Nitric Oxide Influences Blood Flow Distribution in Renovascular Hypertension

David H. Sigmon, William H. Beierwaltes

Abstract

Endothelium-derived nitric oxide contributes to the regulation of regional blood flow. Inhibition of endothelium-derived nitric oxide synthesis increases blood pressure and vascular resistance. Using the substrate antagonist Nω-nitro-L-arginine-methyl ester to block endothelium-derived nitric oxide synthesis, we tested the hypothesis that, in two-kidney, one clip renovascular hypertension, endothelium-derived nitric oxide plays an increased role in maintaining blood flow to the nonclipped kidney and other visceral organs compared with normotensive controls. This could be due to increased vascular shear stress, a primary stimulus for endothelium-derived nitric oxide synthesis, after the onset of hypertension. In hypertensive rats with mild renal artery stenosis, basal renal blood flow normalized by kidney weight was similar in the nonclipped and clipped kidneys. Basal blood pressure of controls was 98±2 mm Hg compared with 145±3 mm Hg in the two-kidney, one clip hypertensive rats. Nω-nitro-L-arginine-methyl ester increased blood pressure by 20±2 and 43±3 mm Hg in control and hypertensive rats, respectively. Compared with normotensive controls, basal resistance was higher in all organ beds in the hypertensive rats including brain, heart, intestine, and kidney. With the exception of the renal circulation, the increase in vascular resistance after Nω-nitro-L-arginine-methyl ester was greater in hypertensive rats compared with normotensive controls. In the hypertensive rats, Nω-nitro-L-arginine-methyl ester caused a similar increase in vascular resistance in both the nonclipped and clipped kidneys, and this was not different from normotensive controls. These results suggest that, in two-kidney, one clip hypertensive rats, as in normotensive rats, endothelium-derived nitric oxide synthesis plays an important role in regulating regional hemodynamics. In this model of hypertension, the endothelium is not dysfunctional but is a critical component in the adaptation of local organ perfusion to increased blood pressure. (Hypertension. 1994;23[suppl I]:I-34-I-39.)

Key Words • nitric oxide • hypertension, renovascular • renal circulation • blood pressure • angiotensins

It has been suggested that various forms of hypertension are characterized by a dysfunctional endothelium, resulting in abnormal endothelium-dependent vasodilation, which contributes to the rise in mean arterial blood pressure (BP).1-7 In various models of hypertension, including two-kidney, one clip (2K1C) Goldblatt,1 aortic coarctation,1,4 Dahl salt-sensitive,3 and deoxycorticosterone acetate-salt1 hypertension as well as in genetically spontaneously hypertensive rats,2 endothelium-dependent vascular relaxation in vitro is impaired but may be restored by reversing the hypertension.1 These observations suggest that endothelial dysfunction associated with hypertension may be due to insufficient production of the intrinsic vasodilator endothelium-derived nitric oxide (EDNO). In normotensive subjects, EDNO contributes to the regulation of regional blood flow.8-13 Inhibition of EDNO synthesis using either Nω-nitro-L-arginine-methyl ester (L-NAME) or Nω-monomethyl L-arginine (L-NMMA) increases BP and vascular resistance and decreases blood flow to a number of vascular beds.9-13 However, the increased resistance is not distributed equally among all vascular beds. This increase is suggested to be the result of removing intrinsic EDNO-mediated vasodilation, allowing the pressor action by inherent myogenic tone or endogenous vasoconstrictors to predominate. Therefore, the extent to which EDNO synthesis inhibition affects a specific resistance bed may indicate the degree to which local vascular tone depends on EDNO.

Using anesthetized rats, we have previously shown that blocking the renin-angiotensin system eliminated the decrease in renal blood flow and attenuated the increase in renal vascular resistance otherwise observed after EDNO synthesis inhibition.14,15 However, angiotensin II (Ang II) blockade did not impair the systemic pressor response to EDNO synthesis inhibition. We concluded that within the renal vasculature, there is a unique interaction between the vasodilator influence of EDNO and the vasoconstrictor influence of Ang II. Therefore, if EDNO buffering of Ang II vasoconstriction of the renal vasculature is important in normal rats, it would probably be even more important in regulating renal perfusion in an Ang II-dependent form of hypertension such as 2K1C renovascular hypertension.

