Oxygen shunting in renal cortical and medullary capillaries

LEVY, MATTHEW N. AND ELIAS S. IMPERIAL. Oxygen shunting in renal cortical and medullary capillaries. Am. J. Physiol. 200(1): 159-162. 1961.—The existence of shunting of oxygen from arterial to venous segments of the renal capillary bed was ascertained from densitometer tracings of renal venous blood after the injection into the renal artery of blood of high oxygen tension and containing optically labeled erythrocytes. The outer region of the renal cortex was functionally separated from the medulla plus inner cortex by means of regional hypothermia. There was observed no consistent exaggeration or attenuation of the diphasic character of the renal densitometer tracing characteristic of oxygen shunting by cooling either the superficial or deeper zones of the kidney. It is concluded that shunting of oxygen occurs in both the renal cortex and medulla, but the degree to which it occurs in each zone cannot be quantified from the present data.

IT HAS RECENTLY BEEN DEMONSTRATED (1) that oxygen traverses the renal circulatory system considerably more rapidly than do the red blood cells, which are the most rapid components of the blood which ordinarily remain within the vascular compartment (2-4). This phenomenon was interpreted to signify that oxygen must diffuse from some point upstream in the renal vascular system to a point further downstream, thereby by-passing a segment of the circulatory bed. It was conjectured that, because of their anatomical configuration, the vasa recta of the renal medulla constituted the most likely site for such diffusion to occur. A more recent study (5), however, failed to reveal any significant difference between the more superficial (outer cortex) and the deeper (inner cortex plus medulla) zones of the kidney relative to the manner in which the rate of oxygen consumption varies with renal blood flow. In both regions, the A-V oxygen difference remains quite constant as renal blood flow is progressively reduced. Since the possibility exists that the relative constancy of renal oxygen extraction is partially dependent on shunting of oxygen from one point in the vascular system to a point further downstream, the present study was designed to test whether such diffusion might occur in both zones of the kidney. These zones were functionally isolated from each other by inducing stratified hypothermia.

METHODS

Seven experiments were performed on isolated, perfused, canine kidneys prepared in a manner previously described (5, 6). The kidney was perfused with arterial blood continually supplied from a peripheral artery of the same dog from which it was excised. Circulation was usually interrupted for no longer than 3 minutes in the process of transferring it to a thermoregulated saline bath. The arterial blood was conducted from a femoral artery through a coil-type condenser in its route to the renal artery. This permitted controlling the temperature of the arterial blood entering the kidney. The temperature at points 4, 10 and 15 mm beneath the renal capsule, as well as that of the kidney bath and of the renal arterial blood, was registered from thermistor probes on one channel of a Sanborn direct-writing recorder. By means of a motor-driven selector switch, the complete cycle of temperature measurements was repeated twice per minute. Pressure at the renal artery and renal venous outflow were recorded as previously described (5, 6).

Cooling of the superficial regions of the kidney was accomplished simply by replacing the normothermic saline in the kidney bath with refrigerated saline (approx. 10°C). Simultaneously, the arterial blood temperature was usually elevated by 1° or 2°C to maintain the temperature at the deepest probe approximately at the control level. The deeper regions of the kidney were cooled by running cold tap water through the jacket of the coil-type condenser. The kidney bath temperature was usually elevated slightly at the same time to maintain the temperature at the most superficial probe at the control level.

In five of the seven experiments, the occurrence of oxygen shunting was ascertained by the same method...
as previously described (1). Methemoglobinemic erythrocytes were prepared by treatment with 1% sodium nitrite. After three saline washes, these cells were added to normal blood, and the mixture was equilibrated with 95% O₂, 5% CO₂. Either 3 or 4 ml of this mixture was introduced into the renal artery at a constant rate of 1 ml/min. by means of a motor-driven syringe. The optical density of renal venous blood was continually recorded at 630 μm by means of a cuvette densitometer. At this wavelength, increased oxygen saturation decreases optical density, while increased methemoglobin content increases the density. If a marked excess of oxygen or methemoglobin were present, its effect on the total optical density of the renal venous blood would mask the influence of the other constituent, since the effect of the mixture represents the algebraic sums of the curves recorded by injecting each component separately (1). Therefore, a suitable mixture was prepared by trial and error until a definite diphasic curve was recorded in the totally normothermic kidney. Sixty milliliters of such a mixture was then prepared and placed in three sealed 20-ml syringes, which were then stored in a water bath at 37°C.

