, none of the transplants functioned. At autopsy the kidneys were soft and small, and appeared poorly perfused. Thrombosis of the main renal artery and its larger branches was seen in 3 pigs and the renal parenchyma was

◀— Footnote to Table 1

a Group I Donor and recipient unrelated
b Group II Pig No. 5-6, 7-8, 9-10, 11-12 were siblings with similar bloodgroups
c Group III Pig No. 13-14, 15-16 were siblings with dissimilar bloodgroups
d Group IV En bloc transplantations

A = Azathioprin

MP = Methylprednisolone (Urbason^{R})

2 The histological examinations were done by Dr. H. G. Kochem, Lecturer, Pathological Institute of the Essen Clinics of the Ruhr University, Bochum (Dir. Prof. Dr. W. Müller).

diffusely necrotic (Experiments 14, 15 and 16). In the 4th animal, the transplanted kidney showed very severe vacuolar degeneration of the tubular epithelium and, in places, luminal casts. The glomeruli appeared normal (Experiment 13).

b) Kidney allotransplants in young animals. 2 isotipic kidney allotransplants were performed in female piglets according to the method described, and without regard to blood groups (Experiments 17 and 18). The first animal died of uraemia with a non-functioning kidney 6 days after transplantation, the second animal survived for 20 days with initially good function of the transplanted organ. After death the transplants showed no macroscopic signs of definite rejection, apart from slight oedema. Microscopically, in 1 animal there were very severe tubular necroses and finely granular epithelial degeneration (Experiment 17). The transplant in the animal surviving for 20 days showed no pathological features of rejection (Fig. 3).

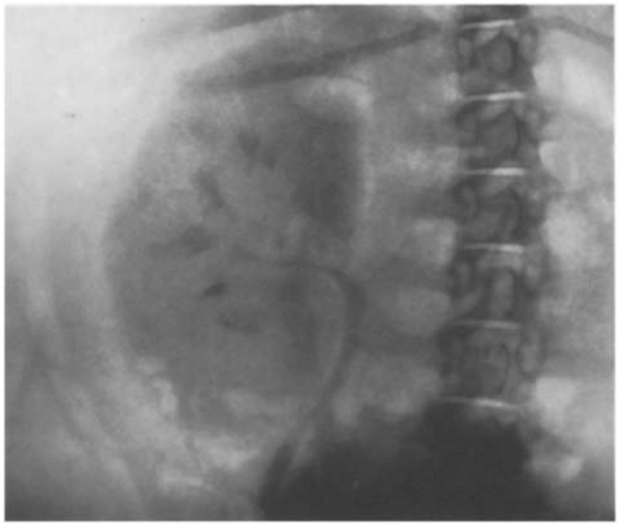

Fig. 3. IVP 10 days after isotopic allotransplantation (experiment No. 18). The 40-minute-film shows the calices and the ureter of the enlarged transplant.

Discussion

Kidney allotransplantation in miniature pigs is technically feasible. In fully grown animals the transplant was placed in the iliac fossa of the recipient and the renal vessels were anastomosed end-to-end and end-to-side with the common iliac artery and vein; this technique was not feasible in young animals (up to 3 months old) because the lumina of the vessels appeared too narrow to be joined successfully. In these animals, therefore, the kidney was transplanted by modification of the methods suggested by Nathan et al. (26) and by Goodwin et al. (13). With the aid of this technique it should be possible to perform kidney transplantations even in babies and small children.

