Role of Renal $\alpha_2$-Adrenergic Receptors in Spontaneously Hypertensive Rats

GERALD F. DIBONA AND LINDA L. SAWIN

SUMMARY To identify a physiological role for renal $\alpha_2$ adrenergic receptors, renal vascular and tubular responses to administration of graded frequencies of renal nerve stimulation or graded doses of adrenergic agonists were determined in anesthetized spontaneously hypertensive, Wistar-Kyoto, and Sprague-Dawley rats. Renal vasoconstrictor responses to renal nerve stimulation and $\alpha_1$-adrenergic receptor agonists (norepinephrine, phenylephrine) were inhibited by an $\alpha_2$-adrenergic receptor antagonist (prazosin) but not by an $\alpha_1$-adrenergic receptor antagonist (rauwolscine). A semilog plot of renal vasoconstrictor responses as fraction of control renal blood flow versus agonist dose (in nanograms) was linear with the slope, $k$, taken as the fractional decrease in renal blood flow per nanogram.

The $\alpha_2$-adrenergic receptor agonists (clonidine, guanabenz) produced minimal renal vasoconstrictor responses (fractional decrease in renal blood flow per nanogram: norepinephrine, 0.011; phenylephrine, 0.003; clonidine, 0.00087; guanabenz, 0.000037). The small renal vasoconstrictor responses to clonidine and guanabenz were more inhibited by rauwolscine than by prazosin. Low frequency renal nerve stimulation produced antidiuresis and antinatriuresis without decreasing glomerular filtration rate or renal blood flow. The antidiuretic and antinatriuretic responses were inhibited by prazosin but unaffected by rauwolscine. The magnitude of the renal vascular and tubular responses and their adrenergic receptor mediation were not different between spontaneously hypertensive, Wistar-Kyoto, and Sprague-Dawley rats. Although increased numbers of renal $\alpha_2$-adrenergic receptors have been described in spontaneously hypertensive rats, these results indicate that the renal vascular and tubular responses to renal nerve stimulation and adrenergic agonists are dependent on renal $\alpha_2$-adrenergic receptors; renal $\alpha_2$-adrenergic receptors are not involved. (Hypertension 9: 41-48, 1987)

KEY WORDS • kidney • renal nerve stimulation • renal blood flow • urinary sodium excretion •

THE kidneys of several species contain $\alpha$-adrenergic receptors, as identified by radioligand binding techniques, with $\alpha_2$-adrenergic receptors predominating numerically over $\alpha_1$-adrenergic receptors. Functional and pharmacological studies have been used to characterize renal adrenergic receptors. With respect to the renal vasculature, the results of studies in rats, cats, and dogs indicate a predominant role for $\alpha_1$-adrenergic receptors in the renal vasoconstrictor response to renal nerve stimulation (RNS) and $\alpha$-adrenergic receptor agonists. However, in the rabbit renal vasculature, there appears to be a greater role for renal vascular $\alpha_2$-adrenergic receptors in the renal vasoconstrictor response to these stimuli. The renin release response to RNS or adrenergic receptor agonists is mediated almost exclusively by renal $\beta_1$-adrenergic receptors; $\alpha$-adrenergic receptors are involved only when associated renal hemodynamic changes occur with decreases in renal blood flow (RBF), glomerular filtration rate (GFR), and urinary sodium excretion. The direct effect of RNS to increase renal tubular sodium and water reabsorption is mediated by renal tubular $\alpha_1$-adrenergic receptors in the dog, and, based on data from an in vitro isolated buffer-perfused kidney preparation, the rat. Therefore, in the normal rat kidney, despite a larger number of $\alpha_2$-adrenergic receptors than of $\alpha_1$-adrenergic receptors, the major renal functional responses to RNS appear to be predominantly mediated by $\alpha_1$-adrenergic receptors. Based on a variety of in vitro studies, it has been postulated that renal $\alpha_2$-adrenergic receptors are
extrajunctional and do not ordinarily mediate the effects of norepinephrine released from renal nerve terminals during RNS but may be more accessible to stimulation by circulating catecholamines.\(^\text{12}\) However, while \(\alpha\)-adrenergic receptor agonists can, through their ability to inhibit adenylate cyclase, modulate the responses to agents known to express their effect on urinary sodium excretion by adenylate cyclase stimulation, \(\alpha\)-adrenergic receptor stimulation alone has no effect on basal urinary sodium excretion.\(^\text{13-16}\)

