Flow as a Function of Arterial Pressure in the Oil Perfused Kidney

By William H. Waugh, M.D.

Isolated canine kidneys were perfused with oil which did not accumulate extravascularly and which prevented renal vasomotor responses. The purely physical effects of changed arterial pressure on renal vascular flow and resistance were studied.

Many workers have found relatively little change in the rate of renal blood flow when the renal arterial pressure is varied within a pressure range of approximately 70 to 180 mm. Hg. This autoregulation of renal blood flow is generally viewed as an intrinsic property of the kidney, wherein resistance increases with a raised arterial pressure. The nature of this response is a moot question. It may be an active vasomotor process or the result of plasma skimming and the anomalous viscosity of blood. Comparative pressure-flow data in the deteriorated blood perfused kidney or in the kidney perfused with an erythrocyte deficient liquid are important but difficult to interpret. With the kidney in an unphysiologic state, edema formation and a generalized increase in interstitial pressure are apt to occur. Thus, as is the case for the kidney perfused with Ringer's solution, the change in renal resistance when arterial pressure is varied may be concerned largely with the factors determining an abnormally high intrarenal pressure. In kidneys poisoned with cyanide, the interstitial pressure rises markedly and rectilinear blood pressure-flow data are found. A similar relationship between renal arterial pressure and flow has also been observed for an oxygenated colloidal perfusate devoid of red blood cells.

A water-immiscible Newtonian liquid would seem to be an ideal perfusate to determine the purely physical effects of arterial pressure on the dimensional vascular component of renal resistance. Interfacial tension should prevent transcapillary passage of a water immiscible fluid into the aqueous tissue compartments and changes in renal resistance to flow of such a fluid should be readily measurable in the absence of edema and vasomotor activity. The use of kerosene was suggested by the work of Cox and Dock who found that renal flow rates post mortem with this oil were not less than the normal rates for renal blood flow during life.

Methods and Materials

Kidneys were excised from 5 to 15 Kg. dogs shortly after death produced by rapid intravenous administration of pentobarbital. In many experiments, 4 mg. of heparin/Kg. were given by vein a few minutes before death. To assure removal of blood, the heparinized excised kidneys were perfused first with 500 ml. of 1.5 per cent sodium chloride solution at an arterial pressure of 100 mm. Hg. The arterial pressure was then reduced to zero.

Perfusion was next performed at room temperature, either with kerosene or with a more viscous oil consisting of a mixture of kerosene and refined mineral oil. The viscosities of the oil perfusates were measured in vitro by a method similar to that of Coulter and Pappenheimer. Preparatory to obtaining the pressure-flow data, at least 500 ml. of oil were perfused at relatively high renal arterial pressures. The effects of serially varying the arterial pressure were then studied, usually 20 min. or more after the initial oil flush.

Desired constant pressure heads were produced by adjusting a mercury valve for air escape which was connected to a perfusion reservoir pressurized by a continuous supply of air. Tygon (vinyl) tubing was employed as a conduit for the oil perfusate. A glass wool filter was interposed in the inflow tract to the kidney to prevent particulate

From the Department of Physiology, Medical College of Georgia, Augusta, Ga.

This work was supported by grant HTS 5011 from the National Heart Institute and by the Life Insurance Medical Research Fund.

Received for publication September 11, 1957.
obstruction of flow. Kidneys were perfused individually while they were supported horizontally on a wire meshwork with occasional topical applications of the perfusate to the major vessels and the renal capsule.

The conduit from the perfusion reservoir was connected to the renal artery by a T-cannula of approximately the same bore as the artery and conduit. An appropriate T-cannula was usually inserted into the renal vein and a small length of tubing attached distally. By placing the outflow exit at the requisite level, the venous pressure at the T-cannula was maintained at 0 or 10 mm. Hg throughout the experiments. In some instances, the intrarenal venous pressure\textsuperscript{10} was also measured by inserting a plastic catheter of 0.94 mm. external diameter into the renal vein and directing the catheter backwards until the tip lay at, or just beyond, the junction of an interlobar and arcuate vein. This position was later verified by renal section. Pressures were determined with mercurial manometers and were referred to the level of the cannulated vessels at the renal hilus. After maintaining the perfusion pressure constant for one-half to several minutes, venous outflow* was measured using a graduated cylinder and stopwatch.

