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Renal Oxygen Delivery and Consumption during Progressive Hypoxemia in the Anesthetized Dog (41749)

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Abstract. The relationship between renal oxygen delivery (RDO_2) and function was evaluated during progressive hypoxemia. Seven anesthetized, spontaneously breathing dogs were given progressively lower oxygen concentrations to breathe while monitoring renal O_2 consumption ($R\dot{V}O_2$), renal hemodynamic and excretory function. In addition, basal $R\dot{V}O_2$ was determined in three models of kidneys without filtration. RDO_2 averaged 3648 μmole O_2/min/100 g during normoxia. Basal $R\dot{V}O_2$ averaged 100 μmole O_2/min/100 g kidney while total $R\dot{V}O_2$ was 466 μmole O_2/min/100 g kidney during normoxia, leaving 366 μmole O_2/min/100 g consumed by those processes involved in tubular transport. During hypoxemia, all renal parameters were well maintained until the lowest P_aO_2 (24.2 Torr). At this level, total $R\dot{V}O_2$ and RDO_2 were significantly reduced. However, RDO_2 remained well above $R\dot{V}O_2$ throughout hypoxemia. The reduction in $R\dot{V}O_2$ was a direct result of decreased O_2 demand, as glomerular filtration and tubular load were also reduced. This associated decrease in O_2 demand and $R\dot{V}O_2$ was indicated by the fact that the renal $(a - v)O_2$ difference remained low and unchanged (1.9 vol%), fractional sodium excretion was unchanged, and the ratio of tubular sodium reabsorption to $R\dot{V}O_2$ also remained unchanged (30.8 meq Na/mmole O_2). It was concluded that hypoxemia, while reducing both RDO_2 and $R\dot{V}O_2$ at the lowest P_aO_2 (24.2 Torr), did not functionally impair renal excretory function by limiting RDO_2 to the tubular transport processes. A reduction in RBF is far more likely to compromise the RDO_2 needed to sustain basal and active transport processes than hypoxemia itself.

A variety of pathological situations leading to hypoxemia are associated with alterations in renal function (1, 2). The question arises as to the sensitivity of the renal transport processes to hypoxemia. The oxygen consumption by a kidney is quite large compared with other organs and normally consumes 4 to 5% of the total body oxygen uptake. This renal oxygen consumption is not only related to the basal oxygen requirement, but for the most part, is determined by the numerous active transport processes of secretion and reabsorption (3–5). A decrement in oxygen delivery as a result of hypoxemia could impair the transport processes and alter renal function.

To evaluate this, we progressively lowered the arterial partial pressure of oxygen (P_aO_2) by decreasing the fractional inspired oxygen (FIO_2) of anesthetized, spontaneously breathing dogs while monitoring renal oxygen consumption, renal hemodynamics, and excretory function. Basal renal oxygen consumption was determined separately to evaluate the relationship of oxygen delivery to both the transport function and the basal metabolism of the kidney.

Materials and Methods. Mongrel dogs of either sex weighing between 19.3 and 26.8 kg were used in this study. Seven dogs were anesthetized with sodium pentobarbital (25 mg/kg) and intubated with a cuffed endotracheal tube. Polyethylene catheters were placed in the abdominal aorta via the femoral artery for the monitoring of arterial blood pressure and blood gases, O_2 content, and plasma sodium and creatinine; in the inferior vena cava via the femoral vein for administration of supplemental anesthesia; and in the jugular vein for the continuous infusion of creatinine (1 ml/kg as a prime of 6% solution, 0.6 ml/min of 3.6% solution as a sustaining infusion). The left kidney was approached retroperitoneally via a flank incision. The ureter was cannulated for the measurement of urine volume, sodium, and creatinine. An electromagnetic flow probe was placed around the renal artery for the measurement of renal blood flow (Carolina Medical Flowmeter Model 501D). A 21-gauge

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needle attached to a small vein infusion set was inserted into the renal vein retrograde to flow for the sampling of renal venous blood.

