

9-1969

Initial Studies of Isolated Kidney Perfusion

Stanley G. Dienst

Michael A. Krieg

Follow this and additional works at: <https://scholarlycommons.henryford.com/hfhmedjournal>



Part of the [Life Sciences Commons](#), [Medical Specialties Commons](#), and the [Public Health Commons](#)

Recommended Citation

Dienst, Stanley G. and Krieg, Michael A. (1969) "Initial Studies of Isolated Kidney Perfusion," *Henry Ford Hospital Medical Journal* : Vol. 17 : No. 3 , 165-170.

Available at: <https://scholarlycommons.henryford.com/hfhmedjournal/vol17/iss3/2>

This Article is brought to you for free and open access by Henry Ford Health System Scholarly Commons. It has been accepted for inclusion in Henry Ford Hospital Medical Journal by an authorized editor of Henry Ford Health System Scholarly Commons.

Initial Studies of Isolated Kidney Perfusion

Stanley G. Dienst, M.D. and Michael A. Krieg, M.D.*

Angiographic and gravimetric studies of dog kidneys perfused with electrolyte, Dextran, or albumin solution are presented to demonstrate the possibility of extending organ preservation for transplantation without loss of function. Findings include a reduction in flow and weight gain with the nonprotein solutions and maintenance of flow with albumin solution. Gross changes of the perfused kidneys are also described.

The objective of isolated kidney perfusion is to extend the period during which normal renal function can be preserved between excising and reimplanting the kidney. In studies toward this objective, the dog has become the standard experimental animal. It has now been shown that, without any perfusion, dog kidneys can be preserved—with subsequent good function on reimplantation—by heparinization and rapid surface cooling for up to 12 hours.¹ This 12-hour "base line" should be significantly extended by the addition of perfusion to a kidney preservation system.

Feemster and Lillehei² were able to preserve dog kidneys for 24 hours by using hyperbaria and perfusing with Dextran in a balanced salt solution. Belzer³ preserved dog kidneys for 72 hours, with sufficient function to allow immediate contralateral nephrectomy, by using filtered cryoprecipitated plasma at 8° to 10° C. Humphries,⁴ pre-

serving dog kidneys with diluted homologous blood, has achieved the preservation of one kidney for five days (or 110 hours) with enough function to maintain the animal after delayed contralateral nephrectomy. These studies are a measure of the success that has been achieved and also show the diversity of procedures that have been applied.

In initiating further studies of isolated kidney perfusion, it was first necessary to determine the most suitable composition of the perfusate. Essentially, the choice lay between electrolyte glucose solution and a protein solution, such as filtered homologous plasma or a commercial albumin solution. For the protein colloid, commercially concentrated human albumin was first chosen because of its availability and the absence of antibody containing globulin fractions. Cryoprecipitated dog plasma filtered through Millipore filters after Belzer³ has been used for subsequent studies.

Procedure:

Angiographic Studies. Dog kidneys weighing near 40 gm were excised and

* Division of Vascular Surgery, Department of Surgery
This work was sponsored in part by The McGraw Foundation

flushed free of blood with 4° to 8° C heparinized Ringer's lactate solution. The renal artery was cannulated and the kidney placed in chipped ice. Slow perfusion was begun from a height of one meter (76 mm Hg) with ice cold saline, saline with 6% clinical Dextran, or saline plus 6 gm/100 ml of concentrated human albumin.* Angiograms were taken using x-ray magnification techniques and an ice cold solution of 50% Conray in saline—also under one meter of hydrostatic pressure.

Isogravimetric Studies: Dog kidneys were prepared as above and placed in an insulated chamber on a pan balance. They were perfused with the same solutions over a period of three to four hours. Arterial and venous perfusion tubings were disconnected momentarily at each weighing. Weight changes and rates of flow were plotted against time.

Gross Changes: All kidneys were hemisected. Changes were noted, particularly in the medullary portion, and representative gross sections were photographed.

