Cardiac and Vascular Effects of Atrial Natriuretic Factor and Sodium Nitroprusside in Healthy Men

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To assess the contribution of venous effects to the hemodynamic changes caused by atrial natriuretic factor (ANF), the cardiac and peripheral effects of ANF were compared with those induced by the venaarterial vasodilator sodium nitroprusside. On 3 different days, eight healthy subjects received 2-hour infusions of either ANF, sodium nitroprusside, or placebo, by a single-blind crossover design. ANF was administered at a rate of 15 ng/kg/min for hour 1 and 50 ng/kg/min for hour 2; each infusion rate was preceded by a 50-μg bolus. The lower ANF infusion rate increased plasma cGMP fourfold, but only modest cardiovascular effects (small decreases in left ventricular end-diastolic and end-systolic volumes) were noted. At the higher ANF infusion rate, left ventricular volumes and intravascular volume, as indirectly assessed by changes in hematocrit levels, decreased further, which resulted in decreases in stroke volume, cardiac index, and systolic blood pressure. No evidence for arterial vasodilation (no decrease in diastolic blood pressure, total peripheral resistance, or forearm resistance) was obtained, and no increase in sympathetic activity was noted. In contrast, sodium nitroprusside caused arterial vasodilation, an increase in cardiac index, and significant increases in sympathetic activity. We conclude that short-term increases in plasma ANF within the physiologic range primarily affect the venous vascular bed (by decreasing intravascular volume or by venodilation) without increasing sympathetic activity. (Circulation 1989;79:383–392)

Atrial natriuretic factor (ANF) is released from mammalian cardiac atria and has potent diuretic and hypotensive actions. Initially, it was assumed that ANF acted as an arterial vasodilator and the blood pressure lowering effect was primarily due to a decrease in total peripheral resistance (TPR). Recent evidence points to a more multifactorial nature of the hypotensive action of ANF. In animals, several studies have demonstrated a relation between the decrease of blood pressure and a decrease in cardiac output after ANF. This reduction in cardiac output may be due to increased vagal activity,3,4 decreased cardiac sympatoadrenal activity,5 or a decrease in the pressure for venous return6 due to venodilation or a reduction in intravascular volume secondary to diuresis or redistribution.7–9 A negative inotropic effect of ANF does not appear to be involved.10,11

Only limited hemodynamic studies have been performed in humans. ANF has lowered TPR and pulmonary wedge and right atrial pressures, which suggests venous and arterial vasodilation in patients with congestive heart failure.12–14 Hemodynamic studies in normotensive subjects are also limited. Cody et al13 reported small decreases in pulmonary wedge and systolic blood pressures in seated subjects but no changes in cardiac output and TPR. In patients without heart failure, however, Saito et al12 observed decreases in pulmonary wedge, right atrial, and mean arterial pressures and TPR and a moderate increase in cardiac output. Thus, ANF may induce venous and arterial vasodilation in normal
humans. However, Saito et al.\textsuperscript{12} used somewhat higher infusion rates (0.1 \( \mu \)g/kg/min), which may be closer to pharmacologic concentrations with possibly different effects than those observed at lower, more physiologic concentrations.\textsuperscript{13} In the present study, we assessed the central and peripheral hemodynamic effects of ANF in healthy subjects at two different rates of infusion producing low-to-moderate increases in plasma ANF concentrations\textsuperscript{7} and small-to-moderate changes in blood pressure.\textsuperscript{7,15} Because ANF may act as a venoarterial vasodilator, the hemodynamic effects of ANF were compared with those of sodium nitroprusside, a venoarterial vasodilator that does not produce negative inotropic or sympatholytic effects,\textsuperscript{16,17} by a randomized, placebo-controlled crossover design and noninvasive methodology.

Methods

Subjects

Eight healthy male volunteers (age, 24±3 years; height, 179±5 cm; weight, 68.7±4.4 kg; mean±SEM) participated in the study. All gave informed, written consent. The study was approved by the Human Ethics Committee of the University of Toronto, Toronto, Canada. The subjects were judged to be healthy from studies of history, electrocardiogram, blood biochemistry, hematology, and physical examination; in addition, urinary drug-screens were negative.