Several features of the neural control of renal function in spontaneously hypertensive rats (SHR) are of related interest. The SHR have a higher level of efferent renal sympathetic nerve activity,\(^\text{17}\) abnormalities of renal vascular and tubular function possibly related to renal sympathetic nerve activity,\(^\text{17}\) abnormalities of renal o\(^\text{u}\)-adrenergic receptor number is increased in SHR compared with normotensive control Wistar-Kyoto rats (WKY) and Sprague-Dawley rats (SD),\(^\text{18}\) a series of studies was undertaken to determine whether renal vascular and tubular responses to RNS and adrenergic receptor agonists were more dependent on renal \(\alpha\)-adrenergic receptors in SHR than in WKY or SD.

### Materials and Methods

Male SHR, WKY (Harlan, Indianapolis, IN, USA), and SD (Biolab, St. Paul, MN, USA), weighing 250 to 350 g, were placed in individual metabolic balance cages and allowed free access to tap water and normal rat chow for not less than 1 week. On the experimental day, the rats were anesthetized with sodium pentobarbital, 50 mg/kg i.p., and placed on a heated micro-puncture table thermostatically regulated to maintain rectal temperature at 37°C. Catheters (PE-60) were placed in the right carotid artery, jugular vein, and the rectal temperature at 37 °C. Catheters (PE-60) were placed in the right carotid artery, jugular vein, and the left ureter for systemic mean arterial pressure (MAP) measurement, blood sampling, fluid administration, and urine collection. The technique of Fink and Brody,\(^\text{31}\) was used to establish a free-flowing extracorporeal circuit between the left carotid artery and an abdominal aortic segment whose only outlet was the left renal artery. The RBF was measured in the circuit, and drugs were administered directly into the renal arterial blood supply through an injection port in the circuit.

Arterial pressures were measured with electronic pressure transducers (Statham P23Db, Otxnard, CA, USA) coupled, as was the electromagnetic flow meter, to a Beckman R611 recorder (Sensor, Anaheim, CA, USA). The left renal nerve bundle was isolated near the aorta, cut centrally, and placed over insulated stainless steel bipolar hook electrodes for nerve stimulation. Bipolar square waves of 0.5-msec duration and supramaximal voltage (10–20 V) were delivered using a Grass S9 stimulator (Quincy, MA, USA). All drugs were dissolved in isotonic saline and either injected (10 \(\mu\)l) or infused (10 \(\mu\)l/min) into the kidney; drug doses refer to the free base.

### Renal Vascular Responses

At the completion of surgery, an intravenous infusion of isotonic saline was initiated at 50 \(\mu\)l/min and maintained for the duration of the experiment. After a 30-minute equilibration period and a 20-minute baseline recording period, renal vascular responses to RNS, norepinephrine, phenylephrine, clonidine, and guanabenz were determined. The RNS (1, 2, 4, and 6 Hz) was performed for 15 seconds, and maximum changes in RBF were determined; norepinephrine (10, 20, 40, and 80 ng), phenylephrine (10, 20, 40, and 80 ng), clonidine (100, 200, 400, 800, 1600, and 3200 ng) and guanabenz (500, 1000, and 5000 ng) were used. The RNS and agonist injections were administered before and after 50 minutes (last 20 minutes served as baseline recording period) after the initiation of a continuous renal arterial infusion of normal saline at 10 \(\mu\)l/min containing prazosin (\(n = 8\)) or rauwolscine (\(n = 8\)) in sufficient quantities to deliver 6.66 ng/min or 10 ng/min, respectively.

### Renal Tubular Responses

At the completion of surgery, an intravenous infusion of isotonic saline containing inulin was initiated at 50 \(\mu\)l/min and maintained for the duration of the experiment. After a 30-minute equilibration period, consecutive 10-minute urine collections were taken continuously. The first two urine collections constituted the control period. Then, RNS was begun at a frequency just beneath that previously determined to cause a perceptible decrease in RBF. Two urine collections constituted the RNS period. The RNS was then stopped, and two subsequent urine collections constituted the recovery period. Then, renal arterial infusion of either prazosin (\(n = 6\) per strain) or rauwolscine (\(n = 6\) per strain), as described in the previous section, was begun and continued for the duration of the experiment. Twenty minutes later, the sequence of control, RNS (same frequency), and recovery periods was repeated. Arterial blood samples (50 \(\mu\)l) bracketed each two urine collections. Urine was collected in preweighed, mineral oil–containing vials.