**RESULTS**

**Evidence for Lack of Extravascular Accumulation of the Renal Perfusate of Oil.** The absence of interstitial edema and transcapillary passage of the oil was demonstrated by the following observations. Ureteral outflow of oil was never observed during arterial perfusion of the kidney and therefore glomerular filtration of oil seemed nonexistent. When the oil perfusate contained Sudan I, a dye which is oil soluble, extravascular localization of the dye was not found upon subsequent examination of cut sections of the kidney. Despite arterial oil pressures as high as 180 mm. Hg to heparinized kidneys, the renal capsule did not become tense and the intrarenal venous pressure remained relatively low. With venous perfusion of the kidney with oil, the organ swelled and the intrarenal pressure downstream rose to nearly the level of inflow venous pressure.\textsuperscript{11} Reduction of venous pressure to normal resulted in an immediate return to normal of intrarenal pressure and of renal size. The immediate reversal of these changes strongly implied that the fluid remained intravascular.

**Kerosene Flow as a Function of Arterial Pressure in Nonheparinized Kidneys.** Eight kidneys, all from different dogs, were perfused without prior heparinization and saline flushing. The kerosene had a viscosity of 0.016 poise at 24 C. With step-wise elevations in arterial pressure up to levels of about 200 mm. Hg, renal resistance usually rose progressively. However, the degree of increased resistance with a raised arterial pressure varied widely in different kidneys. Occasionally, sigmoid pressure-flow curves were observed similar to those found in vivo by Shipley and Study\textsuperscript{12} who used a higher range of arterial pressures.

In 1 case, the intrarenal venous pressure rose to a high level and almost paralleled the elevation in arterial pressure. The resistance upstream from the arcuate veins fell although the venous resistance and the total resistance of the kidney rose at elevated arterial pressures. In another kidney, the resistance both proximal and distal to the arcuate veins increased as the arterial pressure was raised. In a third experiment, the renal artery near the cannula had become dry and contracted to a smaller size than the cannula. The intrarenal venous pressure remained very low when the arterial pressure was raised. Some of the increased resistance in this instance was probably the result of turbulent flow near the contracted arterial segment. Intrarenal venous pressures were not measured in the other 5 kidneys.

**Kerosene Flow as a Function of Arterial Pressure in Heparinized Kidneys.** Quite different results were found in these kidneys. Plows were much greater than in the nonheparinized ones. In 12 heparinized kidneys resistance fell progressively as a function of increased arterial pressure. Figure 1 illustrates data from one of these experiments. The pressure-flow plots were curvilinear and convex to the pressure axis. At the highest levels of arterial pressure used (about 100 mm. Hg), the plots

---

*Outflow through renal collaterals was usually disregarded. It was very small and did not alter the basic pressure-flow relations found when determining only the flow through the main renal vein.
ARterial Pressure and kidney flow

Fig. 1. Typical pressure-flow relationships in a heparinized kidney perfused with kerosene. Constant venous pressure of 10 mm. Hg. Curve A, the total renal arterial-venous pressure differences plotted against flow. Curve P, pressure-flow relations proximal to the arcuate venous system. Kidney weight 22.3 Gm. Ordinate, flow rate (ml./min.); abscissa, pressure gradient (mm. Hg).

closely approached a straight line, which upon extrapolation intersected the pressure axis. At a given arterial pressure, flows were greater after the pressure had been rapidly lowered from a higher level than when slowly increased from a lower level. The pressure-flow relationships did not plot linearly on log-log paper.

