Blood Flow in the Renal Medulla

By Lawrence S. Lilienfield, M.D., Ph.D., Herman C. Maganzini, M.D., and Mark H. Bauer, S.J., Ph.D.

The recent writings of Hargitay and Kuhn, of Wirz, Gottschalk, and Berliner have revived interest in the blood supply to the renal medulla in those animals that produce a concentrated urine. The hyperosmolality of the renal medullary interstitial fluid is now well established, and its function has been surmised. The role of the blood flow in regulation and maintenance of this osmolality needs to be investigated. It was the purpose of this study to devise a method which could be used to measure medullary blood flow. As it developed, the method appears to have serious limitations and has been useful only in providing an approximation of the true flow. Nevertheless, it is presented here in the belief that even such an approximation is of some value.

The renal medulla is perfused with blood which first passes through the juxtamedullary glomeruli, then supplies the renal medullary tissue via the vasa recta. The vasa recta are arranged in bundles admirably suited for countercurrent exchange. Since no one major artery supplies the renal medulla, direct measurement of its blood flow is impossible. In our laboratory, it has been demonstrated that the renal papilla contains a large amount of exchangeable albumin. The compartment, or compartments, in which this albumin is confined have never been accurately defined. The most recent observation in our laboratory of a threefold increase in albumin concentration in vasa recta blood in the tip of the papilla in hamsters lends strong support to the contention that much, if not all, of the exchangeable albumin is intravascular. The anatomical arrangement of the vasa recta makes it likely that blood entering these capillaries displaces the blood already present with relatively little mixing. If this is so, then, with a low velocity of flow and a long capillary distance, considerable time might elapse before blood entering the papilla actually leaves it. Indeed, average transit times of circulating albumin in the renal papilla have been measured photoelectrically by Kramer and coworkers and have been found to be in the one- to two-minute range. If no significant washout of incoming radioactive albumin occurred within the first 20 or 30 seconds, the accumulation rate of radioactivity in this region during this time would be constant and equal to the plasma (albumin) flow.

Methods

Studies were performed in 33 mongrel dogs in the postabsorptive state, anesthetized with sodium pentobarbital or sodium thiopeptinal. Following induction of anesthesia by intravenous administration of the anesthetic agent, an incision was made in the right side of the neck and the right internal carotid artery exposed. A polyethylene catheter was then introduced proximally into the carotid artery and passed down the vessel so that its opening was either in the aortic root or in the left ventricle. The catheter was filled with normal saline solution containing a small amount of heparin and connected to a constant-infusion pump, the syringe of which was filled with an I\(^{131}\) albumin solution in normal saline and adjusted to deliver 4 μc per second. A midline abdominal incision was then made, the intestines gently retracted, and the kidneys exposed. By careful dissection, the renal pedicles were cleared of fat and connective tissue. One ml. of a 1 per cent procaine or Xylocaine solution was then applied to the artery and vein. An umbilical tape was passed around the renal pedicle, and a loosely tied knot was made. Care was taken that the ligation did not in any way occlude renal inflow or outflow. Both the left and the right kidney were prepared in this manner. About 5 to 10 cm. below the kidneys, the ureters were mobilized and fine...
ureteral catheters introduced proximally to permit urine collection.

Immediately following collection of several ml. of urine, infusion of the $^{131}$I-albumin solution into the ascending aorta was begun. From the zero time (the time at which the infusion was begun) until varying times thereafter, samples of arterial blood were collected at one-second intervals into siliconized test tubes containing a small amount of dried heparin solution. At a precisely noted time interval following the beginning of the $^{131}$I-albumin infusion, ligatures around the renal pedicles were suddenly tightened. The kidneys were then rapidly removed, care being taken so that the blood trapped within them could not leak out. The kidneys were then promptly placed in an insulated beaker containing a mixture of dry ice and acetone.

The frozen kidneys were then sliced with a band saw, and portions of the renal papilla were removed and weighed. Tissue radioactivity content was determined in a well-type scintillation counter. Similarly, aliquots of arterial blood collected during the period of infusion were analyzed for radioactivity in the scintillation counter. Blood radioactivity was expressed as counts per ml. of plasma, after making corrections for the hematocrit. Tissue radioactivity was expressed as counts per Gm. of tissue.

After appropriate correction for catheter time delay, the average arterial concentration of radioactivity was determined by summing concentrations of radioactivity in the samples collected between zero time and time of ligation and dividing by this time interval. The ratio of tissue radioactivity to average arterial radioactivity multiplied by 100 was determined and recorded as “apparent volume of distribution” ($V_t$).