Study Protocol

The study was performed as a single-blind, randomized, multiple crossover trial. Each subject was studied on three different mornings, at least 1 week apart, for infusions of ANF, sodium nitroprusside, or placebo. Subjects were instructed to maintain their usual diet throughout the study and to avoid alcohol, caffeine-containing beverages, and tobacco in the 12 hours preceding each study day. A 24-hour urine collection was done on the previous day, showing 24-hour urinary sodium excretion in the range of 100–200 mmol/24 hr and was similar for the 3 study days. On the morning of a study, subjects received a standard liquid breakfast. An indwelling catheter was inserted in a forearm vein in each arm, one for infusion and the other for blood sampling; a blood pressure cuff, electrocardiograph electrodes, occlusion cuffs, and a mercury-in-silicone rubber strain gauge for plethysmography were applied. Subsequently, subjects rested in a semisupine position for 30 minutes in a semidark, quiet study room, after which baseline hemodynamic measurements (blood pressure, heart rate, echocardiogram, and plethysmography) were obtained followed by blood and urine sampling. Blood pressure and heart rate were measured every 2 minutes for 10 minutes; the mean of these five values was used as baseline for statistical analysis. Subsequently, the infusion was started and lasted for 2 hours. Human ANF (Ser99-Tyr126) was purchased from the Protein Research Foundation (Osaka, Japan) and prepared for intravenous administration at the Armand-Frappier Institute (Laval, Canada) as previously described.\textsuperscript{15} It was diluted in 0.9% NaCl and infused at 15 ng/kg/min for hour 1 and at 50 ng/kg/min for hour 2; each rate of infusion was preceded by a bolus of 50 \( \mu \)g.

Sodium nitroprusside was diluted in 0.9% NaCl immediately before the infusion and was protected from light. In a previous run-in study, increasing doses of sodium nitroprusside were given until heart rate increased by 10 beats/min or blood pressure decreased by 10 mm Hg or both. This particular infusion rate was then used in the study (2.9±0.6 \( \mu \)g/kg/min; range, 0.9–6.4). The infusion rate for placebo (0.9% NaCl) was at the same volume as the rate for sodium nitroprusside. Constant infusion rates were maintained with a Compact Infusion Pump (Model 975, Harvard Apparatus, South Natick, Massachusetts).

Echocardiograms were obtained at 0, 15, 30, 60, 90, and 120 minutes, blood samples at 0, 15, 30, 60, and 120 minutes, and plethysmography at 0, 30, and 90 minutes. Blood pressure was measured automatically on the left arm with an Arteriosonde 1225 (Roche, Medical Electronics, Cranbury, New Jersey) every 15 minutes throughout the study, and the mean of three measurements was used for statistical analysis. Heart rate was constantly monitored from the electrocardiogram by a 414 Monitor (Tektronix, Beaverton, Oregon). At the end of the infusion, a second urine sample was collected.

Plethysmography. A mercury-in-silicone rubber strain gauge was placed on the upper third of the right forearm, which was supported in a comfortable position at a level higher than the heart. Occlusion was achieved by a blood pressure cuff applied proximal to the elbow and inflated to 50 mm Hg by a rapid cuff inflator (Fairchild Hiller, Winston-Salem, North Carolina). The hand was excluded from the circulation by inflation of a blood pressure cuff at wrist level to 200 mm Hg 1 minute before the measurements. Forearm blood flow (ml/min/100 ml) was measured as previously described.\textsuperscript{18} Forearm arterial resistance was calculated in arbitrary units by dividing mean blood pressure by forearm blood flow. Total forearm blood flow (ml/min) was determined from forearm blood flow\texttimes(forarm volume/100). The forearm volume was measured by water displacement.

Echocardiography. Echocardiograms were obtained while the subjects were in the supine position, turned 30° on their left side, with a Sonolayer SSH-60A (Toshiba, Osaka, Japan) with a 3.75-MHz transducer in conjunction with a Line Scan Recorder LSR-20B (Toshiba). M-mode echocardiograms were obtained under two-dimensional guidance, and the following variables were calculated or measured: left ventricular end-diastolic and left ventricular end-systolic dimension and volume; stroke volume and cardiac index; percent fractional shortening; ejection fraction; and left ventricular end-systolic wall stress.\textsuperscript{19} TPR was calculated from mean blood pressure/cardiac index,
and pressure-volume ratio was calculated from systolic blood pressure/left ventricular end-systolic volume. Measurements were made by the same observer and were obtained according to the guidelines of the American Society of Echocardiography.