A 1-hr stabilization period followed the surgical preparation. A 30-min control measurement period was accomplished at a FIO_2 of 0.21. This was followed by progressive decreases in inspired O_2 for 20 min at each level. Nitrogen was mixed with ambient air in a meteorological bag to achieve the desired O_2 level (measured with a Beckman OM-11 O_2 analyzer) of 0.14, 0.12, 0.10, or 0.08 FIO_2. Each hypoxic gas was administered from the meteorological balloon through a low-resistance Collins "J" valve connected to the endotracheal tube. Following the final level of hypoxic gas the animal was allowed to recover for a 30-min recovery period. Blood samples for creatinine and sodium determination were drawn at the midpoint of each respective period. Samples for blood gases and O_2 content were drawn 5 min prior to the end of the period.

Blood pressure (Statham P23Db) and renal blood flow (RBF) were continuously recorded on a Gould 2400 strip chart recorder. Glomerular filtration rate was measured by the clearance of creatinine. Plasma and urine sodium concentrations were determined by flame photometry (IL 343). Arterial PO_2, PCO_2, and pH were determined with an IL 213 pH–blood gas analyzer and O_2 content (vol%) with an IL 282 Co-oximeter.

Renal O_2 consumption ($R\dot{V}O_2$) was calculated using a formula that allows for the discrepancy between arterial inflow and venous outflow of blood in the kidney as a result of the formation of urine (6): $R\dot{V}O_2 = RBF \cdot C_aO_2 - (RBF - \dot{V}) \cdot C_vO_2$, where $\dot{V}O_2$ = μmole O_2/min/100 g kidney; RBF = ml/min/100 g kidney, arterial; $\dot{V}$ = ml/min/100 g kidney, urine flow; C_aO_2 and C_vO_2 = oxygen content in μmole/ml for renal arterial and venous blood, respectively.

Basal renal O_2 consumption. In order to establish levels of basal renal O_2 consumption, three different kidney models were used in which glomerular filtration was reduced to essentially zero. Tubular transport related to urine formation is markedly reduced and approaches zero without filtration. Therefore, the resulting O_2 consumption reflects the basal metabolism necessary for maintaining the integrity of the renal tissue. Renal O_2 consumption was measured as previously described.

The three nonfiltering models included the following: (i) In eight normal dogs (17.3–24.2 kg body wt), arterial blood pressure at the level of the kidney was lowered to 40 mm Hg by a clamp placed around the suprarenal aorta. $R\dot{V}O_2$ was measured after 15 min at this pressure. (ii) An additional eight dogs (18.2–23.9 kg body wt) underwent preparation of the left kidney as a nonfiltering kidney (NFK) by the method of Blaine *et al.* (7, 8). Under anesthesia, the renal artery and ureter were exposed aseptically through a flank incision. The ureter was ligated and an atraumatic clamp placed on the artery. After 2 hr of ischemia, the clamp was removed, the incision closed and the animal permitted to recover. This results in a kidney without filtration after 4 days (7, 8). On the fourth day postoperation, $R\dot{V}O_2$ was measured at four consecutive 15-min intervals and averaged. (iii) Since the ischemia may have resulted in a loss of functional tissue thus reducing basal $R\dot{V}O_2$, another set of six dogs (15.9–22.3 kg body wt) underwent the same surgical procedure. However, no period of ischemia was imposed; only ureteral ligation (UO). $R\dot{V}O_2$ was measured in these animals, as for the NFK animals, on the fourth day postoperation.

Statistical analysis involved the use of Dunnett's paired t test for comparing treatment means to a control (9) or Student's group t test where appropriate.

Results. Progressive reductions in inspired O_2 resulted in a progressive decline in P_aO_2 (Table I). The resulting increase in ventilation reduced the P_aCO_2 and increased pH (Table I).

Progressive hypoxemia did not alter $R\dot{V}O_2$ until the lowest FIO_2 (Table II). The renal (a − v)O_2 difference [R(a − v)O_2] did not significantly change, however, indicating a proportional change in $R\dot{V}O_2$ and RBF (Table II, Fig. 1). Renal O_2 delivery (RDO_2) was significantly reduced only at the lowest FIO_2 (Table II). However, RDO_2 remained well above the oxygen requirements of the kidney as reflected by the low R(a − v)O_2 throughout the hypoxemia (Table II).