Technical difficulties with the vascular anastomoses were definitely responsible for failure of the transplants in only 2 animals (Experiments 7 and 9), and all the others appeared satisfactory at autopsy. Similarly, in all cases the ureterocystostomy was patent at necropsy and a bougie could readily be passed from the bladder into the ureters. Despite immunosuppressive therapy during and after transplantation (up to 5 mg kg body weight of both azathioprine and methylprednisolone) a functioning kidney allotransplant was never observed between non-related pigs (Experiments 1 to 4). In seeking the cause of this failure it was deemed possible that differences in blood groups between donor and recipient might be important. In dogs, differences between the blood groups of donor and recipient are of secondary importance as this species does not possess isoagglutinins, but in man and in monkeys, rejection is accelerated if there are blood group differences between a donor and a recipient (5, 32, 35, 36, 39). Since the erythrocytes were washed out of the kidney by arterial perfusion prior to the transplantation, it seemed likely that specific antigens were not confined to the red cells alone, but that blood groupspecific antigens were also present in kidney cells, particularly in the vascular endothelium. Blood group-dependent antigen - antibody reactions have been demonstrated in the renal vascular system in man (37).

In order to show that porcine blood groups could be held responsible for early failure of renal allotransplants, kidneys were grafted between animals with similar blood groups. 18 blood group factors were determined in each animal. Since un-related miniature pigs of identical blood groups were unobtainable, the experiments had to be performed on sister animals, 2 of which always fulfilled the experimental conditions. Sister animals of proven non-identical blood groups served as controls. In a group of 8 sister animals, 2 each with similar blood groups, a total of 7 transplantations was performed. The failure of 2 kidneys could be attributed to mechanical disturbance of the venous outflow (Experiments 7 and 9). 2 of the remaining 5 transplants functioned for 14 and 48 days. The animals died during a massive rejection crisis, the kidneys were enlarged, hard and oedematous, and the parenchyma strewn with innumerable petechial haemorrhages. The large arteries showed intimal proliferation and cell infiltration in

the vicinity of the vessels, and intimal thickening with occasional obstruction of the lumina. Larger focal haemorrhages were found in the interstitium. These microscopic appearances, with particular involvement of arterial vessels, are comparable to accounts of late rejection of dog and baboon kidney allografts (30, 39).

The results suggest that in 2 animals the relatively prolonged functioning of the transplant was due to the compartibility of the blood group factors, whereas in 3 other animals (Experiments 5, 11 and 12) with technically faultless anastomoses, only a few incompatible blood group factors sufficed to produce arterial thrombosis.

The transplants from sister animals with dissimilar blood groups did not function. Microscopically they showed extensive necroses of the kidney parenchyma and thrombosis of the renal artery and sometimes of the interlobular arteries (Experiments 13-16).

The fact that one piglet with an isotopic allotransplant from a sister animal survived for 20 days, whilst another 4 weeks-old animal lived only 5 days after operation, suggests that the first animal probably had similar blood groups to the donor, which came from the same litter.

Conclusion

The experiments have shown 2 types of rejection reaction against allotransplants of porcine kidneys. Hyperacute rejection a few hours after transplantation may be connected with blood group incompatibility between donor and recipient. The immunological reactions take place in the large arterial vessels of the transplant and usually lead to arterial thrombosis. On the other hand, late rejection, 14 to 40 days after transplantation, may lead to renal failure even in animals in whom there is a high degree of compatibility between the blood groups of donor and recipient animals. This form of rejection, characterised by a large, oedematous, hard, functionless kidney with innumerable petechial parenchymatous haemorrhages, and microscopically, by demonstrable lesions in the arterial tree, seems to run a similar course in dogs, baboons and in man. It is due to an antigen-antibody reaction independent of blood groups. Early rejection, which was often seen in the miniature pigs, has rarely been seen in man, and only if there has been incompatibility of the main blood groups between the kidney donor and recipient; it can be provoked in dogs only under certain conditions. The problems posed by blood group incompatibilities in pigs therefore, make this species unsuitable as a transplantation model of man. On the other hand, the present investigations have provided information about the importance of the blood group systems within the general framework of immunological defence reactions.

