The Renal Rheoplethysmogram of the Dog

By G. E. BURCH, M.D. AND J. H. PHILLIPS, JR., M.D.

The renal circulation of the dog was studied by a rheoplethysmographic method capable of simultaneously recording the time courses of volume, rate, and acceleration of inflow, outflow, and difference between inflow and outflow of blood. The studies were done first under control conditions and then under conditions of relatively acute circulatory change induced by intravenous injection of norepinephrine and hexamethonium.

A RHEOPLETHYSMOGRAPHIC method previously developed for the simultaneous recording of the time courses of volume, rate, and acceleration of inflow, outflow, and difference between inflow and outflow of blood for the human digit has been applied to the dog's kidney for the first time. These studies reveal the applicability of rheoplethysmography to the study of the renal circulation as influenced by physiologic and pharmacologic phenomena.

MATERIALS AND METHODS

The electric rheoplethysmograph was employed for the simultaneous recording of the respective curves. The conventional metal renal oncometer was unsuitable and unreliable for these quantitative physiologic studies of the renal circulation, since the dead space around the kidney enclosed within the oncometer was only one or a few cubic centimeters in volume, and an increase of 1 cc. in volume of the kidney resulted in excessive increase in pressure within the pneumatic system. For this reason, an effective Lucite chamber was constructed that would provide a dead space within the chamber of about 400 cc. Since maximal change in volume of the kidney resulted in little change in pressure, the rheoplethysmograph could now function properly as a volume recorder. This is an important factor in such measurements.

Five normal mongrel dogs, having been anesthetized with pentobarbital sodium, were placed on the right side, and the left kidney was delivered extraperitoneally through a lateral abdominal incision. Nonrenal tissue was dissected away from the kidney, and only the renal artery or arteries, veins and ureter remained intact. The kidney was enclosed in the Lucite chamber. The opening of the chamber, through which the renal pedicle entered, was sealed with a printer's roller compound, and absorbent cotton was gently placed over this to retain the sealing material, care being taken to avoid interference with the renal vessels. A small hemostat with rubber tubing over the jaws was used to constrict the renal vein gently during the period of venous occlusion. This insured absolute obstruction to venous outflow and thus prevented leakage.

In these experiments, both kidneys were not studied simultaneously. The volume pulse wave (Dr) just preceding the moment of venous occlusion was subtracted from the volume inflow curve (Iv) of the next pulse cycle to obtain the volume outflow curve (Ov), a procedure that was found to be reliable. Several hundred rheoplethysmograms of renal blood flow for the dogs were obtained, as for digital blood flow, first under controlled conditions and then at intervals during relatively acute increase and decrease in blood pressure produced by intravenous injection of norepinephrine and hexamethonium, respectively. Four milligrams of norepinephrine, in the form of Levophed bitartrate (l-arterenol), were diluted in a 5 per cent solution of glucose in water and administered by slow intravenous infusion until the desired effect was obtained. Injections of hexamethonium, in the form of Bistrium bromide, were administered slowly until a total of 17.5 to 37.5 mg. had been administered. Blood pressure was measured by a mercury manometer connected to a cannula placed in the carotid artery.

RESULTS

Results are summarized in table 1 and in figures 1-3 which reveal quantitative data, time course curves, and the temporal and quantitative relations of the various parameters during the course of the pulse cycle. Certain
REXAL RHEOPLETHYSMOGRAM OF THE DOG