RBF and GFR were not changed by hypoxemia until the lowest FIO_2 where both de-

TABLE I. BLOOD GASES AND pH DURING HYPOXEMIA

	FIO_2					
	0.21 Control	0.14	0.12	0.10	0.08	0.21 Recovery
P_aO_2	76.9 ± 2.2	46.3 ± 2.2*	39.7 ± 2.6*	31.3 ± 2.1*	24.2 ± 1.8*	73.5 ± 2.4
P_aCO_2	37.0 ± 1.7	28.7 ± 0.9*	25.6 ± 1.0*	21.3 ± 1.1*	18.0 ± 1.2*	29.7 ± 2.3
pH	7.40 ± 0.02	7.47 ± 0.01*	7.51 ± 0.02*	7.54 ± 0.02*	7.58 ± 0.03*	7.42 ± 0.02

Note. Values are means ± SE. FIO_2, fractional inspired O_2. P_aO_2, arterial partial pressure of O_2 (Torr); P_aCO_2, arterial partial pressure of CO_2 (Torr); pH, arterial pH.

* $P < 0.05$ compared to control; $N = 7$.

clined (Table II). $UNa\dot{V}$ likewise did not decrease until the lowest FIO_2 and then decreased mainly as a result of the decrease in GFR since FENa remained unchanged (Table II). Tubular sodium reabsorption (TNa) was not changed during hypoxemia until the lower FIO_2 when the filtered sodium was also decreased (Table II, Fig. 2). The relationship between TNa and $R\dot{V}O_2$ ($TNa/R\dot{V}O_2$) remained constant throughout the hypoxemia (Table II). Figure 2 shows the close relationship between the GFR (reflecting changes in sodium filtered), $UNa\dot{V}$, TNa, and $R\dot{V}O_2$. As the filtered load is decreased, the metabolic demand is lowered and $R\dot{V}O_2$ declines.

Basal renal O_2 consumption (Table III) as determined by the three different methods demonstrated no significant difference among the three. The average of the three methods yields a value of 100 μmole O_2/min/100 g kidney. Using this value, the above-basal $R\dot{V}O_2$, which relates mainly to tubular active transport, is 366 μmole O_2/min/100 g kidney (total $R\dot{V}O_2$ − basal $R\dot{V}O_2$). The recalculated ratio of TNa to above-basal $R\dot{V}O_2$ is 30.8 meq of Na/mmole O_2, indicating that it takes 1 mmole of O_2 to transport 30.8 meq of Na.

Discussion. The results of the present study indicate that hypoxemia, even to very low P_aO_2 values (24.2 Torr), does not alter normal tubular function secondary to O_2 deficiency. In fact, RDO_2 remained well above $R\dot{V}O_2$

TABLE II. RENAL OXYGEN, HEMODYNAMIC, AND FUNCTIONAL PARAMETERS DURING HYPOXEMIA

	FIO_2					
	0.21 Control	0.14	0.12	0.10	0.08	0.21 Recovery
$R\dot{V}O_2$	466 ± 27	505 ± 19	502 ± 21	444 ± 32	381 ± 38*	424 ± 39
$R(a-v)O_2$	1.9 ± 0.2	2.1 ± 0.2	1.9 ± 0.3	2.4 ± 0.3	2.3 ± 0.2	2.5 ± 0.4
RDO_2	3648 ± 284	3769 ± 283	3617 ± 239	2596 ± 366	2008 ± 399*	3501 ± 483
RBF	525 ± 22	556 ± 31	565 ± 39	456 ± 38	426 ± 44*	461 ± 42
GFR	75.2 ± 7.2	72.2 ± 7.1	76.7 ± 7.1	64.8 ± 9.5	58.0 ± 9.2*	63.5 ± 10.3
$UNa\dot{V}$	19.7 ± 6.5	19.3 ± 4.9	26.7 ± 7.8	16.7 ± 6.0	15.1 ± 6.0*	22.3 ± 5.0
FENa	0.12 ± 0.02	0.20 ± 0.06	0.25 ± 0.08	0.17 ± 0.07	0.16 ± 0.07	0.12 ± 0.04
TNa	11.1 ± 1.1	10.7 ± 1.1	11.5 ± 1.1	9.7 ± 1.5	8.7 ± 1.4*	9.5 ± 1.6
$TNa/R\dot{V}O_2$	23.8 ± 1.8	21.2 ± 2.1	22.8 ± 2.2	21.9 ± 2.3	22.8 ± 2.3	22.5 ± 2.4