References

1. Bayuk, J. M., Schmidlapp, C. J.: Kidney transplantation in the rabbit: A method for the study of transplantation immunology. Invest. Urol. 4, 378 (1966).
2. Binns, R. M.: Bone marrow and lymphoid cell injection of the pig foetus resulting in transplantation tolerance or immunity, and immunoglobulin production. Nature (Lond.) 214, 179 (1967).
3. Calne, R. Y., White, H. J. O., Yoffa, D. E., Maginn, R. R., Binns, R. M., Samuel, J. R., Molina, V. P.: Observations of orthotopic liver transplantation in the pig. Brit. med. J. 2, 478 (1967).
4. Calne, R. Y.: Cit. Med. Tribune 4, German Ed. No. 17, 3 (1969).
5. Christian, R. M., Ervin, D. M., Young, L. E.: Observations on the in-vitro behaviour of dog isoantibodies. J. Immunol. 66, 37 (1951).
6. Cordier, G., Garnier, H., Clot, J. P., Camplez, P., Gorin, J. P., Clot, P., Rassinier, J. P., Nizza, M., Levy, R.: La greffe de foie orthotopique chez le porc. Premiers résultats. Mém. Acad. Chir. 92, 799 (1966).
7. Cragle, R. G., Stone, W. H.: Preliminary results of kidney grafts between cattle chimeric twins. Transplantation 5, 328 (1967).
8. Eiseman, B., Knipe, P., Mc Coll, H. A., Orloff, M. J.: Isolated liver perfusion for reducing blood ammonia. Arch. Surg. 83, 356 (1961).
9. Eyskens, E., Norman, J. C., Mc Dermott, W. V. jr.: De experimentele "ex vivo" perfusie. Acta chir. belg. 66, 827 (1967).
10. Fisher, B., Lee, S.: Microvascular surgical technique in research with special reference to renal transplantation in the rat. Surgery 58, 904 (1965).
11. Garnier, H., Clot, J. P., Bertrand, P., Camplez, P., Kunlin, A., Corin, J. P., Goaziuo, F. L., Levy, R., Cordier, G.: Greffe de foie chez le porc: Approche chirurgicale. C. R. Acad. Sci. (Paris) 260, 5621 (1965).
12. Gonzalez, E. E., Nathan, P., Miller, B. F.: A method for transplantation of the rat kidney. Ann. N. Y. Acad. Sci. 99, 795 (1962).
13. Goodwin, W. E., Mims, M. M., Kaufman, J. J.: Human renal transplantation: III.