Since Goldblatt et al16 demonstrated the development of hypertension after renal artery stenosis, the pathogenesis of renovascular hypertension has been studied extensively.17 Clipping the renal artery results in an immediate fall in renal blood flow and glomerular filtration rate in the clipped kidney, whereas plasma renin activity (PRA) and BP increase.17,18 Within 4 weeks, PRA increases 5- to 10-fold, and the rats become hypertensive.18 In the nonclipped kidney, renal vascular resistance is elevated,17 but by 4 weeks renal blood flow and glomerular filtration rate in the nonclipped kidney (per gram of kidney weight) are similar to normotensive controls17,19 despite elevated BP, renal vascular resistance, and circulating Ang II. If elevated pressure increases renal perfusion, this should increase

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vascular shear stress, a primary stimulus for EDNO synthesis.\(^{20}\) Thus, we hypothesized that in 2K1C renal-vascular hypertension, EDNO plays an increased role in maintaining blood flow to the nonclipped kidney as well as other visceral organs. Additionally, if renal artery stenosis is mild, so that perfusion to the stenotic, clipped kidney is essentially normalized (pooled gram kidney weight) by the elevated perfusion pressure, we also hypothesized that EDNO will remain an important influence on blood flow in the stenosis-compromised vasculature.

**Methods**

2K1C hypertension was induced as described previously.\(^{16}\) Briefly, male Sprague-Dawley rats (Charles River Laboratories, Wilmington, Mass) weighing 180 to 200 g were anesthetized with sodium pentobarbital (Nembutal, Abbott Laboratories, North Chicago, III). Under antiseptic conditions, the left renal artery was exposed through a retroperitoneal flank incision and carefully dissected free of the renal vein. A silver clip with an internal diameter of 0.23 mm was placed around the renal artery, causing partial occlusion. The wound was closed, and the rat was allowed to recover for 4 weeks before the experiments detailed below.

Our protocol used the hemodynamic response to L-NAME as an indicator of the involvement of EDNO in the regulation of regional blood flow. Normotensive controls (n=7) or 4-week 2K1C hypertensive rats (n=7) were fasted overnight but allowed free access to water. Rats were anesthetized by an intraperitoneal injection of 125 mg/kg body wt of thiobutabarbital (Inactin, Andrew Lockwood Co, Milwaukee, Wis) and placed on a heating pad to maintain constant body temperature. A PE-10 catheter was introduced through the right common carotid artery and passed into the left ventricle for infusion of microspheres. The position of the catheter tip in the left ventricle was adjusted until the left ventricular pulse pressure could be read without artifacts. The right femoral vein and artery were catheterized with PE-50 tubing. The venous catheter was used for constant infusion of saline (40 \(\mu\)L/min), infusion of drugs, and blood replacement; the arterial catheter was used for monitoring of BP and for reference blood sampling. Blood pressure was recorded with a Statham pressure transducer (Viggo-Spectramed, Oxnard, Calif) connected to a chart recorder (Gould Instruments, Valley View, Ohio). After surgery, the rats were allowed a 60-minute stabilization period, during which BP was monitored.

The effect of EDNO synthesis inhibition on regional blood flow was measured using radioactive microspheres\(^{21}\) (Du Pont—New England Nuclear, Boston) with a diameter of 15±1.5 \(\mu\)m and labeled with either \(^{14}\)Ce or \(^{85}\)Sr. Microspheres suspended in 3.5 mol/L glucose with 0.01% Tween 90 (an antiaggregant) at a concentration of 400 000/mL were mechanically agitated for approximately 15 minutes. A volume of 0.2 mL of the suspension, corresponding to approximately 80 000 microspheres, was then drawn up into a syringe. The microspheres, together with 0.2 mL saline, were infused into the left ventricle over 20 seconds while at the same time arterial reference blood was withdrawn mechanically at a rate of 0.48 mL/min over 75 seconds. The withdrawn blood was replaced with blood obtained from a donor rat nephrectomized 16 to 24 hours earlier. The rats were then allowed to reheat every 15 minutes, after which an established intravenous bolus blocking dose of 10 mg/kg body wt of L-NAME was administered to inhibit EDNO synthesis.\(^{21}\) Fifteen minutes later, a second set of microspheres was injected using the same technique. Fifteen minutes after the last injection of microspheres, a blood sample was obtained for determination of PRA from hypertensive rats. PRA was determined by radioimmunoassay as described previously.\(^{22}\) The animals were then killed with an intravenous injection of sodium pentobarbital (150 mg/kg), and tissue samples were obtained from the brain, heart, hind limb, kidneys, intestine, and lung. Samples were counted in a Packard gamma counter using dual window settings of 10 to 250 and 400 to 700 MeV.