Results

Figure 1 shows the angiographic appearance of a controlled kidney without perfusion after 3½ hours. The only differences noted between this and angiograms taken immediately after excision is a blurring of the smaller vessel outlines and a decreased filling of the medullary portion. In the kidney perfused with saline, the perfusion rate has fallen over three hours from eight to less than 2 ml/min. The weight gain of these kidneys is 10% or more and they are grossly edematous. It was

found that placing the kidney in a hyperbaric chamber at three atmospheres of oxygen allowed saline perfusion to five hours with the rate of flow falling to 3 ml/min. Weight gain of these kidneys was generally less. However, angiographic appearances were similar. The angiogram of the saline perfused kidney at atmospheric pressure (Fig 1) demonstrates the marked slowing of the dye (15 seconds). Later films at 45 seconds show only a few additional secondary and tertiary branches filling.

In Figure 2, the vascular pattern resulting from perfusing with Dextran and albumin solution are compared. In the Dextran perfused kidney, the cortex is well perfused, but the medullary portion does not fill. The vessel outlines have become appreciably blurred and the flow rate has fallen to less than 3 ml/min. The finest reticular angiographic pattern with homogeneous filling of both cortex and medulla was consistently obtained with the albumin solution. There is some edema of the outer cortex of the albumin perfused kidney from prolonged exposure to the hypotonic ice bath. The flow rate through the albumin perfusion was controlled at 7 to 8 ml/min, but readily increased to 14 ml at 3½ hours. Weight gain by albumin perfused kidneys was less than 2%.

Weight changes of the colloid and the saline perfused kidney are compared on a single kidney in Diagram 1. With albumin perfusion, there is no weight gain. Immediately after starting saline, there is a progressive gain of 10 to 15% per hour over the two hours measured and an associated reduction in flow. Restarting the albumin stopped the increase in weight but did

* Albumisol

Initial Studies of Isolated Kidney Perfusion

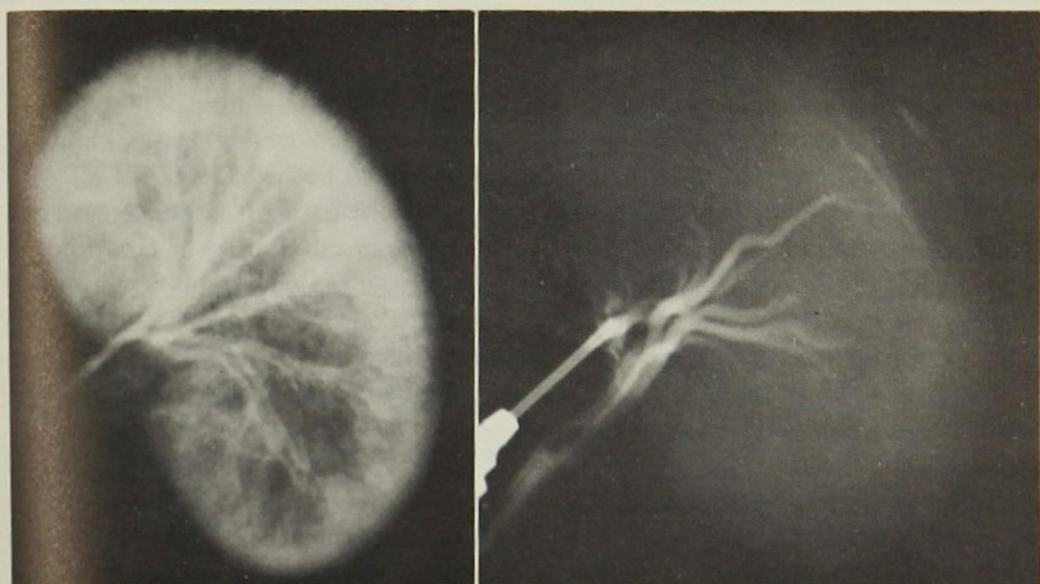


Figure 1

Angiograms of dog kidneys after $3\frac{1}{2}$ hours at 0 to 40° C. The kidney on the left has not been perfused after initial flushing with Ringer's lactate. The kidney on the right was perfused with saline at 6 mm Hg pressure.

