Effects of Low Oxygen and of Carbon Monoxide on the Renal Circulation in Unanesthetized Rabbits

By Paul I. Korner, M.D.

With the technical assistance of Yvonne Pascoe

The circulatory response of the normal unanesthetized rabbit to acute hypoxia differs from that of man or the dog.\(^1\)\(^2\) For the first few minutes after breathing low O\(_2\) mixtures, bradycardia and a small rise in blood pressure were observed.\(^1\) The steady state response following more prolonged exposure was variable with an increase in cardiac output and heart rate in some animals and persistent bradycardia and a reduction in cardiac output in others.\(^2\) In contrast to this variable response, man and the dog usually develop an increase in cardiac output and heart rate when breathing low O\(_2\) mixtures. The experiments of Bernthal et al.,\(^4\) Daly and Scott,\(^3\)\(^6\)\(^7\) and Downing et al.\(^5\) suggest that in the dog this response is not primarily the result of stimulation of the arterial chemoreceptors. When the carotid chemoreceptors were perfused with hypoxic blood in dogs with controlled ventilation, bradycardia, reduction in cardiac output and systemic vasoconstriction were observed.\(^4\)\(^5\) When chemoreceptor perfusion was carried out in the same animals during spontaneous respiration a variable response not unlike the picture in the conscious rabbit during the steady state was obtained; for example, under these conditions the heart rate remained unchanged, or increased or decreased.\(^6\)\(^7\) These results suggest that the circulatory effects of chemoreceptor stimulation in the dog may be modified in the spontaneously breathing animal.

In contrast to the variable effects of low O\(_2\) mixtures in the rabbit, breathing small concentrations of carbon monoxide in air resulted in a uniform increase in cardiac output, tachycardia and relatively little increase in respiratory minute volume.\(^2\) Breathing CO reduces the O\(_2\)-carrying capacity of the blood and produces an "anemic" type of hypoxia at the tissue level. The results with CO in the rabbit were similar to the effects observed in man by Asmussen and Chiodi\(^8\) and in the dog by Chiodi et al.\(^9\) These workers found that breathing small concentrations of CO produced slight elevation in arterial carbon dioxide pressure (P\(_{\text{aCO}_2}\)), but left the arterial oxygen pressure (P\(_{\text{aO}_2}\)) essentially within normal limits. The differences between the rabbit's response to low O\(_2\) mixtures and CO might thus depend on differences in ventilation, P\(_{\text{aCO}_2}\) and P\(_{\text{aO}_2}\). The effects of P\(_{\text{aCO}_2}\) and ventilation on cardiac output and heart rate were excluded by the experiments of Korner and Edwards,\(^3\) who showed that little effect was observed when P\(_{\text{aCO}_2}\) was elevated in the presence of a normal or elevated P\(_{\text{aO}_2}\); however, in the presence of a low P\(_{\text{aO}_2}\) elevating the P\(_{\text{aCO}_2}\) produced bradycardia and reduction in cardiac output. This response differs considerably from the effects with CO. The difference in the arterial oxygen tension in the two types of hypoxia thus appeared to be an important factor in accounting for the difference in the circulatory response of the rabbit to low O\(_2\) mixtures and CO. A comparison of the circulatory effects in these two types of hypoxia thus offers the possibility of assessing the role of the P\(_{\text{aO}_2}\) in various aspects of circulatory regulation in the intact, unanesthetized rabbit.

The renal blood flow accounts for a large
fraction of the resting cardiac output and might be expected to play a part in the circulatory adjustments to low O2 mixtures and carbon monoxide. In moderate arterial hypoxia in man and the dog only minor changes in renal blood flow (RBF) and glomerular filtration rate (GFR) have been observed, but in severe arterial hypoxia the RBF and GFR were markedly reduced. In asphyxia marked reductions in RBF have been described in the anesthetized rabbit and in diving mammals. The effects of CO on the renal circulation have not been investigated. However, in anemia the reduced O2-carrying capacity of the blood leads to the development of a somewhat similar type of "tissue" hypoxia with an essentially normal $P_{aO_2}$. The changes in the renal circulation reported in anemia have been variable, probably as a result of differences in the types of anemia studied, and due to uncertainty regarding the renal PAH extraction ratio in anemia. The present study was therefore undertaken to determine the part played by changes in the renal circulation in the circulatory adjustments to low O2 mixtures and to carbon monoxide in the unanesthetized rabbit, and to investigate which components of the renal vascular response were under direct nervous control.