**Analytical Methods**

Blood samples were centrifuged at 4°C. Plasma catecholamines were determined by radioenzymatic assay, and plasma renin activity was determined by radioimmunoassay. Plasma immunoreactive ANF levels were determined after Sep-Pak cartridge extraction and radioimmunoassay. However, plasma ANF samples were exposed to too high temperatures during transportation to Montreal, and their assay produced unreliable results. Plasma and urinary cGMP were determined by radioimmunoassay after extraction and purification on Dowex-Alumina columns for plasma. Serum aldosterone levels were measured by a modification of the method of Underwood and Williams. Hematocrit (Hct) was measured in capillary tubes after centrifugation; the relative intravascular volume change (ΔHct) was calculated with the formula [(Hct−baseline Hct)/baseline Hct], assuming no change of red blood cell volume and shape during the 2-hour infusion of nonosmotically active drugs.

**Statistical Analysis**

Data were analyzed by ANOVA within study days to assess the effects of each drug and between study days to compare the effects of ANF with sodium nitroprusside and with placebo. For ANF infusion, an additional comparison was made between the two different doses. This was performed with the SAS program (Statistical Analysis Systems, SAS Institute, Cary, North Carolina). The statistical analysis of blood pressure, heart rate, echocardiography, and plethysmographic data was done on absolute changes from baseline. The catecholamine and plasma renin activity values were logarithmically transformed to meet homogeneity of variance requirements. All data are mean ± SEM. A \( p \) value less than 0.05 was considered significant.

**Results**

**Blood Pressure**

During placebo infusion, systolic blood pressure and diastolic blood pressure showed minor, nonsignificant changes (Figure 1). Infusion of sodium nitroprusside caused small (about 5 mm Hg) decreases in systolic and diastolic blood pressures. These decreases were significant \( (p<0.001) \) compared with baseline and placebo values.

At the lower rate of ANF infusion, systolic blood pressure did not change, whereas diastolic blood pressure increased \( (p<0.002) \) compared with baseline and placebo values. At the higher rate of ANF infusion, systolic blood pressure decreased significantly \( (p<0.001) \), similar to the effect of sodium nitroprusside. Diastolic blood pressure remained slightly increased compared with baseline \( (p<0.004) \) but not compared with placebo values.

**Cardiac Function**

During placebo infusion, no significant changes in the echocardiographic measurements were observed.
Sodium nitroprusside infusion decreased left ventricular end-diastolic volume (by 15–20 ml) and left ventricular end-systolic volume (by 10–15 ml) (Figure 2). As a consequence, stroke volume decreased only slightly (NS) (Table 1). However, because heart rate (Figure 1) increased by 15–20 beats/min ($p<0.001$), cardiac index increased from baseline by about 0.5 l/min/m$^2$ ($p<0.001$). Indexes of left ventricular performance such as ejection fraction and fractional shortening also showed significant increases during sodium nitroprusside infusion as did the pressure-volume ratio ($p<0.001$), an index of myocardial contractility. End-systolic stress, an index of afterload, decreased within 15 minutes and remained decreased throughout the sodium nitroprusside infusion.

During the lower rate of ANF infusion, left ventricular end-diastolic and end-systolic volumes decreased to a small extent; only the decrease in left ventricular end-systolic volume was significant ($p<0.002$). Stroke volume, heart rate, cardiac index, and indexes of left ventricular performance showed minor, nonsignificant changes. Left ventricular end-systolic stress decreased significantly compared with placebo values ($p<0.004$) but to a lesser extent than during sodium nitroprusside infusion ($p<0.001$).

At the higher infusion rate of ANF, left ventricular end-diastolic and end-systolic volume decreased significantly. Stroke volume also decreased significantly compared with both baseline and placebo values ($p<0.01$). Heart rate increased compared with baseline values only ($p<0.002$). Cardiac index decreased significantly compared with baseline ($p<0.001$) but was not significant compared with placebo values. Indexes of left ventricular performance showed small increases ($p<0.01$) but less than the increases caused by sodium nitroprusside. Left ventricular end-systolic stress decreased significantly ($p<0.001$) from baseline and from placebo and similarly to the decrease on sodium nitroprusside.

**Peripheral Circulation**

During placebo, TPR and forearm resistance showed minor changes (Figure 3). Sodium nitroprusside caused persistent decreases in TPR, which was significant compared with baseline and placebo values ($p<0.001$). In contrast, both rates of ANF infusion caused small increases in TPR, similar to those occurring during placebo infusion. In accordance with the observed effects on TPR, sodium nitroprusside decreased forearm resistance ($p<0.002$), whereas ANF did not change forearm resistance significantly.