Urine (\(U_\text{Na}\) and plasma (\(P_\text{Na}\)) inulin concentrations were measured by an anthrone method.\(^\text{19}\) Urine and plasma sodium concentrations were measured by flame photometry. The GFR was taken as the clearance of inulin equal to \(U_\text{Na}/P_\text{Na} \times V\), where \(V\) denotes urine flow rate, determined gravimetrically. Renal vascular resistance (RVR) = RAP/RBF (mm Hg/ml/min).

For renal vascular responses, a semilog plot of fraction of control RBF against either RNS frequency (Hz) or agonist dose (ng) was linear in each rat. The slope (\(k\)), fractional decrease in RBF per hertz or nanogram, was determined for each rat's response to RNS and each agonist before and after either prazosin or.
Results

Renal Vascular Responses

Baseline (i.e., before RNS or agonist injections) values of RAP, RBF, and RVR for WKY and SHR are shown in Table 1; of the 16 rats in each strain used for control measurements, eight went on to receive prazosin and eight went on to receive rauwolscine. During the control period (i.e., before prazosin or rauwolscine administration), RAP and RVR were significantly higher (p < 0.01) in SHR than in WKY while RBF was similar. Following renal arterial administration of either prazosin or rauwolscine, there were slight increases in RBF and slight decreases in RVR that were not significant in either WKY or SHR; RAP was not affected.

Figure 1 shows the RBF responses as values of k to graded frequencies of RNS before and after administration of either prazosin or rauwolscine. Before the administration of the adrenergic receptor antagonists, renal vasoconstrictor responses to RNS were similar in WKY and SHR. While rauwolscine had no effect, prazosin produced a similar degree of inhibition (p<0.01) of renal vasoconstriction in WKY and SHR.

Figure 4 shows the RBF responses as values of k to graded doses of phenylephrine before and after administration of either prazosin or rauwolscine. Before the administration of the adrenergic receptor antagonists, renal vasoconstrictor responses to phenylephrine were similar in WKY and SHR. While rauwolscine had no effect, prazosin produced a similar degree of inhibition (p<0.01) of renal vasoconstriction in WKY and SHR.

Figure 5 shows the RBF responses as values of k to graded doses of clonidine before and after administration of either prazosin or rauwolscine. Before the administration of the adrenergic receptor antagonists, renal vasoconstrictor responses to clonidine were similar in WKY and SHR. Prazosin inhibited the renal vasoconstrictor responses to clonidine in WKY by 32% (p<0.05) and in SHR by 35% (p<0.05), whereas rauwolscine inhibited the responses by 73% (p<0.01) in WKY and 78% (p<0.01) in SHR.

Figure 6 shows the RBF responses as values of k to graded doses of guanabenz before and after administration of either prazosin or rauwolscine. Before the administration of the adrenergic receptor antagonists, renal vasoconstrictor responses to guanabenz were similar in WKY and SHR. While rauwolscine had no effect, prazosin produced a similar degree of inhibition (p<0.01) of renal vasoconstriction in WKY and SHR.

Figure 7 shows the RBF responses as values of k to graded doses of clonidine before and after administration of either prazosin or rauwolscine. Before the administration of the adrenergic receptor antagonists, renal vasoconstrictor responses to clonidine were similar in WKY and SHR. Prazosin inhibited the renal vasoconstrictor responses to clonidine in WKY by 32% (p<0.05) and in SHR by 35% (p<0.05), whereas rauwolscine inhibited the responses by 73% (p<0.01) in WKY and 78% (p<0.01) in SHR.

Figure 8 shows the RBF responses as values of k to graded doses of guanabenz before and after administration of either prazosin or rauwolscine. Before the administration of the adrenergic receptor antagonists, renal vasoconstrictor responses to guanabenz were similar in WKY and SHR. While rauwolscine had no effect, prazosin produced a similar degree of inhibition (p<0.01) of renal vasoconstriction in WKY and SHR.
Fractional reduction in renal blood flow per nanogram (k) for norepinephrine (NE), phenylephrine (PE), clonidine (CLON), and guanabenz (GUAN) in WKY and SHR.