The intrarenal venous pressures rose to levels up to 35 mm. Hg at arterial pressures of 100 mm. Hg when the external venous pressure was 10 mm. Hg. Plots of the differences in arterial and arcuate venous pressure against flow rates (see curve P of fig. 1) suggested a large progressive reduction in arteriolar resistance with increasing arterial pressure.

Atypical relations were found in 5 other experiments. In 4 of these resistance rose at high rates of flow. In the fifth case, the renal artery had become dry and contracted near the cannula and the entire pressure-flow curve was concave to the pressure axis. These atypical results were probably due to turbulent flow.

Effect of Partial Vascular Occlusion on Resistance as a Function of Arterial Pressure. The following experiments were performed to determine whether turbulence could account for the increased resistance to kerosene flow with elevated arterial pressures observed frequently in the nonheparinized kidney and atypically in the heparinized kidney. A thin ligature was tied around either the renal artery or vein tightly enough to impede flow. The arterial ligature was placed downstream and the venous tie upstream to the respective manometer connections. Either procedure converted the typical convex pressure-flow plots of the heparinized kidney to plots concave to

Fig. 2. Effect of constant arterial constriction on the pressure-flow relationship. Heparinized kidney (24.1 Gm.) was perfused with kerosene. Curve A, without ligature; curve B, with a ligature severely narrowing a segment of the renal artery. Constant venous pressure of 10 mm. Hg. Ordinate, flow rate (ml./min.); abscissa, pressure gradient (mm. Hg).
the pressure axis. Resistance rose, rather than fell, with increased arterial pressure and varied with the degree of stricture. Figure 2 illustrates an experiment of this type. With a stricture of the renal artery, the intrarenal venous pressure remained very low even with very high arterial pressures. With partial venous occlusion, the arcuate venous pressure and the venous resistance in the region of the stricture rose considerably as the arterial pressure was elevated.

In the hope of localizing the change in the nature of the pressure-flow plot with segmental arterial stenosis, manometers were also placed a short distance on both sides of the arterial stricture. The pressure drop across the stricture when plotted against flow gave a curve concave to the pressure axis, the pressure gradient across the kidney a convex curve, while that across the whole system was concave. When the arterial pressure upstream was increased from 35 to 198 mm. Hg, resistance in the region of the narrowed arterial segment rose from a value of one half to a value 2.5 times the actual renal resistance, which decreased 41 per cent. It may well be that blood clots remaining in the nonheparinized excised kidney also produced turbulence which was responsible for resistance rising with increased arterial pressure.

Renal Pressure-Flow Relations with Oil Perfusates of Higher Viscosity. In order to obtain lower flow rates at higher arterial pressures and to reduce the possibility of turbul-ent flow, two kerosene-mineral oil mixtures of higher viscosity (0.033 and 0.079 poise at 25 C.) were employed in heparinized kidneys, perfused at temperatures between 24 and 26 C. Three kidneys from different dogs were perfused with the oil of 0.079 poise without venous catheterization. At pressure gradients of 90 mm. Hg, the flow rates for this oil were 3.6, 3.7 and 4.3 ml./min./Gm. of kidney weight, respectively. Figure 3 records data from 2 of these experiments. In all 3 kidneys, the pressure-flow plots were curvilinear and convex to the pressure axis and approached rectilinearity at high arterial pressures. Since the nearly or apparently linear portions did not extrapolate backwards to the zero pressure-flow origin, resistance was not constant even in the linear parts of the pressure-flow diagrams. Renal resistance progressively fell with increasing arterial pressures up to the highest level studied, 180 mm. Hg. Using logarithmic co-ordinates, the pressure-flow data did not plot as a straight line. Hysteresis was demonstrated upon reducing the pressure step-wise over a 5 to 8 min. period (fig. 3).