**Methods**

The experiments were carried out on 91 hutch bred male rabbits of mixed breed varying in weight from 1.5 to 3.5 kg. Details of operative, experimental and analytical procedures have been described elsewhere. In 50 animals all operative procedures were carried out using local anesthesia. In 16 rabbits where renal vein catheterization was carried out, and in 25 animals subjected to bilateral ureteric catheterization, the preliminary operative procedures were carried out using light sodium thiopental anesthesia. In the latter two groups the determination of renal clearances, cardiac output, etc. commenced about four hours after recovery from anesthesia. There was no obvious difference in the response of these animals to the various inspired gas mixtures when compared to completely unanesthetized animals.

The general plan of the experiment was, except where stated otherwise, as shown in figure 1. All clearance determinations during control and "treatment" periods were carried out during moderate water and mannitol diureses as described previously. Following the control observations the animals breathed one of the following inspired "treatment" mixtures: 21% O2 in N2; 9.4-9.8% O2 in N2 (9.6% O2); 0.1% CO + 21% O2 in N2 (0.1% CO); 0.2% CO + 21% O2 in N2 (0.5% CO). In some experiments different low oxygen mixtures ranging from 8% O2 in N2 to 11.8% O2 in N2 were used in relation to special test procedures described in the text. The gas mixtures were freshly prepared just before use, from cylinders of air, N2, and 0.5% CO in 21% O2. The gases were passed through rotameters at appropriate flow rates, and the mixtures were stored in a 100-liter Douglas bag. The animals breathed the mixtures through a respiratory valve from a very light polythene bag, as described...
### TABLE 1

Results of Mean Values for Renal PAH Extraction Ratios, \( S_{oa} \) (or \( S'_{oa} \)), Renal Vein \( S_{oa} \) (or \( S'_{oa} \)), Renal O2 Consumption and Renal Blood Flow (RBF), in 16 Animals Subjected to Renal Vein Catheterization. Each Group Breathed Room Air During the Control Period (C), but Breathed 21\% \( O_2 \), or 9.6\% \( O_2 \), 0.2\% CO + 21\% \( O_2 \) in N2, During the Treatment Period (T). The Calculation of the Standard Error (SE) Has Been Determined for Individual (Control-Treatment) Differences Since Each Animal Acts as its Own Control.

<table>
<thead>
<tr>
<th>Treatment No. of animals</th>
<th>21% ( O_2 )</th>
<th>9.6% ( O_2 )</th>
<th>0.2% CO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal PAH extraction ratio per cent</td>
<td>C</td>
<td>T</td>
<td>C</td>
</tr>
<tr>
<td>( S_{oa} ) or ( S'_{oa} ) per cent</td>
<td>92.4</td>
<td>91.7</td>
<td>1.48</td>
</tr>
<tr>
<td>Renal vein ( S_{oa} ) per cent</td>
<td>81.1</td>
<td>1.10</td>
<td>81.5</td>
</tr>
<tr>
<td>Renal ( V_{O2} ) ml/min</td>
<td>21.9</td>
<td>3.29</td>
<td>0.86</td>
</tr>
<tr>
<td>RBF, ml/min</td>
<td>84</td>
<td>81</td>
<td>5.5</td>
</tr>
</tbody>
</table>

**Results in brackets represent mean from 4 animals breathing 9.6\% \( O_2 \), omitting results from 1 animal where extraction ratio fell by 19%.

### RESULTS

**EFFECT OF BREATHING 9.6\% \( O_2 \) AND 0.2\% CO ON RENAL PAH EXTRACTION RATIO**

Renal vein catheterization was carried out in 16 animals. Each animal breathed room air during the control period. During the subsequent treatment period five animals breathed 21\% \( O_2 \), five animals breathed 9.6\% \( O_2 \) and six animals breathed 0.2\% CO. The results in table 1 show that the effect on the renal PAH extraction ratio of breathing low \( O_2 \) mixtures was small and barely significant. In these experiments there was significant reduction in renal vein \( S_{oa} \) (or \( S'_{oa} \) in the CO experiments), indicating that there was probably significant reduction in the renal \( O_2 \) consumption occurred in the experiments with 9.6% \( O_2 \) and 0.2% CO only when there was a reduction of more than 30% in the RBF.