**Figure 2.**

Fractional reduction in renal blood flow per nanogram (k) for phenylephrine (PE) in WKY and SHR in the absence (−) and presence (+) of prazosin and rauwolscine.

**Figure 4.**

Fractional reduction in renal blood flow per nanogram (k) for norepinephrine (NE), phenylephrine (PE), clonidine (CLON), and guanabenz (GUAN) in WKY and SHR.

**Figure 3.**

Fractional reduction in renal blood flow per nanogram (k) for clonidine (CLON) in WKY and SHR in the absence (−) and presence (+) of prazosin and rauwolscine.

**Figure 5.**

Fractional reduction in renal blood flow per nanogram (k) for clonidine (CLON) in WKY and SHR in the absence (−) and presence (+) of prazosin and rauwolscine.

Before the administration of the adrenergic receptor antagonists, renal vasoconstrictor responses to guanabenz were similar in WKY and SHR. Prazosin inhibited the renal...
Renal Tubular Responses

Tables 2, 3, and 4 show the data for RAP, GFR, RBF, and RVR in the low frequency RNS experiments in SD, WKY, and SHR, respectively. The RAP (p < 0.01) and RVR (p < 0.01) were higher in SHR than in WKY and SD. The GFR and RBF were higher (p < 0.05) in SD than in WKY and SHR. The renal arterial administration of prazosin or rauwolscine did not affect basal values of RAP, GFR, RBF, or RVR in SD, WKY, or SHR. The frequency of RNS employed, averaging 0.4 Hz for all studies, did not significantly alter RAP, GFR, RBF, or RVR in SD, WKY, or SHR. Baseline urinary sodium excretion was similar in SD, WKY, and SHR, averaging 2.82 ± 0.22 μEq/min. In the control phase, low frequency RNS produced a 40 to 50% reversible decrease (p < 0.01) in urinary sodium excretion in SD, WKY, and SHR (Figure 7). Rauwolscine administration had no effect on either the basal levels of urinary sodium excretion or the antinatriuretic response to low frequency RNS in SD, WKY, or SHR. However, prazosin, while not affecting basal levels of urinary sodium excretion, essentially abolished (p < 0.01) the antinatriuretic response to low frequency RNS in SD, WKY, and SHR. Changes in urinary flow rate paralleled those in urinary sodium excretion.

Discussion

These studies demonstrate that, although renal α₂-adrenergic receptor number is greater in SHR than in WKY, the renal vascular and tubular responses to RNS and adrenergic receptor agonists are not mediated to any significant extent by renal vascular or tubular α₂-adrenergic receptors in either SHR or WKY. These findings are in agreement with in vivo studies in the isolated perfused rat kidney by Schmitz et al. (Sprague-Dawley) and Imbs et al. (Wistar). In both studies, the renal vasoconstrictor responses to α-adrenergic receptor agonists were measured. Both studies concluded that the postsynaptic α-adrenergic receptors that cause vasoconstriction are exclusively α₂-adrenergic receptors. In addition, recent in vivo studies of renal vasoconstrictor responses in Wistar rats have shown that, while norepinephrine and the α₂-adrenergic receptor agonists cirazoline and phenylephrine acted as full agonists, the α₂-adrenergic receptor agonist guanabenz, BHT 920, and UK 14304, were neither potent nor efficacious. For example, the dose eliciting a 20% decrease in RBF was 0.323 ng/kg for phenylephrine, whereas it was 500-fold greater, 165 ng/kg, for UK 14304. Therefore, both in vitro and in vivo studies indicate that the renal vasoconstrictor response to α-adrenergic receptor agonists in normotensive strains of rats is solely dependent on renal vascular α₂-adrenergic receptors.