TABLE 1.—Influence of Norepinephrine and Hexamethonium on Renal Blood Flow

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>Mean arterial B.P. (mm./Hg)</th>
<th>Mean inflow (mm./cc. part/sec.)</th>
<th>Maximum inflow (mm./cc. part/sec.)</th>
<th>Basal inflow (mm./cc. part/sec.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16.0</td>
<td>124</td>
<td>214</td>
<td>64</td>
</tr>
<tr>
<td>2</td>
<td>23.5</td>
<td>130</td>
<td>170</td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td>17.0</td>
<td>156</td>
<td>216</td>
<td>110</td>
</tr>
<tr>
<td>4</td>
<td>22.3</td>
<td>150-160</td>
<td>230</td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>32.0</td>
<td>100-110</td>
<td>180</td>
<td>70</td>
</tr>
<tr>
<td>Mean</td>
<td>22.2</td>
<td>134</td>
<td>201</td>
<td>76</td>
</tr>
<tr>
<td>Range</td>
<td>16.0</td>
<td>100</td>
<td>170</td>
<td>48</td>
</tr>
</tbody>
</table>

* Levophed bitartrate (l-arternol).
†Histrion bromide.

1 Is the rate of inflow.

aspects of the data deserve special comment. The values for rate of blood flow can be converted to the more conventional units of ml./100 Gm./min. by multiplying them by 1.2.

Control Renal Blood Flow. With the animal resting quietly, several recordings of renal blood flow were obtained. The configuration of the curves and the quantitative data are shown in figures 1 and 2 and table 1. In all instances, renal flow was pulsatile in both the arterial and the venous segments of the circulation, as illustrated in the inflow and outflow curves. The basal flow was extremely high in every instance, the superimposed complementary pulsatile flow being present for both inflow and outflow, i.e., for the arterial as well as the venous segments of the circulation. The first major increase in flow occurred with the systolic phase of the pulse cycle; this was followed by a fairly rapid decline and then a less rapid, and at times even an increase in, flow to produce a secondary peak in flow after the diastolic notch, followed finally by another increase in the rate of decline. Early in the pulse cycle, the curves of the rate of outflow were still decreasing when the systolic phase of the cycle began and inflow was increasing fairly rapidly. The mean basal flow for the 5 dogs studied was 163.2 mm.3/5 cc. kidney/sec., and the mean rate of inflow was 178.8 mm.3/5 cc. kidney/sec. Although rates of flow were relatively stable, variations were sometimes fairly large (table 1).

Influence of Norepinephrine. The mean rise in arterial blood pressure produced by norepinephrine was 67 mm. Hg (table 1). As the blood pressure rose after injection of norepinephrine, rheoplethysmographic recordings were obtained. The influence of the drug on the time course curves is shown in figures 1 and 2 and table 1. Norepinephrine produced a decrease in basal flow in 4 of the 5 dogs and a diminution in maximal rate of flow, as well as the mean rate of flow for the entire pulse cycle, in all 5 animals (table 1). The changes were not extreme, however, even though the mean carotid arterial blood pressure reached 200 mm. Hg or more.

Influence of Hexamethonium. The mean decline in arterial blood pressure produced by hexamethonium was 58 mm. Hg (table 1). The basal, maximal and mean rates of blood flow decreased in every instance except one after injection of hexamethonium (figs. 1 and 2 and table 1). When the mean carotid arterial blood pressure was made to approach zero, or minimal levels, by administration of additional amounts of hexamethonium, renal blood flow ceased. The magnitude of the changes is summarized in table 1.

DISCUSSION

The rheoplethysmographic method can easily be applied to a detailed study of the time course of renal inflow and outflow of blood to demonstrate variations in magnitude and
Fig. 1. Typical simultaneous volume-time course curves of inflow (\(I_v\)), outflow (\(O_v\)), and the difference (\(D_v\)) between the volume of inflow and outflow for a single pulse cycle for the kidney of dog no. 3, demonstrating the effects of norepinephrine and hexmethonium. Even though these drugs altered arterial blood pressure appreciably, the time course of volume flow was not altered significantly. Mean rate of blood flow was not changed remarkably by norepinephrine, as first glance at the curves might suggest, because the pulse rate was greater than in the control dog.