Organ blood flow (milliliters per minute per gram tissue weight) was measured as Blood Flow=counts per minute (cpm) per Organ \times Pump Speed/cpm in Blood \times Tissue Weight (grams); organ vascular resistance (millimeters of mercury per milliliter per minute per gram tissue weight) (referred to as resistance units, or RU) was determined as Vascular Resistance=Mean BP/Organ Blood Flow. Cardiac output (milliliters per minute per 100 grams body weight) was measured as (cpm per Injection \times Pump Withdrawal Rate)/cpm in Blood.

Changes induced by L-NAME were analyzed using Student’s paired \(t\) test. Comparisons of changes occurring under different conditions or of basal values were carried out using Student’s unpaired \(t\) test. A value of \(P<.05\) was considered significant. In these experiments, we selected 2K1C rats in which the clip produced a mild renal artery stenosis based on renal blood flow; when corrected by kidney weight, renal blood flow was the same in both clipped and nonclipped kidneys.

**Results**

Effect of EDNO Synthesis Inhibition on Regional Hemodynamics in Normotensive and Two-Kidney, One Clip Hypertensive Rats

Rats with mild stenosis had an average nonclipped-to-clipped corrected renal blood flow ratio of 0.94±0.07, although absolute flow was 36% greater in the nonclipped kidney \((P<.025)\). Basal BP of the normotensive rats was 98±2 mm Hg compared with 145±3 mm Hg in the hypertensive rats. Changes in BP in response to L-NAME are shown in Fig 1. L-NAME significantly increased BP 20±1 mm Hg \((P<.001)\) in normotensive rats. The pressor response in 2K1C rats with mild stenosis was more than twice as potent (43±3 mm Hg, \(P<.001\)) as in normotensive rats. Basal cardiac output was 29.5±3.3 mL \(\cdot\) min\(^{-1}\) \(\cdot\) 100 g body wt\(^{-1}\) in normotensive rats compared with 23.7±1.4 mL \(\cdot\) min\(^{-1}\) \(\cdot\) 100 g body wt\(^{-1}\) in 2K1C hypertensive rats. L-NAME caused a similar decrease in cardiac output in both normotensive (11.5±2.3 mL \(\cdot\) min\(^{-1}\) \(\cdot\) 100 g body wt\(^{-1}\), \(P<.005\)) and 2K1C hypertensive rats with mild stenosis (9.9±1.7 mm Hg, \(P<.005\)). PRA in hypertensive rats was 9.0±1.5 ng angiotensin I \(\cdot\) mL\(^{-1}\) \(\cdot\) hr\(^{-1}\) after L-NAME.

Changes in regional hemodynamics to various organs in normotensive and 2K1C hypertensive rats are shown in the Table and Figs 1 and 2.

In normotensive rats, L-NAME had no effect on cerebral blood flow but increased vascular resistance by 39% \((P<.05)\). In 2K1C rats, L-NAME also had no effect on cerebral blood flow but increased resistance by 70% \((P<.005)\). The increase in vascular resistance after EDNO synthesis inhibition was greater in 2K1C hypertension \((P<.05)\). In normotensive rats, L-NAME had no effect on cardiac blood flow but increased vascular resistance by 40% \((P<.05)\). In 2K1C rats, L-NAME decreased cardiac blood flow by 38% \((P<.05)\) and increased vascular resistance by 105% \((P<.02)\). The increase in vascular resistance after EDNO synthesis inhibition was greater in 2K1C hypertension \((P<.05)\).