### EFFECT OF BREATHING 9.6\% \( O_2 \)

Following control observations with all animals breathing room air, 24 animals breathed 9.6\% \( O_2 \) during the treatment period (fig. 1), and 12 animals breathed 21\% \( O_2 \). There was a considerable increase in respiratory minute
FIGURE 2

$S_{aO_2}$ (or $S'eO_2$) in relation to the change in ventilation, expressed as percentage of each animal's own control value (upper panels), and the Right Atrial $O_2$ (or $O'eO_2$) (lower panels). Open circles—breathing 21% $O_2$ during treatment period; black circles—breathing 9.6% $O_2$; half-black circles—breathing 0.1% or 0.2% $CO$ in 21% $O_2$.

volume (upper left panel fig. 2). Although the animals breathed a gas mixture of approximately constant composition the magnitude of the respiratory response varied between individual animals. The range of $S_{aO_2}$ values varied from 84% to 46%, reflecting variation in ventilation:perfusion ratios between different animals. The right atrial $S_{aO_2}$ was reduced below normal values whilst breathing 9.6% $O_2$. In the 24 animals breathing 9.6% $O_2$ during the treatment period the $O_2$ consumption was 23.7 ml/min STPD when breathing room air, and 30.9 ml/min STPD when breathing the low $O_2$ mixture (difference 2.8 ± 0.85 (SEM) ml/min). In the 12 animals breathing 21% $O_2$ during the treatment period corresponding values for $S_{aO_2}$ were 25.6 ml/min STPD while breathing room air, and 24.8 ml/min STPD whilst breathing 21% $O_2$ (difference 0.8 ± 1.5 (SEM) ml/min).

The effect of arterial hypoxia on the urine flow was variable. The mean urine flow whilst breathing room air was 0.72 ml/min and 0.50 ml/min whilst breathing 9.6% $O_2$.

The changes in cardiac output and RBF are shown in figure 3. In the present experiments the proportion of animals showing an increased cardiac output while breathing low

FIGURE 3

Arterial $S_{aO_2}$ in relation to changes in cardiac output (C.O.), renal blood flow (RBF), ear artery pressure (BP), and filtration fraction (FF) in animals breathing 9.6% $O_2$ during treatment period (open circles), and 21% $O_2$ (black circles). Changes in above measurements are expressed as percentage of the animals own control value. Each animal is represented by only one point.
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O₂ mixtures was greater than observed previously, possibly as a result of further reduction in the amount of handling and excitement to which the animals were subjected. The heart rate at the time of the clearance determinations in animals breathing 9.6% O₂ was 93.5 ± 2.9 (se) % of the control value (taken as 100%). There was no significant change in arterial pressure with increasing hypoxia. There was reduction in RBF related to the degree of severity of hypoxia (fig. 3). Although the GFR was also reduced, the effect was smaller than the effect on the RPF and there was thus an increase in filtration fraction at low SaO₂ values. The results indicate that there was an overall increase in the renal vascular resistance with a selective increase in postglomerular resistance with increasing severity of hypoxia.

EFFECT OF BREATHING 0.1 AND 0.2% CO

Twenty-seven animals breathed 0.1 or 0.2% CO during the treatment period. There was a small, but statistically significant increase in respiratory minute volume. The percentage of carboxyhemoglobin varied between 30% and 58% depending on the concentration of inspired CO. The mixed venous SaO₂ was reduced in relation to the reduction in arterial O₂-carrying capacity (fig. 2). The O₂ consumption was 26.4 ml/min STPD while breathing room air, and 22.9 ml/min STPD when breathing CO mixtures (difference 3.5 ± 0.60 (se) ml/min).

There was usually some reduction in urine flow in the course of breathing CO mixtures, the urine flow of the group being 0.60 ml/min while breathing room air and 0.37 ml/min while breathing CO.

Figure 4 shows that the cardiac output increased in relation to the reduction in SaO₂. The mean heart rate while breathing carbon monoxide was 112.9 ± 2.45 (se) % of the control value and tachycardia was observed in most animals. There was reduction in ear artery pressure, RBF and GFR, each variable being reduced by approximately 20%. The GFR and RPF were reduced to approximately the same degree, so that there was no significant change in filtration fraction with reduction in SaO₂. There was no significant effect in the group on the renal vascular resistance.

The fall in arterial pressure, RBF and GFR, did not appear to be closely related to the degree of reduction in arterial O₂-carrying capacity.