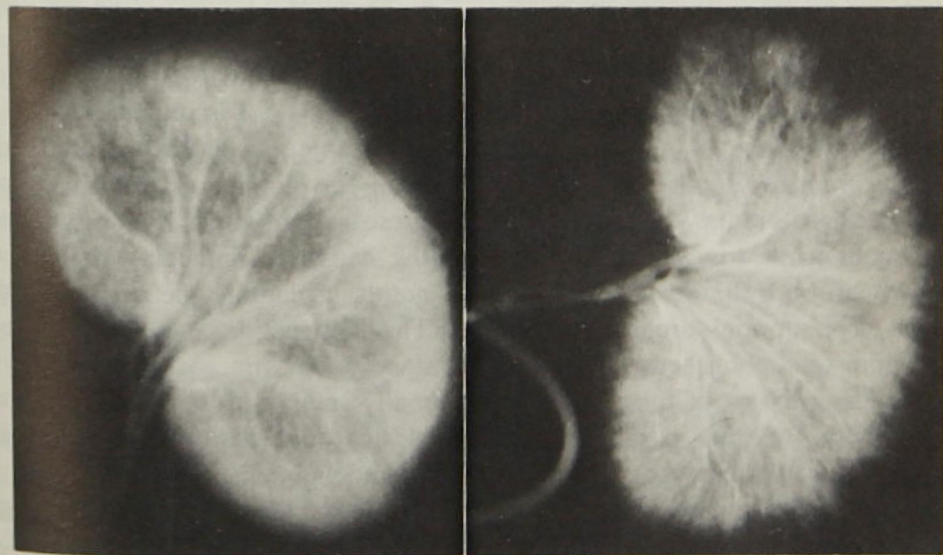


Figure 2

Angiograms of dog kidneys perfused for $3\frac{1}{2}$ hours at 0 to 40° C with Dextran in saline (left) and Albumisol in saline (right).

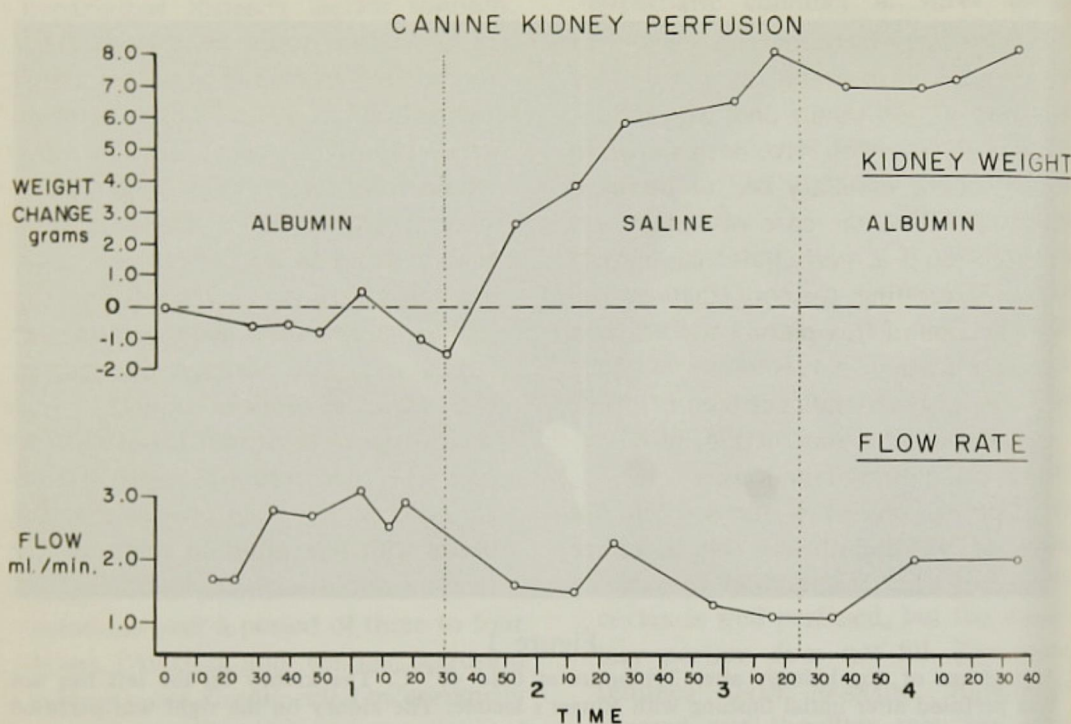


Diagram 1

This shows the weight and flow rate changes of a dog kidney perfused consecutively with albumin solution, saline, and then returning to albumin. Flow during the first period of albumin perfusion is limited to 3.0 ml/min. Flow rates during the saline perfusion and the final albumin perfusion represent maximum rates at the constant pressure of 50 mm Hg.

not reduce it toward normal and did not re-establish flow.