Throughout the procedure, arterial blood pressure was monitored employing a strain-gauge transducer and direct-writing recorder. Only those animals whose mean arterial pressure remained above 90 to 100 mm. Hg are included in this series. Osmolality or specific gravity of the urine was determined in each case with the use of a Fiske osmometer or urine hydrometer.

Results

All the dogs in this series were producing hypertonic urine. Urine flow rates ranged from 0.02 to 1.0 ml./100 Gm. of kidney per minute, and arterial blood hematocrit from 35 to 57.

In the series of kidneys ligated 0.08 minute after the beginning of the radioalbumin infusion, papillary radioactivity averaged 1.9 per cent of arterial plasma radioactivity (table 1). In the series ligated after 0.12 and 0.17 minute, the averages increased to 2.2 and 2.8 per cent respectively. In the kidneys ligated after 0.25 minute and 0.5 minute, papillary activity was found to average 4.3 and 12.7 per cent, respectively. Kidneys ligated after one, two, and three minutes showed 25.2, 28.3, and 29.3 per cent of arterial plasma radioactivity in their papillae, respectively.

When the radioactivity percentage (or apparent volume of distribution) is plotted against time for all groups, it appears that tissue radioactivity increases at an approximately constant rate during the first minute and approaches a maximum after three to five minutes (fig. 1). The slope of the initial portion of the constructed best-fit line is 25 ml./100 Gm./min., which may be taken as the plasma perfusion rate in the papilla.

Discussion

It is worth noting that the flow rate being determined here is not actually the volume flow, but rather an equivalent flow based on arterial radioactivity. In other words, an accumulation rate of 25 ml./100 Gm./min. would mean that 100 Gm. of medulla is perfused with blood plasma at a rate which would provide an amount of albumin per minute which is carried by 25 ml. of renal arterial plasma. The actual volume flow to
this region would be somewhat less than 25 ml./100 Gm., as a result of the filtration of water as the plasma passed through the juxta-medullary glomeruli. Assuming a 0.20 filtration fraction, the actual plasma flow would be approximately 20 ml./100 Gm./min.

In their report, Kramer and co-workers have estimated the medullary blood flow to be 24 ml./100 Gm./min. This was done by measuring the average transit time of Evans blue dye photoelectrically as it traversed this region and using estimates of the vascular volume. Since it has been previously demonstrated in our laboratory that the hematocrit of medullary blood in the dog is approximately 8, whole-blood flow calculated from our data (plasma flow and red-blood-cell flow) would be approximately 22 ml./100 Gm./min., which is in excellent agreement with Kramer's computation.

A blood perfusion rate of 22 ml./100 Gm./min. in the renal medulla, although considerably less (by one order of magnitude) than that of the cortex, is still higher than the rate in most other body tissues. However, when this perfusion rate is considered from the point of view of oxygen supply, the very low red-cell content of the blood becomes an important factor. No doubt, the recently observed low oxygen tension of the urine as it leaves the kidney is, in part at least, a reflection of this, although the anatomical distribution of vessels, favorable for countercurrent exchange of diffusible substances, probably also plays a role.

The wide range of individual values for papillary radioactivity found in this study imposes severe limitations on the usefulness of this method for investigating induced alterations in blood flow. No reason for the wide variations could be ascertained. Good agreement between left and right kidneys in individual dogs indicates that incomplete intra-arterial mixing was probably not a factor. Except for the variations in individual dog urine flow rates over a wide but low range, the animals appeared comparable. The relationship to the urine flow rate is not obvious and is currently under further investigation.

Circulation Research, Volume IX, May 1961
Summary
The accumulation of intra-arterially injected 1131 albumin in the papilla of the kidney was measured in a series of 33 anesthetized dogs producing hypertonic urine. Although the data were widely scattered, an estimate of the average rate of this accumulation during the first half-minute following the start of the infusion was made. From the data, the plasma perfusion rate in the papilla under the experimental conditions was calculated and appears to average 25 ml./100 Gm./min.

Acknowledgment
The authors gratefully acknowledge the technical assistance of Mrs. Jean B. Young and Mr. Thomas F. Doyle.

References

BOOK REVIEW


A few of the most fundamental aspects of immersion hypothermia are discussed in this short monograph. The author presents his technique of hypothermia for neurosurgery and discusses six clinical cases. In addition, he considers briefly the responses of the cardiovascular and respiratory systems to hypothermia, and the acid-base balance with changing temperature.
Blood Flow in the Renal Medulla

LAWRENCE S. LILIENTHIELD, HERMAN C. MAGANZINI and MARK H. BAUER

Circ Res. 1961;9:614-617
doi: 10.1161/01.RES.9.3.614

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1961 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/9/3/614

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://cires.ahajournals.org/subscriptions/