With the saline bath and arterial blood both at normothermic levels, several curves of optical density of renal venous blood were recorded after the successive injections of 3- or 4-ml aliquots of this mixture into the renal arterial blood stream at a rate of 1 ml/min. by means of a constant-rate infusion pump. The more superficial regions of the kidney were then rendered hypothermic by cooling the saline bath. After temperatures had stabilized (usually within 5-10 min.) the second syringe was inserted into the infusion pump, and the optical density of renal venous blood was recorded after injections of identical volume, rate, and composition were introduced into the renal arterial blood stream. Finally, the saline bath was restored to its original temperature, and the renal arterial blood was cooled. After renal temperatures had again stabilized, the third syringe was installed in the infusion pump, and a final series of curves were similarly secured. The sequence of cooling the kidney bath and arterial blood was alternated in successive experiments.

In the two remaining experiments, the procedures were identical, with the exception that the passage of red cells through the kidney was signaled by a change in their concentration, rather than by production of methemoglobin. This was done to rule out the possibility that the methemoglobinemic erythrocytes might pass through the kidney more slowly than the normal red cells. To prepare the mixtures for injection into the renal artery, an aliquot of arterial blood was centrifuged, approximately half of the plasma was withdrawn and returned to the dog, and the remaining blood of higher hematocrit ratio was equilibrated with 95% O₂, 5% CO₂.

RESULTS

In figure 1 are reproduced segments of original records obtained from one of the two experiments in which blood with high hematocrit ratio and high oxygen tension was injected into the renal artery. In the records in segment a, the temperatures (T) at 4-, 10-, and 15-mm depths were 40°C, 38°C, and 38°C, respectively. Renal venous outflow (F) was 173 ml/min., or 3.02 ml/min/gm tissue. In the densitometer tracing (D), the beginning and end of the injection of 3 ml of the blood preparation
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into the renal artery are signaled by the two downward spikes. The optical density of the renal venous blood first decreases (upward deflection) 10.5 seconds (un corrected for dead space in the venous blood withdrawal tubing) after the beginning of injection. This is then followed by a downward deflection, indicative of an increase in optical density. Such a diphase curve is characteristic of that recorded in the intact kidney in situ, as reported previously (I). The upward deflection is indicative of the preponderant optical effects of increased oxygen saturation, while the ensuing downward deviation marks the prepotent influence of the passage of the increased erythrocyte concentration. Thus, oxygen traverses the renal vascular bed more rapidly than the normal erythrocytes, confirming previous observations (1) in which the red cells were labeled with methemoglobin.

Cooling the kidney bath (segment b) produced temperatures of 21°, 36° and 35° at depths of 4, 10 and 15 mm, respectively. Renal blood flow decreased to 132 ml/min. The changes in optical density of renal venous blood after introduction of the high hematocrit, high oxygen tension mixture into the renal artery were quite similar to those observed with the entire kidney at normothermic temperatures.

Cooling the renal arterial blood (segment c) produced a more severe diminution of renal blood flow—to a value of 77 ml/min. Temperatures were 35°, 21° and 21° C, respectively. The changes in optical density of renal venous blood were directionally the same, but greater in magnitude, than in the two previous segments.

In all of the experiments in this series, similar diphase curves of optical density of renal venous blood were recorded. When methemoglobin was used to label the red cells, the curves resembled those in figure 1 in which the cells were marked by increased concentration. The initial deflection was always upright, signaling the predominant optical effect of increased oxygen saturation, and the later deflection was downward, marking the predominant influence of methemoglobin or increased red cell concentration. This occurred when the entire kidney was normothermic as well as when either the superficial or deep regions were selectively cooled. The configuration and time relationships of the curves usually differed under the three temperature conditions, but the diphase character was neither emphasized nor attenuated consistently by cooling either the more superficial or deeper regions of the kidney.