Our studies using α-adrenergic receptor agonists and antagonists in an in vivo evaluation of renal vasoconstrictor responses in WKY and SHR are in agreement. Norepinephrine and phenylephrine were full agonists, whereas clonidine and guanabenz were neither potent nor efficacious. In addition, the renal vasoconstrictor responses to norepinephrine and phenylephrine were markedly inhibited by the α₂-adrenergic receptor antagonist prazosin and unaffected by the α₂-adrenergic receptor antagonist rauwolscine. The small renal vasoconstrictor responses to clonidine and guanabenz were reduced by rauwolscine; prazosin attenuated the clonidine response but did not affect the guanabenz response, reflecting the relative α₂-adrenergic versus α₁-adrenergic selectivity of clonidine (some α₁ with α₂) and guanabenz (less α₁ with α₂).

In the context of considering the contribution of renal mechanisms governed by sympathetic neurohumoral stimuli to hypertension, the influence of the renal sympathetic nerves clearly predominates over that of circulating plasma catecholamines. This is of
TABLE 2. Renal Hemodynamics in Low Frequency Renal Nerve Stimulation Experiments in Sprague-Dawley Rats

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n = 6)</th>
<th>Prazosin (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C</td>
<td>E</td>
</tr>
<tr>
<td>RAP (mm Hg)</td>
<td>95 ± 3</td>
<td>94 ± 3</td>
</tr>
<tr>
<td>GFR (ml/min)</td>
<td>0.81 ± 0.03</td>
<td>0.82 ± 0.04</td>
</tr>
<tr>
<td>RBF (ml/min)</td>
<td>5.7 ± 0.2</td>
<td>5.6 ± 0.2</td>
</tr>
<tr>
<td>RVR (mm Hg/ml/min)</td>
<td>17.3 ± 0.8</td>
<td>17.0 ± 0.8</td>
</tr>
</tbody>
</table>

Values are means ± SE. C = control period; E = experiment; R = recovery; RAP = renal arterial pressure; GFR = glomerular filtration rate; RBF = renal blood flow; RVR = renal vascular resistance.

TABLE 3. Renal Hemodynamics in Low Frequency Renal Nerve Stimulation Experiments in WKY

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n = 6)</th>
<th>Prazosin (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C</td>
<td>E</td>
</tr>
<tr>
<td>RAP (mm Hg)</td>
<td>108 ± 4</td>
<td>109 ± 3</td>
</tr>
<tr>
<td>GFR (ml/min)</td>
<td>0.73 ± 0.07</td>
<td>0.72 ± 0.08</td>
</tr>
<tr>
<td>RBF (ml/min)</td>
<td>4.5 ± 0.7</td>
<td>4.4 ± 0.7</td>
</tr>
<tr>
<td>RVR (mm Hg/ml/min)</td>
<td>23.9 ± 1.0</td>
<td>24.6 ± 1.0</td>
</tr>
</tbody>
</table>

Values are means ± SE. See Table 2 for key to abbreviations.

TABLE 4. Renal Hemodynamics in Low Frequency Renal Nerve Stimulation Experiments in SHR

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n = 6)</th>
<th>Prazosin (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C</td>
<td>E</td>
</tr>
<tr>
<td>RAP (mm Hg)</td>
<td>165 ± 5</td>
<td>164 ± 4</td>
</tr>
<tr>
<td>GFR (ml/min)</td>
<td>0.74 ± 0.03</td>
<td>0.74 ± 0.03</td>
</tr>
<tr>
<td>RBF (ml/min)</td>
<td>4.7 ± 0.1</td>
<td>4.7 ± 0.1</td>
</tr>
<tr>
<td>RVR (mm Hg/ml/min)</td>
<td>35.2 ± 1.9</td>
<td>34.9 ± 1.9</td>
</tr>
</tbody>
</table>

Values are means ± SE. See Table 2 for key to abbreviations.

FIGURE 7. Effect of low frequency renal nerve stimulation on urinary sodium excretion (UNaV) in SD, WKY, and SHR during control (open bars) and administration of either prazosin or rauwolscine (solid bars). Numbers in parentheses indicate number of rats.

special relevance to SHR, in which basal efferent renal sympathetic nerve activity is increased17 and renal de- nervation delays hypertension development through an effect on renal sodium handling.19 Therefore, we also evaluated the renal vascular α-adrenergic receptor med- iation of the renal vasoconstrictor responses to RNS.
The renal vasoconstrictor responses to RNS were similar in WKY and SHR; furthermore, in both WKY and SHR, they were similarly inhibited by prazosin and unaffected by rauwolscine.