In kidneys catheterized by way of the renal vein, the resistance upstream from the arcuate veins fell continuously as a function of raised arterial pressure while the resistance between the arcuate veins and main renal vein fell initially and then usually rose moderately at high arterial pressures and flow rates. In 5 kidneys perfused at an arterial pressure of 100 mm. Hg, the arcuate venous pressures were between 9 and 24 mm. Hg when the extrarenal venous pressure was 0. When both the arterial and main venous pressures were raised 10 mm. Hg, arcuate venous pressures were about 10 mm. Hg higher than the above cited values. Upon graded withdrawal of the intrarenal venous catheter, the venous...
arterial pressure and kidney flow

pressure fell at the renal sinus to a value almost equal to the pressure in the main renal vein. Thus, the chief place of resistance in the distal renal venous system was in the region of the renal capsule and was normally about 9 to 24 percent of the total renal resistance.

**Major Circulatory Pathway of the Oil Perfused Kidney.** In 2 kidneys which exhibited the typically reduced resistance upon raising the arterial pressure, a few milliliters of oil containing a heavily colored suspension of finely powdered indigo carmine were injected intra-arterially when the perfusion pressure was high. This dye was insoluble in the oil perfusate and none of the dye returned through the renal vein. Section of these 2 kidneys showed the vessels of the cortex to be diffusely and deeply colored with the dye particles. However, no dye was found in the medulla of either kidney. Therefore, the reduction in resistance with a raised arterial pressure in the oil perfused kidney was not due to a medullary by-pass of the cortical circulation or to circulation through large pre-capillary arterial-venous shunts.

**Effect of Vascular Fixation on Renal Pressure-Flow Relationships.** The following experiment showed that fixation of the renal vessels largely prevented both the reduced resistance with a raised arterial pressure and the hysteresis of the oil perfused kidney. A heparinized kidney was prepared by perfusion with 500 ml. of 1.4 per cent saline solution containing 3.4 per cent formaldehyde and then by immersion of the kidney in the formaldehyde solution for 48 hours. The organ became enlarged and hardened by this procedure. Subsequent perfusion with kerosene revealed low rates of flow with a nearly rectilinear pressure-flow diagram (fig. 4). No evidence of hysteresis was found upon rapidly reducing the arterial pressure.

**Critical Pressure for Flow in the Oil Perfused Kidney.** To ascertain the critical pressure difference necessary for flow, total rather than main renal venous outflow was measured in 4 heparinized kidneys where the extrarenal venous pressure was maintained at zero. In every case, renal flow perceptibly stopped while there remained a pressure difference of less than 6 mm. Hg between the renal artery and vein. In 2 of these kidneys, the renal artery was also completely occluded to entirely prevent the possibility of an almost imperceptible rate of flow. There were left both a downstream arterial pressure and an arcuate venous pressure of 2 mm. Hg. With no flow and a pressure drop of 2 mm. Hg between the arcuate veins and main renal vein, the resistance between these two sites was therefore infinite. It was apparently caused by complete collapse of the intrarenal effluent veins due to an interstitial pressure of 2 mm. Hg.

Critical closure of pre-venous pathways was not demonstrable since flow continued when arterial pressure was just barely above the critical venous closing pressure of 2 mm. Hg (table 1). Thus, no residual vessel tension or force of elasticity in Burton's sense was demonstrated as sufficient to close all the parallel channels of the oil perfused kidney. However, the resistance to small flow rates, even upstream from the arcuate veins, increased the longer the arterial pressure had been maintained at the critical venous closure value of 2 mm. Hg. This suggested that the caliber of the high resistance vessels gradually became smaller when the distending pressure was removed.