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TABLE 2
Mean Values in 3 Groups of Rabbits Subjected to Following Treatment Sequences. Group A: Each Animal Breathed Successively Room Air—21% O₂—9.6% O₂. Group B: Each Animal Breathed Successively Room Air—0.1% CO—0.2% CO. Group C: Each Animal Breathed Successively Room Air—0.2% CO—9.6% O₂

| Group   | number of animals | Treatment | | | A | B | C |
|---------|-------------------|-----------|---|---|---|---|---|---|
|         | Control period    | 21% O₂    | 9.6% O₂ | 0.1% CO | 0.2% CO | 9.6% O₂ | 0.1% CO | 0.2% CO | 9.6% O₂ |
|         | Cardiac output ml/min | 537 | 530 | 565 | 530 | 728* | 768* | 515 | 704* | 861* |
|         | Heart rate/min | 256 | 256 | 259 | 256 | 251* | 202* | 206* | 232* |
|         | B.P. mm Hg | 96 | 93 | 93 | 95 | 83* | 671 | 95 | 71* | 831 |
|         | R.B.F. ml/min | 111 | 111 | 114 | 119 | 105* | 105* | 120 | 91* | 631 |
|         | O.F.R. ml/min | 17.4 | 17.4 | 16.6 | 20.2 | 17.0 | 17.4 | 16.6 | 15.5* | 13.0* |
|         | Ventilation ml/min atD 0, | 1200 | 1370 | 1400 | 1400 | 1460 | 1610* | 1178 | 1700* | 2580* |
|         | S'a0₂ or S'a0₂ | 95 | 95 | 95 | 95 | 65* | 81* | 94 | 55* | 68* |
|         | S'a0₂ or S'a0₂ | 40 | 61 | 57 | 69 | 45* | 271 | 57 | 25* | 331 |

*Significantly different from control value (P < 0.05)
†Significantly different from first treatment value (P < 0.05)
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nately the same degree with 9.6% O₂ as with CO for a given value of SaO₂ or S'ao₂, but there were significant differences in the response of the heart rate of the two groups.

The RBF was reduced to a greater extent in animals breathing 9.6% O₂ than in those breathing CO despite the fact that the blood pressure remained unchanged in the former group, but was reduced in the latter. This suggests that renal vasoconstriction occurs with 9.6% O₂. The difference in the renal vascular response between low O₂ mixtures and CO can be demonstrated more clearly by observing the response to both mixtures in a given animal (table 2, Group C). Figure 5 shows that when a rabbit breathed 0.2% CO the arterial and mixed venous O₂ content were reduced. There was increase in cardiac output, some increase in ventilation, and reduction in arterial pressure, RBF and GFR. When the inspired gas was changed to 9.8% O₂ further increase in ventilation occurred. The O₂ content of the arterial and mixed venous blood increased slightly. The blood pressure increased from its previous level, but despite this there was further significant reduction in RBF, clearly indicating the occurrence of renal vasoconstriction. This effect was observed in all four animals tested in this way and is in agreement with the results observed in the main groups shown in figures 3 and 4.

THE ROLE OF THE RENAL VASOMOTOR NERVES IN THE RESPONSE TO 9.6% O₂

Whilst the above experiments demonstrate the occurrence of renal vasoconstriction in animals breathing 9.6% O₂, they do not indicate the mechanism involved. Vasoconstriction could be due to increased sympathetic constrictor tone, or due to the liberation of humoral agents such as epinephrine. 35 The part played by the renal vasomotor nerves was studied in 14 animals where separate clearance estimations for each kidney were carried out. In seven of these the left kidney was denervated six to eight days before an experiment.

Figure 6 shows the effects of 9.6% O₂ on the innervated and denervated kidney of an unanesthetized rabbit. The RBF was reduced to a greater extent in the innervated kidney when breathing 9.6% O₂ than in the denervated kidney. On resuming air breathing the RBF increased in the innervated kidney, but there was little change in flow in the denervated kidney. Breathing 8% O₂ again resulted in a marked difference between the two sides. The results of all experiments are summarized in figure 7. In animals with both kidneys in-
Experiment showing effect of breathing 9.6% O₂ and 8% O₂ on cardiac output, arterial pressure, RBF and GFR in rabbit with chronic denervation of left kidney. Separate clearance determinations were carried out from each kidney. White—breathing room air. Black—breathing low O₂ mixture.

In animals with one kidney denervated there was relatively little change in RBF on the denervated side with increasing severity of hypoxia, but a marked reduction in RBF on the innervated side. The experiments demonstrate the importance of the renal vasomotor nerves in the production of renal vasoconstriction with low oxygen mixtures. The effect on the GFR was similar to the effect on the RBF in these experiments (fig. 7) and it is thus likely that the vasoconstrictr nerves terminate near the afferent arteriole. Figure 7 shows that there was no difference in filtration fraction on innervated and denervated sides, and the increase in filtration fraction with reduction in SaO₂ (figs. 3 and 7) is thus not the result of direct nervous action on the renal blood vessels.