Thus, the renal vasoconstrictor responses to both RNS and adrenergic receptor agonists are similar in WKY and SHR. In addition, they are entirely dependent on renal vascular \( \alpha_{1} \)-adrenergic receptors with no evidence of major involvement of \( \alpha_{2} \)-adrenergic receptors. The \( \alpha_{1} \)-adrenergic receptor is the predominant \( \alpha_{1} \)-adrenergic receptor subtype mediating renal vasoconstriction in cats\(^1\) and dogs\(^6,7\) whereas in the rabbit renal vasculature,\(^6\) renal vascular \( \alpha_{1} \)-adrenergic receptors appear to play a greater role in the renal vasoconstrictor response to both \( \alpha_{1} \)-adrenergic receptor agonists and RNS.

Although prior in vivo studies in both dogs\(^6\) and rabbits\(^9\) had demonstrated that the renal tubular adrenergic receptor mediating the antinatriuretic response to low frequency RNS was exclusively of the \( \alpha_{1} \) subtype, similar in vivo studies are not available for the rat. Recent in vitro studies\(^10,11\) using an isolated perfused rat kidney preparation (RVR = 4–5 mm Hg/ml/min vs in vivo normal range of 15–20 mm Hg/ml/min) have shown that the antinatriuretic response to low frequency RNS (no change in GFR or perfusate flow rate) is abolished by renal \( \alpha_{1} \)-adrenergic receptor blockade with prazosin and unaffected by renal \( \alpha_{2} \)-adrenergic receptor blockade with yohimbine. Additional in vitro studies have suggested a possible modulatory effect of \( \alpha_{2} \)-adrenergic receptor agonists on the urinary sodium excretion response to agents that operate through adenylyl cyclase stimulation.\(^13,14\) Therefore, using an in vivo preparation, we examined the effect of prazosin and rauwolscine on the antinatriuretic response to low frequency RNS, which does not affect RBF, RVR, or GFR and, therefore, increases renal tubular sodium reabsorption by a direct action on the renal tubule. In SD, WKY, and SHR, prazosin essentially abolished the antinatriuretic response to low frequency RNS whereas rauwolscine had no effect. Evidence that the doses of prazosin and rauwolscine produced selective blockade of renal \( \alpha_{1} \)-adrenergic and \( \alpha_{2} \)-adrenergic receptors, respectively, is shown in Figures 4 and 6. Therefore, the ability of low frequency RNS to directly increase rat renal tubular sodium reabsorption in SD, WKY, and SHR is mediated exclusively by renal tubular \( \alpha_{1} \)-adrenergic receptors; \( \alpha_{2} \)-adrenergic receptors...
are not involved. These results are in agreement with findings from similar in vivo studies in the dog and rabbit as well as in vitro studies in the rat.

Thus, while \(\alpha_2\)-adrenergic receptors numerically predominate over \(\alpha_1\)-adrenergic receptors in the kidneys of SHR and normotensive SD and WKY and \(\alpha_2\)-adrenergic receptor number is selectively further increased in the kidneys of SHR, there is no convincing evidence that \(\alpha_2\)-adrenergic receptors mediate the renal vascular or tubular responses to \(\alpha_1\)-adrenergic receptor agonists or RNS in these rat strains. Rather, these responses are mediated exclusively by renal vascular and tubular \(\alpha_1\)-adrenergic receptors. However, based on in vitro studies, it would appear that renal tubular \(\alpha_1\)-adrenergic receptors, through their inhibitory effect on adenylate cyclase, may be involved in modulating the overall urinary sodium excretion response to other agents (hormonal, pharmacological) that influence renal tubular sodium reabsorption through stimulation of adenylate cyclase.

References

4. Horn PT, Kohl JD, Listinsky JJ, Goldberg LI. Regional variations in the alpha adrenergic receptors in the canine resistance vessel. Naunyn Schmiedebergs Arch Pharmacol 1982;318:166–172
Role of renal alpha 2-adrenergic receptors in spontaneously hypertensive rats.
G F DiBona and L L Sawin

*Hypertension*. 1987;9:41-48
doi: 10.1161/01.HYP.9.1.41

*Hypertension* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1987 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/9/1/41