Note. Values are means ± SE. FIO_2, fractional inspired O_2; $R\dot{V}O_2$, renal O_2 consumption (μmole O_2/min/100 g kidney); $R(a-v)O_2$, renal arterial − venous O_2 difference (vol %); RBF, renal blood flow (ml/min/100 g kidney); RDO_2, renal O_2 delivery (μmole O_2/min/100 g kidney); GFR, glomerular filtration rate (ml/min/100 g/kidney); $UNa\dot{V}$, urinary sodium excretion (μeq/min/100 g kidney); FENa, fractional sodium excretion (%); TNa, tubular reabsorption of sodium (meq/min/100 g/kidney); $TNa/R\dot{V}O_2$, reabsorption of sodium per unit of O_2 consumed (meq Na/mmole O_2).

* $P < 0.05$ compared to control; $N = 7$.

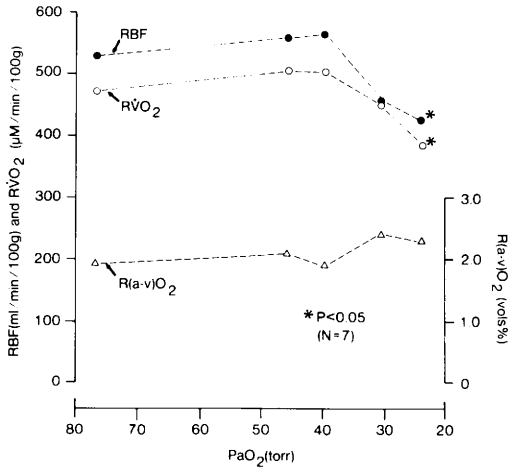

FIG. 1. Effect of progressive hypoxemia on the mean values of renal blood flow (RBF), renal oxygen consumption ($R\dot{V}O_2$), and renal arterial − venous oxygen difference, R(a − v)O_2. P_aO_2, arterial partial pressure of oxygen.

throughout the progressive hypoxemia (Table II). RDO_2 was significantly reduced at the lowest P_aO_2 value as a result of the reduction

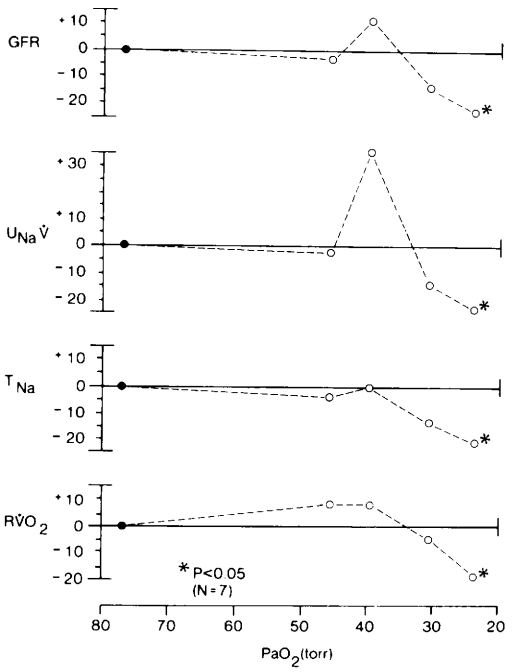

FIG. 2. Effect of progressive hypoxemia on the percentage change from control (●) of glomerular filtration rate (GFR), urinary sodium excretion rate ($U_{Na}\dot{V}$), tubular sodium reabsorption rate (TNa), and renal oxygen consumption ($R\dot{V}O_2$). P_aO_2, arterial partial pressure of oxygen.

TABLE III. BASAL RENAL OXYGEN CONSUMPTION

Normal	NFK	UO
101 ±13	91 ±17	107 ±15

Note. Values are means ± SE, μmole O_2/min/100 g kidney. Normal (N = 8), normal kidneys at an arterial blood pressure of 40 mm Hg; NFK (N = 8), nonfiltering kidneys; UO (N = 6), ureteral obstructed kidneys.

in RBF, but remained well above renal O_2 demands as indicated by the low R(a − v)O_2 difference (1.9–2.3 vol%) maintained during hypoxemia.