**Table 1.**—*Pressures and Resistances in the Oil Perfused Kidney when Arterial Pressure is Varied Serially from the Critical Venous Closure Pressure* *

<table>
<thead>
<tr>
<th>Arterial pressure</th>
<th>2</th>
<th>6.5</th>
<th>20</th>
<th>120</th>
<th>20</th>
<th>3</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arcuate venous pressure</td>
<td>2</td>
<td>2.1</td>
<td>2.5</td>
<td>28</td>
<td>5.5</td>
<td>2.4</td>
<td>2</td>
</tr>
<tr>
<td>Total flow rate</td>
<td>0</td>
<td>0.19</td>
<td>1.1</td>
<td>144</td>
<td>11.0</td>
<td>0.50</td>
<td>0</td>
</tr>
<tr>
<td>Resistance between artery and arcuate veins</td>
<td>–</td>
<td>23</td>
<td>16</td>
<td>6</td>
<td>1.3</td>
<td>1.2</td>
<td>–</td>
</tr>
<tr>
<td>Resistance between arcuate and external veins</td>
<td>∞</td>
<td>11</td>
<td>2.3</td>
<td>0.2</td>
<td>0.5</td>
<td>4.8</td>
<td>∞</td>
</tr>
</tbody>
</table>

* The arterial inflow tube had been totally occluded for 20 min. before the arterial pressure was changed from the critical pressure of 2 mm. Hg. Extrarenal venous pressure kept constant at 0. Pressures in mm. Hg, flows in ml./min., resistances in (mm. Hg X min.)/ml.

**Fig. 5.** Flow as a function of arterial pressure in hindlimbs perfused with oil. A (895 Gm.), viscosity of the oil was 0.033 poise and venous pressure, 10 mm. Hg. In limb B (215 Gm.), the values were 0.079 poise and 0 mm. Hg. *Ordinate,* flow rate (ml./min.); *abscissa,* pressure gradient (mm. Hg).

**Comparative Pressure-Flow Relationships in the Oil Perfused Hindlimb.** In order to demonstrate that the total resistance of the oil perfused kidney with increased arterial pressure did not change in a manner unique for vascular beds, pressure-flow data were similarly obtained in 3 heparinized canine hindlimbs. A tight ligature encircled the upper third of the thighs exclusive of the femoral vessels and the amputated limbs were perfused through the femoral artery. Femoral venous outflow was measured. In all 3 experiments with mixtures of kerosene and mineral oil, the pressure-flow data plotted curvilinear and convex to the pressure axis (fig. 5). The hindlimb curves were similar to the typical renal pressure-flow relationships and also did not plot linearly on log-log paper.

**Discussion**

The typical pressure-flow plots for the canine kidney cleared of blood and perfused with oil were curvilinear and convex to the pressure axis and were similar to those found in the oil perfused hindlimb. Flow was not a constant parabolic function of pressure gradient since the plots on log-log paper were not linear. Furthermore, the reduced renal resistance at elevated arterial pressures was not the result of arteriovenous or transmedullary shunting of the perfusate.

Autoregulation of flow as a function of arterial pressure could not be demonstrated in heparinized and oil perfused kidneys when care was taken to avoid turbulence. The introduction of turbulent flow reversed the directional change in resistance and was able to increase markedly the total resistance of the circuit when the renal arterial pressure was raised. This investigation does not indicate whether renal autoregulation of blood flow with a varying arterial pressure is dependent upon the heterogeneous nature of the...
blood perfusate or upon an active vasomotor mechanism. However, it is noteworthy that the viscosity of oil must be 3 to 3.5 times greater than the effective viscosity of normal whole blood as measured in the hindlimb in order to obtain, at normal pressures, renal flows equal to normal rates of renal blood flow.

In the unanesthetized dog, renal blood flow is normally about 3.5 to 4.0 ml./min./Gm. of kidney. The low resistance of the oil perfused kidney may be simply because the vessels are more dilated than in the normal blood perfused kidney; however, the effective viscosity of renal blood may be considerably higher than that of hindlimb blood.