temporal relations. These curves also make possible quantitative measurement of the basal component, upon which is superimposed the complemental component, of the over-all pulsatile flow produced by the heart beat (figs. 1 and 2).\(^3\) The fact that basal flow in the kidney is much higher than that in the digit of man\(^1\) indicates that there is less resistance to renal than to digital blood flow. Thus, in the kidney blood slips through at a high rate during the entire pulse cycle, the maximal flow being reached during the systolic phase. The magnitude of the complemental component of renal blood flow exceeds that for digital flow only slightly, if at all. For example, the basal flow is so rapid that a volume of blood equal to the volume of a kidney weighing 17 Gm. (dog no. 3) flowed through this organ in about 19.4 sec. This same volume of blood would flow through in about 16 sec. if the maximal flow prevailed throughout the pulse cycle. Thus, the basal flow is mainly responsible for the high rates of renal blood flow.

The flow of blood from the arterial to the venous side of the circulation must be mainly through functionally large arteriovenous connections or shunts that offer relatively little resistance to flow. The state of the renal circulation and renal flow may be likened to an arteriovenous fistula; this circulatory state insures large quantities of fresh blood flow to the kidney at all times for satisfactory renal function and formation of urine. The gushing renal flow provides an adequate quantity of blood to be diverted to both the glomerular and the tubular components of the renal circulation. The rich flow in the main channels can be "tapped off" at constantly varying quantities to meet the individual needs of the various components of the nephrons.

In general, the configurations of the time course of blood flow through the kidney are similar to those for the finger and toe tips of man.\(^1\) Among the differences are the high basal rate of flow and the decline in outflow during the early phases of the pulse cycle while inflow is increasing. The discordancy in inflow and outflow early in the pulse cycle resembles that in the curves for the digit of patients with aortic insufficiency.\(^4\) This may reflect the circulatory characteristics of large central arteries noted by Gregg and associates,\(^5,6\) who described reversal of flow. This type of rheoplethysmogram (RPG), which has been discussed previously,\(^4\) may also reflect the occlusion or narrowness of the renal vessels and the inertia of relatively large volumes of blood filling large vascular channels.
The kidneys were fairly distensible by comparison with the human digits. With clamping of the renal vein and obstruction to venous outflow, the kidneys distended readily and, in many instances, the A-V pressure gradient did not change appreciably for the first pulse cycle. In such cases, the inflowing blood was accommodated without appreciable change in the rate of inflow in the next pulse cycle, a characteristic that makes the kidney particularly suitable for rheoplethysmographic studies. Furthermore, in these renal rheoplethysmographic studies, venous outflow from the renal pedicle adjacent to the plethysmographic chamber was gently and completely obstructed by means of a hemostat, and leakage past the obstruction was thus eliminated. In previous digital rheoplethysmographic studies, in which a pneumatic cuff was distended, leakage past the collecting cuff occurred when venous pressure in the collecting veins rose sufficiently. This error was eliminated, of course, by proper analysis and interpretation of the RPG or by special recording procedures. Since use of a hemostat obstructed venous outflow completely, the application of rheoplethysmography to the kidney made possible a study of the nature of the changes in the recording produced by a progressive decline in the A-V pressure gradient independent of any leakage factor that might produce confusion. Such a study can be made from careful examination of the curves illustrated (figs. 1-3). These curves reflect a progressive decline in renal blood flow as the pulse cycle continues, so that the rates recorded by the end of the cycle are lower than actually occurred. This is well supported by the lower basal rate of flow recorded at the end of the pulse cycle than at the beginning (fig. 2). This error can be eliminated if an RPG is selected that fails to manifest this or if only the initial portion of the pulse cycle after venous occlusion is used and, by means of successive fractions, the curves are reconstructed for the pulse cycle as previously described.