In normotensive rats, L-NAME had no significant effect on hind limb blood flow or vascular resistance. In 2K1C rats, L-NAME had no effect on hind limb blood flow but increased vascular resistance by 112% \((P<.01)\).
In normotensive rats, L-NAME decreased pulmonary blood flow by 68% (P<.005). In 2K1C rats, L-NAME similarly decreased pulmonary blood flow by 64% (P<.005). Pulmonary resistance could not be calculated because we were unable to measure pulmonary perfusion pressure in our preparation.

**Discussion**

We have found that, in 2K1C renovascular hypertensive rats with only mild renal artery stenosis, inhibition of EDNO synthesis results in an exaggerated increase in systemic pressure and vascular resistance compared with normotensive rats. However, the kidneys behaved differently. First, renal vascular resistance was elevated to a degree that basal renal blood flow was depressed (compared with normotensive rats) in both clipped and nonclipped kidneys. Second, the renal blood flow response to L-NAME was attenuated in both kidneys of the hypertensive rats. The increase in renal vascular resistance was not exaggerated but was similar to that in kidneys of normotensive rats. Thus, in this model of hypertension, the systemic responses suggest that there is no deficiency in EDNO, except perhaps in the renal endothelium. Our hypothesis that EDNO is a critical component in maintaining renal perfusion is inappropriate because renal blood flow is depressed in this form of 2K1C hypertension. This differs from our previous observations in 2K1C rats with severe renal artery stenosis. In those studies, we found normalized blood flow in the nonclipped (but not the clipped) kidney that was largely maintained by EDNO.

In 2K1C renovascular hypertension, renal artery stenosis produced with a clip is characterized by a fall in renal perfusion to the clipped kidney, a rise in PRA and circulating Ang II, and a steady increase in BP. Additionally, a number of in vitro studies have reported diminished endothelium-dependent vascular relaxation in 2K1C hypertensive rats, suggesting that this model is characterized by a dysfunctional endothelium and diminished nitric oxide, which is permissive for the increase in resistance. However, compared with normotensive rats, 2K1C hypertensive rats have elevated Ang II, which should increase vascular resistance, while a rise in BP should increase organ perfusion. These factors should result in greater vascular shear stress, a potent stimulus for EDNO synthesis.

The increase in vascular resistance after EDNO synthesis inhibition was greater in 2K1C hypertension (P<.01).

In normotensive rats, L-NAME decreased renal blood flow by 39% (P<.001) and increased renal vascular resistance by 97% (P<.001). In 2K1C rats, L-NAME decreased renal blood flow by 18% (P<.02) and increased renal vascular resistance by 50% (P<.005) in both nonclipped and clipped kidneys. Although the decrease in blood flow after EDNO synthesis inhibition was less in 2K1C rats compared with normotensive controls (P<.001), the increase in vascular resistance observed for the two groups was not different.

In normotensive rats, L-NAME decreased intestinal blood flow by 49% (P<.001) and increased vascular resistance by 152% (P<.005). In 2K1C rats, L-NAME decreased intestinal blood flow by 50% (P<.001) and increased vascular resistance by 186% (P<.005). The increase in vascular resistance after EDNO synthesis inhibition was significantly greater in rats with 2K1C hypertension (P<.025).

During the early phase of 2K1C hypertension, while BP is increasing, the pathogenesis of the disease has been attributed to a combination of elevated Ang II, altered plasma volume, changes in renal function, and increased renal nerve activity. We found that at 4 weeks, EDNO synthesis inhibition increased BP by 43 mm Hg in 2K1C hypertensive rats, whereas in normotensive rats L-NAME increased BP by only 20 mm Hg. Although EDNO is an important mediator of vascular tone, we have previously reported that the systemic pressor response to L-NAME is exaggerated in various models of hypertension, regardless of the intrinsic involvement of the renin-angiotensin system. Therefore, the exaggerated systemic pressor response to L-NAME may be a function of elevated systemic resistance in hypertension but is not necessarily caused by Ang II. The exaggerated pressor response to L-NAME also implies that the endothelium is probably not dysfunctional in 2K1C hypertension (4 weeks after clipping), as
Effect of Endothelium-Derived Nitric Oxide Synthesis Inhibition on the Hemodynamic Response in Normotensive and Two-Kidney, One Clip Hypertensive Rats With Mild Renal Artery Stenosis