**Hormonal and Hematocrit Level Responses**

Infusion of placebo did not cause significant changes in any of the blood variables measured. Plasma epinephrine did not change during any of the infusions (data not shown). Sodium nitroprusside infusion increased plasma norepinephrine significantly from baseline and placebo ($p<0.001$) (Figure 4). Sodium nitroprusside infusion did not alter the hematocrit level (Table 2). During infusion of ANF, plasma norepinephrine did not change significantly. Hematocrit level increased signifi-
Table 1. Cardiac Effects of Atrial Natriuretic Factor, Sodium Nitroprusside, or Placebo

<table>
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<th>Baseline</th>
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Data are mean±SEM and absolute changes from baseline.

Atrial natriuretic factor was infused at 15 ng/kg/min for hour 1 and at 50 ng/kg/min for hour 2; each infusion was preceded by a 50 µg bolus.

ANF, atrial natriuretic factor; SNP, sodium nitroprusside; PLA, placebo.

*p<0.05 vs. PLA; †p<0.05 vs. SNP; ‡p<0.05 vs. lower infusion rate. Significance indicates overall treatment effect.

Significantly compared with placebo values (p<0.01), the increase becoming more marked (p<0.05) at 120 minutes (+11±1%) than at 60 minutes (+5±1%).

During sodium nitroprusside infusion, plasma renin activity increased significantly compared with placebo values (p<0.001) as did plasma aldosterone concentrations (p<0.02). During ANF infusion, plasma renin activity (p<0.05) and plasma aldosterone (p<0.006) decreased significantly compared with placebo values.

**Plasma and Urinary Cyclic GMP**

At the lower rate of ANF infusion, plasma cGMP increased fourfold, and an additional similar increase occurred after infusion of the higher rate (p<0.001) (Figure 4). A marked increase was also noted for the 2-hour excretion of urinary cGMP (p<0.004) (Table 3). In contrast, plasma cGMP did not change during the infusion of sodium nitroprusside or placebo. Urinary excretion of cGMP also was not influenced by placebo, whereas sodium nitroprusside caused a small, nonsignificant rise.

**Urine Volume and Sodium**

Urine volume during the 2-hour ANF infusion was higher than during sodium nitroprusside or placebo, but the difference was not statistically significant (Table 3). Urinary sodium excretion was similar for the three different infusions.

**Adverse Effects of Atrial Natriuretic Factor and Sodium Nitroprusside**

No clinically significant complications were observed during and after the infusion of sodium nitroprusside or ANF. One subject complained of nausea and sweating during the final 30 minutes of the ANF infusion, and these symptoms subsided without any special intervention 15 minutes after the infusion. Side effects were observed during sodium nitroprusside infusion in five subjects; one had nausea and vomiting during the run-in study, which did not recur during the rest of the study, and four subjects had slight-to-moderate nasal stuffiness.

**Discussion**

The central and peripheral hemodynamic effects induced by moderate doses of ANF were compared with those induced by the venoarterial vasodilator sodium nitroprusside and by placebo. At the lower rate of infusion (15 ng/kg/min), ANF increased plasma cGMP fourfold, but it caused only modest hemodynamic effects. Small decreases in left ventricular end-diastolic and end-systolic volumes were noted, which were associated with a small rise in the hematocrit level and diastolic blood pressure. At the higher rate of infusion (50 ng/kg/min), more marked hemodynamic effects occurred. Left ventricular end-diastolic and end-systolic volumes
decreased further, resulting in decreases in stroke volume, cardiac index, and systolic blood pressure. However, diastolic blood pressure, TPR, and forearm resistance did not decrease. Heart rate, pressure-volume ratio, and plasma norepinephrine (reflecting increased sympathetic or decreased parasympathetic activity or both) tended to increase but only to a minor extent. The effects of sodium nitroprusside were distinctly different from those of ANF; in particular, sodium nitroprusside did cause arterial vasodilation (i.e., decreases in diastolic blood pressure, TPR, and forearm resistance). Similar to ANF, sodium nitroprusside decreased left ventricular end-diastolic volume, but this effect was associated with improved left ventricular emptying and an increase in heart rate resulting in a significant increase in cardiac output (compared with a decrease in cardiac output by ANF). Moreover, heart rate, pressure-volume ratio, and plasma norepinephrine clearly showed significant increases after sodium nitroprusside infusion.