The influence on the RPG of such factors as posture, obstruction to the inferior vena cava, administration of mercurial diuretics and other drugs, cardiac lesions, and congestive heart failure, as well as many other physiologic and pathologic phenomena, may be observed. For example, these acute experiments suggested that norepinephrine and hexamethonium, administered in therapeutic doses to change blood pressure in man, would probably cause no significant decrease in renal flow. When large doses of hexamethonium were given, however, with great reductions in mean arterial blood pressure, renal blood flow declined to low levels, even zero. Norepinephrine, on the other hand, even in fairly large doses, raised arterial blood pressure greatly but did not alter renal blood flow as much as might be expected. Whereas neither glomerular flow, as such, nor glomerular filtration rate was measured, it is possible, although not likely, that over-all renal flow is high when glomerular flow is extremely low.

With existing knowledge of the mechanism
of glomerular flow, it would be safe to predict, even with plasma skimming and high rates of pulsatile inflow and renal outflow, that the rate of glomerular filtration must be pulsatile. The rate of lymph flow and the reabsorptive phenomena dependent upon the circulation along the tubules are probably also pulsatile. As for the circulation, these functions should be recorded continuously throughout the pulse cycle as soon as methods can be developed to trace even the smallest changes caused by chemical and other physical phenomena. The continuous phasic quantitative variations and interrelations during the pulse cycle must be more than merely interesting.

The large lucite chamber, which provides a large dead space, is necessary for accurate rheoplethysmographic recording. If the dead space is small, the pressure within the chambers can reach high levels and fluctuate widely, so that the rheoplethysmograph ceases to function as a volume recorder. High pulsatile extrarenal pressure will also produce errors by displacing the seal of the pedicle and will result in pressure on the renal veins and the kidney; this, of course, will influence renal venous outflow and renal tissue pressure. Displacement of the seal will not only distort the veins but will also cause errors in measurement and leakage in the system.

**SUMMARY**

The rheoplethysmogram for the kidney of the normal dog has been described. The time course curves of volume, rate, and acceleration of inflow, outflow, and difference between inflow and outflow of renal blood have essentially the same configurations as those for the digits of man. Basal renal blood flow is extremely high and accounts in large measure for the total high rates of renal blood flow for the entire pulse cycle. In fact, the flow through the kidney may be compared to an arteriovenous fistula. For example, at mean basal rates of flow, a volume of blood equal to the average-sized kidney used in this series (22 Gm.) flowed through the organ in 31 sec. If maximal rates encountered during systole in these experiments were to prevail throughout the pulse cycle, this could be reduced to 21 sec.

**BURCH AND PHILLIPS**

The kidney is an excellent organ for rheoplethysmographic studies of physiologic and pharmacologic circulatory phenomena.

**SUM.MARIO IN INTERLINIA**

Es descrisibite le rheoplethysmogramma del ren pro canes normal. Le curvas tempore-curo pro volumine, intensitate, e acceleration de influxo, effluxo, e differentia inter influxo e effluxo de sanguine renal exhibi essentialmente le mesme configurationes como illos trovate in le caso del digitos de humanos. Le influxo renal basal es extremely alte e explica in grande mesura le alte intensitate total del influxo renal pro le complete cyclo pulsatile. De facto, le influxo a transverso le ren pote esser comparate con un fistula arterivenose. Per exemplo, a valores medie del basal intensitate de influxo, un volumine de sanguine equal al volumine medie del renes usate in iste serie (22 g) passava a transverso le organo in 31 secundas. Si le intensitate maximal in-contrate durante le systoles in iste experimentos perdurava a transverso le integre cyclo, le valor de 31 secundas se reducerea a 21. Le ren es un organo excellente pro studios rheoplethysmorphic de phenomenos physiologic e pharmacologic in le circulation.

**ACKNOWLEDGMENT**

We wish to acknowledge the surgical assistance of Dr. Salem Sayegh of the Department of Surgery.

**REFERENCES**

The Renal Rheoplethysmogram of the Dog
G. E. BURCH and J. H. PHILLIPS, JR.

Circ Res. 1958:6:72-76
doi: 10.1161/01.RES.6.1.72

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/6/1/72

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/