Relationship of arterial SaO₂ to changes in RBF, GFR and filtration fraction (FF) in animals breathing 9.6% O₂ during the treatment period. Open circles—denervated kidney; black circles—innervated kidney. Results from one animal are joined together by a line.

Because of variation in the renal vascular response between animals it is not obvious from the results in figure 7 if there is a threshold for the occurrence of renal vasoconstriction. The effects of a number of different low O₂ mixtures were studied in greater detail in two animals, and the result of one experiment

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is shown in Figure 8. There was no difference in the behaviour of RBF and GFR on innervated and denervated sides when the animal breathed 11.8% O₂ (SαO₂ 85%). A small degree of vasoconstriction could be demonstrated on the innervated side when breathing 10.4% O₂ and 9.6% O₂ (SαO₂ 79% and 77% respectively), and this became marked with increasing severity of hypoxia. This result demonstrates that renal vasoconstriction requires the presence of a more severe degree of arterial hypoxia than is required to bring about an increase in ventilation.

In order to further investigate the relationship of the PaO₂ to renal vasoconstriction, bilateral denervation of the carotid and depressor nerves was carried out in two animals in two stages, eight days before the experiment. Figure 9 shows the result of one experiment. The animals were not able to tolerate 9.6% O₂ and higher inspired O₂ pressures were used. The ear artery pressure was 103 mm Hg preceding the test period and was 114 mm Hg in the other animal. These values are lower than might be expected following complete baroreceptor denervation. It is possible that baroreceptor denervation may not have been complete, or the prolonged period of rest in the experimental cage following the operative procedures may have reduced the blood pressure. Chemoreceptor denervation was probably adequate as judged by the very small increase in ventilation with very severe
Experiment showing effect of breathing 0.2% CO in 21% O₂ and 8% O₂ in N₂ on cardiac output, arterial pressure, RBF and GFR on rabbit with chronic denervation of left kidney. Separate clearance measurements were carried out from each kidney. White—breathing room air; stippled—breathing 0.2% CO in 21% O₂; black—breathing 8% O₂.

**FIGURE 10**

The renal vascular response differed considerably from the response produced normally by this degree of hypoxia. The degree of reduction in RBF was much smaller than usual, and it appeared to be related to the reduction in blood pressure. There was a fall in renal vascular resistance instead of the usual rise. The results suggest that the arterial chemoreceptors are normally of importance in the renal vasoconstriction of arterial hypoxia.

**THE ROLE OF THE RENAL VASOMOTOR NERVES IN THE RESPONSE TO 0.2% CO**

This was investigated in nine animals, in five of which left renal denervation had been carried out. There was much less difference in the response between innervated and denervated kidney with CO than with 9.6% O₂ (fig. 10). In all animals there was a slightly greater reduction in RBF (table 3) and GFR on the innervated side during the first 10 to 20 minutes of breathing CO. During steady state conditions, however, there was no difference in behaviour between the two sides. In all animals the characteristic constrictor response to low O₂ mixtures was demonstrated at the end of the experiment (fig. 10). The part played by the renal vasomotor nerves in the reduction in RBF and GFR in the CO experiments thus appears to be small.

Figure 10 shows that the maximum fall in RBF occurred in both innervated and denervated kidney during the initial fall in blood pressure. Subsequently there was no change or a slight increase in RBF despite further fall in arterial pressure. This suggests the occurrence of some renal vasodilatation with 0.2% CO.

**Discussion**

The experiments demonstrated significant differences in the response of the renal circulation of the rabbit following exposure to low oxygen mixtures and to carbon monoxide. The mean reduction in RBF was greater in animals breathing 9.6% O₂ than in those breathing carbon monoxide and occurred as a result of renal vasoconstriction. The renal vasomotor nerves constricting the afferent arteriole played an important part in this response. The physiological evidence regarding the site of action is in accord with anatomical demonstration by Mitchell™ that the afferent arteriole is more richly innervated than the post-glomerular vessels. Increased nervous vasoconstriction did not however account for the increased filtration fraction observed in animals with the most severe degrees of hypoxia. A similar increase in filtration fraction can be produced by infusions of epinephrine.
TABLE 3