Technical problems encountered in 6 cases of renal transplantation. J. Urol. (Baltimore) 89, 349 (1963).
14. Guttmann, R.D., Lindquist, R.R., Parker, R.M., Carpenter, C.B., Merrill, J.P.: Renal transplantation in the inbred rat. Transplantation 5, 668 (1967).
15. Herrmann, J.B.: Renal transplantation in the rhesus monkey. Use of the American vascular stapler. Invest. Urol. 2, 264 (1964).
16. Huser, H.J., Murphy, G.P.: Renal transplantation in the ehesus monkey. 3. Hematologic and immunologic studies. Invest. Urol. 2, 273 (1964).
17. Johnston, G.S., Murphy, G.P.: Renal transplantation in rhesus monkey. IV. Correlation of renal alterations with the radioisotope renogram. Invest. Urol. 2, 286 (1964).
18. Kerr, W.S. jr.: Maximum clearances (GFR and ERPF) in dogs. J. Urol. (Baltimore) 80, 205 (1958).
19. Kierfeld, G., Mellin, P., Schwalm, E., Brehmer, B.: Erfolgreiche Nierenkonservierung bis zu 48 Stunden im Experiment am Miniaturschwein. Urol. int. (Basel) 26, 196 (1971).
20. Lauschke, H., Hermann, G.: Versuche zur heterotopen Nierentransplantation bei der Ratte. In: Organtransplantation. (A. Heymer, D. Ricken) Stuttgart - New York: F.K. Schattauer (1969).
21. Liem, D.S., Waltuch, T.L., Eiseman, B.: Function of the ex vivo liver perfused with human blood. Surg. Forum 15, 90 (1964).
22. Mieny, C.J., Moore, A.R., Homatus, J., Eisenman, B.: Homotransplantation of the liver in pigs. S. Afr. J. Surg. 5, 109 (1967).
23. Mieny, C. J., Eiseman, B.: Liver preservation: Unperfused cold storage and continuous cold perfusion. Surgery 63, 923 (1968).
24. Murphy, G.P., Lawson, N.L., Johnston, G.S.: Renal transplantation in the rhesus monkey. II. Alterations in renal function and morphology. Invest. Urol. 2, 261 (1964).
25. Murphy, G.P., Melby, E.C., Mirand, E.A., Huser, H.F., Weldon, C.S.: Renal transplantation in the rhesus monkey. VI. Observations in homotransplanted animals. Invest. Urol. 3, 244 (1965).
26. Nathan, P., Gonzalez, E.E., Fowler, R., Pescovitz, H., Miller, B.F.: A method for transplantation of the rabbit kidney. Proc. Soc. exp. Biol. (N.Y.) 107, 51 (1961).
27. Nerstrom, B., Gyrd-Hansen, N., Iversen-Hansen, R., Lokkeraard, H.: Renal autotransplantation in the pig: Surgical aspects. Scand. J. Urol. Nephrol. 6, 151 (1972).
28. Norman, J.C., Franco, F.O., Brown, M.E., Saravis, C.A., Ackroyd, F.W., Dermott, W.V.: Techniques of obtaining and preparing the porcine liver for experimental and clinical temporary ex vivo perfusion. J. surg. Res. 6, 117 (1966).
29. Petterson, T.J.: The survival of skin flaps in the pig. Brit. J. plast. Surg. 21, 113 (1968).
30. Porter, K.A., Calner, R.Y., Zukoski, C.F.: Vascular and other changes in 200 cantine renal homotransplants treated with immunosuppressive drugs. Lab. Invest. 13, 809 (1964).
31. Rosenberg, J.C., Broersma, R.J., Bullemer, G., Mammen, E.F., Lenaghan, R., Rosenberg, B.F.: Relationship of platelets, blood coagulation, and fibrinolysis to hyperacute rejection of renal xenografts. Transplantation 8, 152 (1969).
32. Sheil, A.G.R., Stewart, J.H., Tiller, D.J., May, J.: ABO blood group incompatibility in renal transplantation. Transplantation 8, 299 (1969).
33. Simonsen, M.: The acquired immunity concept in kidney homotransplantation. Ann. N.Y. Acad. Sci 59, 448 (1955).
34. Suarez, C.A., Guerrero, A.A., Musil, G., Hulet, W.H.: Renal function and nephron structure in the miniature pig. Amer. J. vet. Res. 29, 995 (1968).
35. Starzl, T.E., Marchioro, T.L., Hermann, G., Brittain, R.S., Waddell, W.R.: Renal homografts in patients with major donor-recipient blood group incompatibility. Surg. Forum 14, 214 (1963).
36. Starzl, T.E., Marchioro, T.L., Holmes, J.H., Hermann, G., Brittain, R.S., Stonington, O.H., Talmage, D.W., Waddell, W.R.: Renal homografts in patients with major donor-recipient blood group incompatibilities. Surgery 55, 195 (1964).
37. Szulman, A.E.: The histological distribution of the blood. group substances A and B in man. J. exp. Med. 111, 785 (1960).
38. Terblanche, J., Peacock, J.H., Bowes, J., Davies, R.J., Tierris, E.J., Palmer, D.B., Hunt. A.C.: The use of the pig as an experimental animal for orthotopic liver homotransplantation. Brit. J. Surg. 54, 231 (1967).

39. Weber, H.W., Brede, H.D., Retief, F. P., Retief, C.P., van Zyl, J.A., Gronewald, J.H., van Zyl, J.J.W., Murphy, G.P.: Morphological and functional alterations noted after baboon renal allotransplantation. J. Urol. (Baltimore) 101, 465 (1969).

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