<table>
<thead>
<tr>
<th>Blood flow, mL min⁻¹·g tissue wt⁻¹</th>
<th>2K1C Hypertension</th>
<th>Normotensive Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue (n=7)</td>
<td>L-NAME</td>
<td>Basal</td>
</tr>
<tr>
<td>Brain</td>
<td>0.74±0.07</td>
<td>0.57±0.07</td>
</tr>
<tr>
<td>Heart</td>
<td>4.69±0.61</td>
<td>2.90±0.36*</td>
</tr>
<tr>
<td>Hind limb</td>
<td>0.06±0.01</td>
<td>0.05±0.01</td>
</tr>
<tr>
<td>Nonclipped kidney</td>
<td>4.17±0.50</td>
<td>3.47±0.36*</td>
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<tr>
<td>Clipped kidney</td>
<td>4.30±0.38</td>
<td>3.45±0.34*</td>
</tr>
<tr>
<td>Intestine</td>
<td>1.33±0.10</td>
<td>0.67±0.11*</td>
</tr>
<tr>
<td>Lung</td>
<td>1.22±0.22</td>
<td>0.44±0.09*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vascular resistance, mm Hg · mL⁻¹·min⁻¹·g tissue wt⁻¹</th>
<th>2K1C Hypertension</th>
<th>Normotensive Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue (n=7)</td>
<td>L-NAME</td>
<td>Basal</td>
</tr>
<tr>
<td>Brain</td>
<td>212.5±31.6</td>
<td>359.9±37.3*</td>
</tr>
<tr>
<td>Heart</td>
<td>36.5±6.0</td>
<td>75.0±13.1*</td>
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<tr>
<td>Hind limb</td>
<td>2019±345</td>
<td>4286±531*</td>
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<tr>
<td>Nonclipped kidney</td>
<td>38.7±5.9</td>
<td>59.1±9.5*</td>
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<tr>
<td>Clipped kidney</td>
<td>40.9±6.8</td>
<td>61.2±11.3*</td>
</tr>
<tr>
<td>Intestine</td>
<td>112.5±10.2</td>
<td>321.3±42.8*</td>
</tr>
</tbody>
</table>

2K1C indicates two-kidney, one clip; L-NAME, N⁶-nitro-L-arginine-methyl ester.

*Significant difference from basal, P<.05.

Values represent mean±SEM for each experimental group: Normotensive controls (n=7) and 2K1C hypertension with mild renal artery stenosis (n=7).

Pulmonary vascular resistance could not be calculated because pulmonary pressure was not measured.

Previously suggested by in vitro studies, but rather serves as an important buffer of hypertensive factors or influences.

We have previously reported that in anesthetized normotensive rats, acute blockade of Ang II largely diminished the increase in renal vascular resistance seen with EDNO synthesis inhibition, suggesting that local EDNO production balances the renal vasoconstrictor effect of Ang II and thereby maintains renal blood flow. Based on these observations, we hypothesized that in 2K1C hypertension with elevated Ang II but only mild renal artery stenosis, EDNO should have a greater influence on regional blood flow compared with normotensive controls. Our results generally support this hypothesis. We found that in normotensive rats, EDNO synthesis inhibition increased vascular resistance in all vascular beds that were investigated. With the exception of the renal circulation, these responses were uniformly greater in 2K1C hypertension. Additionally, in 2K1C hypertension with mild renal artery stenosis, L-NAME had qualitatively similar hemodynamic effects on both the nonclipped and clipped kidneys. Despite depressed basal renal blood flow, the kidneys responded to L-NAME by reducing flow to a level similar to that seen in kidneys of normotensive rats.

The endothelium reportedly modulates vascular tone through the production of various vasoactive factors. Inhibition of EDNO synthesis results in increased BP and total peripheral resistance and decreased heart rate and cardiac output. The rise in total peripheral resistance is mirrored by various degrees of increased resistance in many vascular beds. Loeb and Longnecker and Wang et al reported that in normotensive rats, EDNO synthesis inhibition with L-NMMA resulted in heterogeneous changes ranging from a 15% decrease in bronchial resistance to an increase of more than 200% in brown fat. These findings suggest that EDNO influences the distribution of blood flow and that the extent to which it affects a specific resistance bed may indicate how much local perfusion depends on EDNO. Our study demonstrates that in 2K1C hypertension, EDNO appears to have a similar or even exaggerated influence on regional hemodynamics compared with normotensive controls.