The following comparison indicates that, with oil perfusion of a vascular bed at normal pressures, the vessels were actually in a dilated state. For the oil perfused hindlimb subjected to relatively rapid reductions in arterial pressure, the flow rates, when corrected to correspond to the average viscosity of dog plasma at 37°C (0.012 poise) apparently exceeded those previously reported for the 'maximally' dilated hindlimb perfused with plasma. At a pressure gradient of 90 mm. Hg, the calculated flows with oil were 515 and 553 ml/min. for the 2 hindlimbs studied from 5 Kg. dogs and 890 ml/min. for the limb from a 14 Kg. dog. They compare with plasma flows of 450 ml/min./hindlimb (of an 8 to 10 Kg. dog) and 610 ml/min./hindlimb found at the same pressure gradient of 90 mm. Hg during 'maximal' dilation.

Although they are contrary to the linear pressure-flow plots found by Whittaker and Winton and Levy and Share for the dilated hindlimb, the renal and hindlimb pressure-flow relations typically found in this investigation are similar to the data of Folkow and Lofving who reported curvilinear pressure-flow plots for the 'maximally' dilated cat limb perfused with aqueous colloidal solutions. Differences in technique probably explain the variable pressure-flow plots reported by different observers. As pointed out by Alexander, changes in pressure result in changes in vascular distensibility as a function of (1) the length of time over which the new pressure acts, (2) the magnitude of the pressure change and (3) the previously existing pressure. It is noteworthy that, in the oil experiments, a much less curved pressure-flow relationship was observed when arterial pressure was rapidly lowered rather than raised serially.

In these experiments, the changes in resistance when the perfusion pressure was altered over a wide range may be due to one or more of several factors. Both water-oil interfacial tension and critical opening or closing of certain vascular channels according to Burton's concept could be involved. However, closing of pre-venous parallel pathways was not demonstrable and intrarenal pressure accounted for the venous stoppage of flow at very low perfusion pressures. On the other hand, a time dependent change in size of patent vessels does seem to be an important factor. The marked curvilinearity of the pressure-flow plots when the arterial pressure was increased step-wise may have been solely due to progressive distension of residually small but patent vascular channels. A high degree of curvilinearity which indicates a large reduction in resistance with increased pressure does not necessarily depend upon the actual opening of previously closed channels as the pressure is raised. It is noteworthy that curvilinearity was virtually absent and hysteresis was not found in the formaldehyde fixed and relatively nondistensible kidney subsequently perfused with oil.

**SUMMARY**

Flow as a function of arterial pressure was investigated in isolated dog kidneys and hindlimbs perfused with kerosene or kerosene-mineral oil mixtures which remained intravascular and which eliminated vasomotor activity. In nonheparinized and nonsaline-flushed kidneys, resistance inconsistently rose as a function of increased arterial pressure. With a constant narrowed segment of the renal artery or vein which produced turbulence, the total resistance of the previously
heparinized renal circuit also rose as the arterial pressure was elevated.

In kidneys and limbs free of blood clots, the pressure-flow relationships were typically curvilinear and convex to the pressure axis. The reduction in renal resistance with increased arterial pressure was largely upstream from the arcuate veins, was not due to the operation of arteriovenous or transmedullary shunts, was associated with hysteresis, and was almost entirely prevented by formaldehyde fixation of the renal vasculature.

At normal arterial and venous pressures, the resistance between the arcuate veins and main renal vein consisted of 9 to 24 per cent of the total resistance of the kidney devoid of blood. As the arterial pressure was lowered, flow stopped because of a small residual intrarenal pressure. Critical closure of vessels due to vascular tension was not demonstrable in the oil perfused organ.

ACKNOWLEDGMENT

The writer is indebted to Dr. W. F. Hamilton for his criticism and advice.

REFERENCES

11. WAUGH, W. H. AND HAMILTON, W. F.: Physical effects of increased venous and extrarenal


Flow as a Function of Arterial Pressure in the Oil Perfused Kidney
WILLIAM H. WAUGH

Circ Res. 1958;6:107-115
doi: 10.1161/01.RES.6.1.107

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1958 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/6/1/107

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/