<table>
<thead>
<tr>
<th>Period</th>
<th>Right BBF</th>
<th>Left RBF</th>
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</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>0.92</td>
<td>0.89</td>
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<tr>
<td>(left kidney</td>
<td>0.81</td>
<td>0.83</td>
</tr>
<tr>
<td>denervated)</td>
<td>0.96</td>
<td>0.84</td>
</tr>
<tr>
<td>1-10</td>
<td>1.01</td>
<td>0.97</td>
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<td></td>
<td>0.98</td>
<td>0.91</td>
</tr>
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<td></td>
<td>0.96</td>
<td>0.96</td>
</tr>
<tr>
<td>Mean</td>
<td>0.94</td>
<td>0.94</td>
</tr>
<tr>
<td>Group 2</td>
<td>0.96</td>
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<tr>
<td>(both kidneys</td>
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</tr>
<tr>
<td>innervated)</td>
<td>0.99</td>
<td>1.05</td>
</tr>
<tr>
<td></td>
<td>1.01</td>
<td>1.04</td>
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<tr>
<td></td>
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<td>1.00</td>
</tr>
<tr>
<td>Mean</td>
<td>1.01</td>
<td>1.04</td>
</tr>
</tbody>
</table>

*In two additional animals only steady state response studied.

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and norepinephrine. Since these substances are known to be liberated in severe hypoxia it is possible that they may have played a part in the post-glomerular constriction in the rabbit, but the present experiments provide no proof of this. It appears that more severe reduction in PaO₂ is required to bring about renal vasoconstriction, than is required to produce an increase in ventilation, and that the filtration fraction increases only during the most severe degrees of hypoxia.

Denervation of the carotid sinuses region and of the depressor nerve was carried out in two animals and in both of these reduction in renal vascular resistance with relatively slight effects on renal blood flow was observed in place of the usual constrictor response. The renal vasoconstriction which occurs in the innervated kidney of the rabbit breathing 9.6% O₂ would thus appear to be reflexly mediated with excitation of the carotid and aortic chemoreceptors initiating the reflex.

In contrast to the results with low O₂ mixtures there was no evidence of reduction in RBF due to nervous constriction during the steady state in the CO experiments and the response appeared to be partly passive due to fall in blood pressure, and partly the result of local renal dilatation. The passive reduction in RBF due to the fall in arterial pressure is consistent with the results of pressure-flow studies in the isolated kidney.

Transient and slight renal vasoconstriction occurred in the initial period of breathing CO, at the time of the steepest fall in blood pressure and it is possible that this may have been of baroreceptor origin, though the present experiments provide no proof of this. The experiments were not designed to test the role of catechol amines (whose liberation might be expected in relation to the fall in blood pressure from the experiments of Heymans and Neil, and Tournade and Chabrol, cited in ref. 19) in the response to CO mixtures.

In addition to the differences in the renal vascular response there were significant differences in ventilation, heart rate, and blood pressure in the response of the rabbit to low O₂ mixtures and CO, and agreement with previous findings. In these two types of hypoxia differences in Pao₂, Paco₂, Pvo₂, blood pH and possibly direct tissue effects (in the case of CO) might be expected to contribute to the difference in circulatory response. The results suggest that differences in Pvo₂ probably do not account for the different responses since there was considerable overlap in the estimated Pvo₂ in both types of hypoxia. Similarly direct interference with tissue oxygen transport by CO is unlikely since the changes observed in total and renal oxygen consumption were very similar with CO and low O₂ mixtures. Changes in blood pH were not measured and are likely to be different in the
The effects of breathing 9.6% O₂ in N₂ and of breathing 0.1% to 0.2% CO in air on the renal blood flow (RBF), glomerular filtration rate (GFR) and renal PAH extraction ratio were studied in the unanesthetized rabbit in relation to changes in cardiac output, heart rate, blood pressure and ventilation. All experiments were carried out during moderate water and mannitol diuresis. The RBF and GFR were reduced in both types of hypoxia but this effect was produced by different mechanisms. With low O₂ mixtures reduction in RBF and GFR occurred mainly as a result of nervous vasoconstriction acting on the arterial chemoreceptors played a part in the production of vasoconstriction. With carbon monoxide, reduction in RBF and GFR occurred mainly as a result of passive reduction in blood pressure, and only slight transient nervous vasoconstriction could be demonstrated in the early period of exposure to this gas. The results suggest that differences in arterial oxygen pressure (Pao₂) were of major importance in accounting for the differences in renal circulatory effects of low O₂ mixtures and CO in the rabbit.

References
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PAUL I. KORNER and Pascoe Yvonne

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