In normotensive rats, L-NAME increased BP but decreased blood flow to the kidneys, intestine, and lung with no change in brain, heart, or hind limb. Resistance increased in all vascular beds, with the greatest increase in the intestine. This is consistent with previous findings and suggests that basal production of EDNO is a factor in maintaining the perfusion of all visceral organs.

In 2K1C hypertensive rats with mild renal artery stenosis, L-NAME decreased blood flow to the heart, nonclipped and clipped kidneys, intestine, and lung, with no change in either brain or hind limb. Resistance increased in every organ; increases seen in hypertensive rats were uniformly greater than in normotensive con-
were not different from those in the normotensive controls, with the surprising exception of the kidneys. It is possible that the normalization or adaptation of blood flow (in vasculatures other than the renal) is due to an increased influence of EDNO, maintaining perfusion against increased circulating Ang II and elevated BP. This may be due to elevated EDNO synthesis or decreased degradation. In contrast, in the renal circulation, L-NAME caused a similar increase in resistance in both nonclipped and clipped kidneys, and these changes were not different from those in the normotensive controls. Interestingly, the nonclipped and clipped kidneys were the only organs in which basal blood flow was significantly lower in hypertensive compared with normotensive animals. Therefore, in the renal circulation, there was no apparent compensatory increase in EDNO in either kidney. This implies that either the kidneys could not produce sufficient EDNO to counteract the onset of hypertension or that the renal vasculature has not yet achieved the hypothesized balance between Ang II and EDNO, the resulting imbalance being responsible for the decreased basal renal blood flow. This is contrary to what we have previously observed in 2K1C rats with a more severe stenosis in which basal renal blood flow to the nonclipped kidney is similar to controls, with an exaggerated response to L-NAME.22

In these studies the response to L-NAME was used as an index of the participation of endogenous EDNO in regulating regional hemodynamics. Contrary to our results, it has been reported that agonist-induced, endothelium-dependent vasodilation is impaired in various forms of hypertension.1 7 However, most of these studies have been done in vitro in conduit rather than resistance vessels. There may be inherent differences in the responsiveness of these model systems compared with the hemodynamic responses in situ. There are also in vivo studies that demonstrate a diminished dilator response to endothelium-dependent vasodilators such as acetylcholine. This apparent reduced in vivo response could be due to the limitation of using equimolar doses of agonist (rather than the EC50) to compare vasculatures with different structural characteristics and/or basal vascular resistance. In contrast, under the same conditions, when the vasodilator influence of EDNO is removed in vivo, the elevated basal tone could result in an augmented hemodynamic response in the absence of any increase in EDNO synthesis. It is not clear whether the mechanism of agonist-induced vasodilation differs from that of intrinsic EDNO-induced vasodilation.

In conclusion, our data suggest that in 2K1C renovascular hypertensive rats with mild renal artery stenosis studied 4 weeks after clipping, EDNO synthesis plays an important role in regulating regional hemodynamics and maintaining organ perfusion. The exaggerated increase in systemic pressure and vascular resistance to EDNO synthesis inhibition in 2K1C hypertension suggests that, overall, the endothelium is not dysfunctional. This response could be attributed to (1) increased EDNO synthesis associated with hypertension, (2) Ang II-mediated stimulation of EDNO synthesis, and/or (3) decreased degradation of EDNO. Surprisingly, the kidneys of mildly stenotic 2K1C rats were the only visceral organs with reduced basal blood flow caused by a relatively higher basal resistance. Thus, there appears to be an imbalance between renal EDNO and endogenous (and increased) constrictor influences in these hypertensive rats. This suggests an absence of EDNO-mediated renal adaptation (suggested by the depressed renal blood flow) that may be contributing to the pathogenesis of this model of hypertension. Overall, the local influence of EDNO appears to be a critical component of the compensatory response or normalization of organ blood flow in this angiotensin-dependent model of hypertension.

Acknowledgment
This work was supported by grant HL-28982-11 from the National Institutes of Health, Bethesda, Md.

References
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Hypertension. 1994;23:I34
doi: 10.1161/01.HYP.23.1_Suppl.I34

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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