Total $R\dot{V}O_2$ was 466 μmole O_2/min/100 g kidney while basal $R\dot{V}O_2$ was determined to be 100 μmole O_2/min/100 g kidney; values which compare well to those in the literature (3–5, 10–12). The majority of total $R\dot{V}O_2$ is utilized in tubular transport (mainly sodium) in the formation of urine. $R\dot{V}O_2$ was not significantly altered during moderate hypoxemia and was decreased only at the lowest P_aO_2 value. $R\dot{V}O_2$ was reduced as a result of a decrease in renal tubular transport requirements. At the P_aO_2 of 24.2 Torr, RBF and GFR were signficantly reduced. Therefore, tubular sodium load was reduced and less sodium was reabsorbed and excreted (Fig. 2). With less sodium to be transported, $R\dot{V}O_2$ was proportionally reduced. This close relationship between GFR, sodium reabsorption, and $R\dot{V}O_2$ has been demonstrated under a variety of experimental conditions through a wide range of GFR values (5, 11, 12).

The calculated ratio of TNa/$R\dot{V}O_2$ in this study during normoxia was 30.8 meq of Na/mmole O_2 consumed above basal $R\dot{V}O_2$. This value compares favorably with those reported in the literature (10–12). The study by Thurau (10) reported, like the present study, that the ratio TNa/$R\dot{V}O_2$ remained unchanged by hypoxemia while $R\dot{V}O_2$ was reduced. His conclusions were that the reduction in O_2 availability reduced the $R\dot{V}O_2$ and consequently TNa. The results of the present study indicate, however, that the reduction in $R\dot{V}O_2$ occurs as a result of a decrease in renal O_2 demand. This statement is supported by three pieces of evidence. First, R(a − v)O_2 remained unchanged, indicating a proportional decrease in both RBF and $R\dot{V}O_2$. Second, FENa remained unchanged which indicates that GFR

and sodium transport changed proportionally. And, third, the ratio $TNa/R\dot{V}O_2$ remained unchanged, indicating a proportional decrease in sodium reabsorption and $R\dot{V}O_2$. Based upon the additional evidence presented in the current study, it would appear more likely that the observed reduction in $R\dot{V}O_2$ reflected the decrease in RBF, GFR, and hence TNa.

The data of the present study enable a concise evaluation of the relationship between O_2 availability and consumption by the kidney and lend further support to our conclusions. As indicated in Table II, 3648 μmole O_2/min/100 g kidney is delivered to the kidney under normal conditions. This is 3182 μmole O_2/min/100 g kidney above the total $R\dot{V}O_2$ and 3548 μmole O_2/min/100 g above the basal $R\dot{V}O_2$. Thus, with a normal RBF, RDO_2 far exceeds $R\dot{V}O_2$.

The most important determinant of RDO_2 is RBF. The high blood flow which normally goes to the kidney must be markedly reduced to limit RDO_2. If we assume the kidney can extract up to 3–4 vol% O_2 (3, 5), then in the present study, RBF could be lowered to approximately 75–56 ml/min/100 g kidney before RDO_2 would begin to fall below basal $R\dot{V}O_2$ ($RBF = R\dot{V}O_2/C_aO_2 - C_vO_2$). Lowering the arterial PO_2, therefore, has a minor influence on RDO_2 compared to RBF. With a normal blood flow, P_aO_2 would have to be lowered well below 20 Torr to reduce RDO_2 to less than 466 μmole O_2/min/100 g kidney and even lower to reduce RDO_2 to less than 100 μmole O_2/min/100 g kidney. At these low P_aO_2 values, other organs with a high (a − v)O_2 difference (i.e., the heart with an (a − v)O_2 of 15 vol%) would be functionally impaired significantly sooner than the kidney. The high RBF and the fact that renal O_2 requirements are reduced as RBF is decreased, makes it unlikely that lowering of P_aO_2 per se could functionally impair the kidney or result in renal tissue damage.

From the data presented in this study, it is apparent that reductions in renal excretory function which occurred during acute hypoxemia are not the result of a direct effect of hypoxemia on renal tubular function, but are due to changes in renal hemodynamics and filtration. RDO_2 to the renal transport processes was not functionally limited by reducing P_aO_2. RDO_2 is more likely to be limited by significant reductions in RBF, or a combination of both lowered RBF and P_aO_2. Therefore it is ischemia (reduced blood flow) which is more important in inducing renal functional compromise than is hypoxemia.

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