Gross Changes: Hemisection of the saline perfused kidneys showed an homogenous white translucent appearance through both the inner and outer medulla. The normal architecture in this region was abolished. This was true to a lesser extent of those kidneys perfused with Dextran in saline. The albumin perfused kidneys, on the other hand, showed the normal striated pattern of collecting tubules converging toward the pyramids. There were few gross changes in the cortices of the kidneys studied.

Discussion

Obstruction of the vascular bed has been the dominant problem in organ preservation work. It is recognized as the cause of immediate failure when autotransplanting the perfused kidney. The obstruction is considered secondary to the macroaggregation of normally soluble proteins in the perfusing plasma and to swelling of capillary endothelial cells.

The problem of obstructing aggregates, though not entirely clarified, has found a partial solution in the use of Belzer's³ cryoprecipitated plasma. This process removes a portion of

Initial Studies of Isolated Kidney Perfusion

the lipoproteins from the plasma. Without cryoprecipitation, these lipoproteins form large macromolecules or aggregates presumably as a result of trauma in the pump and oxygenator. These microemboli have been shown to lodge in the capillary bed of perfused organs and in the case of kidney are concentrated in peritubular capillaries. It is interesting to note that in the preparation of this plasma the primary clotting factor (X) is removed. This may be also a significant factor in preventing vascular obstruction by blocking initial clotting reactions.

Current interest is focused on the role of the endothelial cell in either "swelling" or "contracting" to produce capillary obstruction. This work has been given impetus by the increased availability of the electron microscope. The swelling of these cells, as well as various degrees of dissolution of mitochondrial cristae resulting from perfusion, have been demonstrated. Though these changes have been documented, specific etiological factors have not been identified.

Colloid osmolality of the perfusing solution may well be a factor in preventing or partially controlling endothelial swelling. It may be significant in the first hours, whereas alterations such as anoxia, acidosis, substrate and amino depletion may be prominent later in the course of preservation.

These studies were designed to compare kidney perfusion, using isotonic electrolyte solution alone, to perfusion with Dextran or protein colloid added to the electrolyte solution. The perfusion time was kept short and tempera-

tures low enough to minimize cellular anoxic changes. Therefore, differences in perfusion would be due primarily to the effect of colloid oncotic pressure. Intermittent or pulsatile flow were not used for this study. The measures would have allowed for longer perfusion at higher flows. These adjuncts were deleted to accentuate the angiographic and flow differences.

The results show a progressive obstruction to flow through the vascular bed when noncolloid solutions were used for perfusion; and lesser obstruction when Dextran was used. No obstruction to flow was produced at 3½ hours with 6% albumin solution. The relative importance of endothelial cell swelling, interstitial edema and cellular parenchymal swelling cannot be differentiated by this type of study. Grossly, most of the changes occur in the medullary portion of the kidney. The usual hypertonicity of cells in the inner medulla make this region the most prone to swelling when the rate of metabolism is acutely reduced and filtration slowed. In the case of saline perfusion, this is probably accentuated by the presence of noncolloid fluid in the peritubular capillaries. The use of albumin or cryoprecipitated plasma for perfusion will minimize the problem of early vascular bed obstruction. Longer perfusion will depend on the close regulation of metabolic factors such as oxygen and substrate supply, control of pH, the establishment of extracellular-intracellular amino acid balance, and the provision of soluble respiratory enzymes.

REFERENCES

1. Collins, G.M.; Shugarman, M.B.; and Terasaki, P.I.: NIH Progress Report. Jun 1969.
2. Feemster, J.H., and Lillehei, R.C.: Hypothermic, hyperbaric pulsatile perfusion for preservation of the canine kidney, unpublished, 1968.
3. Belzer, F.O., et al: Etiology of rising perfusion pressure in isolated organ perfusion, *Ann Surg* 168:382-91, Sept 1968.
4. Humphries, A.L., et al: Successful five-day kidney preservation, *Invest Urol* 5:609-18, May 1968.

tali
of t
pro
ope
repe
surv
dio-
ited
caus
onst
mal
varia
subo
tics o
pecte
desig
mitra
satisf
availa
valves
mitral
group
morb
cardia
iod. B

* Divisi