**DISCUSSION**

In a previous study (6), in which the experimental conditions for perfusion of the isolated kidney were virtually identical with those of the present experiments, a homogeneous reduction of temperature of the entire isolated kidney to 27° C resulted in a decrease of flow to approximately 45% and of oxygen consumption to about 28% of the normothermic values. In the present study, by cooling of either the kidney bath or renal arterial blood, the temperatures of the more superficial or deeper zones of the kidney were reduced to at least this temperature. Therefore, in whichever region the temperature was selectively diminished, it may be anticipated that the rate of blood flow was diminished and, of even greater importance, that the oxidative metabolism was severely depressed. On this basis, it is probable that the oxygen tension gradient from arterial to venous capillary segments would be diminished in the hypothermic zone. Furthermore, the blood flow to this zone would be curtailed, so that the relative contribution of this zone to the total renal venous outflow would be reduced. Also, consequent to the decreased velocity of flow, any evidence of oxygen shunting in the hypothermic zone would be delayed and hence lost in the later portions of the densitometer tracing recorded from the renal venous blood.

The variations in temperature experimentally produced in the present study do not divide the kidney sharply into two distinct zones, but produce continuous temperature gradients. On the basis of evidence previously discussed (5), it is probable that cooling the kidney bath severely depresses the outer zone of the cortex, while lowering the temperature of the renal arterial blood exerts its predominant effect on the medulla and inner zone of cortex. Since the diphase character of the densitometer tracing was equally prominent under either set of temperature gradients, it is probable that oxygen diffusion occurs in both superficial and deeper zones of the kidney.

When segment c of figure I was recorded, it is probable that only the outer portion of the renal cortex was normothermic, while the medulla and inner cortex were severely hypothermic. The diphase densitometer tracing strongly suggests that oxygen must be bypassing a portion of the vascular pathway in the outer renal cortex. Although it is widely recognized that the individual capillaries of the renal medulla are arranged in the form of "hairpin loops," it is usually not realized that the peritubular capillary plexus in the renal cortex also possesses a hairpin-like configuration (7). The efferent arterioles of the cortex have a variable structure histologically. They range from endothelial vessels to typical arterioles with well-developed smooth muscle layers. The efferent arterioles lead directly to the capillary networks which supply the medullary rays (composed of loops of Henle and collecting tubules), which lie midway between the interlobular vessels. These constitute the arterial portion of the peritubular capillary bed (ref. 8, pp. 161 164). The capillary network then doubles back toward the interlobular vessels to furnish the proximal and distal convoluted tubules with less well-oxygenated blood. The glomerular tufts are enclosed by capillaries from the venous end of the capillary bed (ref. 8, pp. 161-164). Thus, the glomerular capillaries, efferent arterioles and their initial peritubular capillary subdivisions pass through, and are intimately surrounded by, capillaries with a lower oxygen
tension. This anatomical arrangement provides the opportunity for diffusion of oxygen from arterial to venous segments of the capillary bed.

The tracings in figure 1b were recorded under conditions in which the metabolism of the outer cortex was severely depressed. The diphasic densitometer curves are therefore indicative of oxygen shunting in either the deeper cortical layers or the medulla, or in both regions. Since the preceding discussion asserts that oxygen shunting does occur in the renal cortex, then this same phenomenon within the deeper zones of the cortex must be at least partially responsible for the tracings reproduced in figure 1b. Since the experimental conditions did not functionally isolate the medulla from an appreciable portion of the inner cortex, it is not possible, from the present data, to assess to what extent oxygen shunting may occur in the medulla. Other considerations, however, lead to the conclusion that this phenomenon probably does occur here. The vasa recta, the capillaries of this region, are arranged in the form of hairpin loops. In the outer medullary zone, they form vascular bundles, with a large number of arterial and venous segments in intimate contact with each other (ref. 8, pp. 60-64). Evidence has already been adduced which indicates that the highly diffusible gas, Kr, diffuses across a similar gradient in the medulla.

It is probable, therefore, that a shunt for oxygen occurs at all levels in the kidney. Unfortunately, the present data do not permit quantitation. Elucidation of the physiological role of this phenomenon must await a quantitative evaluation of the degree of shunting under a variety of experimental conditions.

REFERENCES