This hemodynamic profile of ANF suggests that at the plasma concentrations achieved, the primary effect of ANF was a decrease in venous pressure. This conclusion is based on the significant decrease in left ventricular end-diastolic volume, stroke volume, cardiac index, and systolic blood pressure. The small increase in heart rate can explain only a minor part of the decrease in left ventricular end-diastolic volume. The decrease in left ventricular end-systolic volume is likely secondary to the decreases in left ventricular end-diastolic volume and afterload (somewhat improving left ventricular emptying) and, possibly, to a small positive inotropic effect (small increase in pressure-volume ratio). In agreement with previous studies in animals, the decrease in cardiac output caused by ANF was not related to a negative inotropic effect of ANF. If anything, left ventricular performance was slightly increased, which was probably related to the decrease in afterload and, perhaps, to increased cardiac sympathetic activity. In agreement with our
Table 2. Hormonal and Hematocrit Level Responses During Infusion of Atrial Natriuretic Factor, Sodium Nitroprusside, or Placebo

<table>
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<th>Baseline</th>
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<td>Plasma renin activity (ng/ml/hr)</td>
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<td>Hematocrit level (%)</td>
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Data are mean±SEM. ANF, atrial natriuretic factor; SNP, sodium nitroprusside; PLA, placebo.

Table 3. Urine Variables Before and During Infusion of Atrial Natriuretic Factor, Sodium Nitroprusside, or Placebo

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<td>Urine volume (ml)</td>
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</table>

Data are mean±SEM. ANF, atrial natriuretic factor; SNP, sodium nitroprusside; PLA, placebo.

Table 2 shows that ANF decreases the peripheral venous pressure. ANF has been shown to decrease central venous pressure in rats and right atrial and pulmonary wedge pressures in normotensive subjects and patients with heart failure. Considering that atrial stretch is a potent stimulus for ANF release and that, at least under physiologic circumstances, increased atrial stretch usually is consequent to increased venous return, ANF probably decreases atrial stretch primarily by decreasing venous return. Also, at higher concentrations or more prolonged stimulation, ANF may decrease atrial stretch by other mechanisms such as unloading the heart by arteriolar vasodilation.

ANF may decrease venous pressure by several mechanisms. A reduction in intravascular volume may occur secondary to a volume shift or to diuretic effects. As reported previously, ANF significantly increased the hematocrit level; at the lower infusion rate, the increase was small, and at the higher rate, the increase was more marked. Considering that no real diuretic effect of ANF was noted in the present study, this increase in the hematocrit level probably relates to a volume shift from the intravascular to the extravascular compartment, presumably because of increased capillary hydraulic conductivity. ANF, sodium nitroprusside, and plasma renin activity (decreasing any compensatory effect of angiotensin II on efferent arterioles). It is not possible to assess whether or not the decrease in intravascular volume as noted is sufficient to explain the whole decrease in venous pressure and cardiac output. Other effects of ANF also may have participated, such as venodilation or localized arterial vasodilation, which increases blood volume in high capacitance venous beds and decreases effective circulating blood volume and the mean systemic pressure.

In the present study, no evidence for arterial vasodilation by ANF was found because TPR, forearm resistance, and diastolic blood pressure did not decrease. Other studies have shown that ANF induces arterial vasodilation in vitro in isolated vascular beds and in healthy humans, which causes decreases in diastolic blood pressure or TPR or both. These different findings may partly relate to different study designs, such as position of the subject, supine in the present study compared with sitting in a previous study, but particularly to different infusion rates. One may tentatively conclude that at lower, more physiologic concentrations, ANF primarily affects the venous circulation.
(although localized arterial vasodilation may participate), whereas at higher concentrations,\textsuperscript{7,12} more generalized arterial effects also occur.

Considering that left ventricular end-diastolic volume was decreased by ANF and that other studies\textsuperscript{6,12-14} demonstrated lowering of right-sided pressures, one may expect that deactivation of cardiopulmonary receptors occurred and resulted in increases in peripheral sympathetic activity, reflected by increases in plasma catecholamines or forearm vascular resistance.\textsuperscript{33} However, only minor, nonsignificant increases in plasma norepinephrine were noted. These small rises may, however, reflect sufficient sympathetic activation to explain the moderate increases in heart rate and myocardial contractility as assessed by the pressure-volume ratio and perhaps offset any arterial vasodilatory actions of ANF at the infusion rates used. Because central pressures were not measured in the present study, it is not possible to assess whether the minor increases in sympathetic activity reflect only minor deactivation of the cardiopulmonary receptors or that clear deactivation did occur but that the expression on peripheral sympathetic activity was counterbalanced by other effects of ANF, such as stimulation of vagal afferents,\textsuperscript{34} inhibitory effects on central neurons,\textsuperscript{35} or an inhibitory effect on the efferent sympathetic pathway.\textsuperscript{36}

As reported previously,\textsuperscript{37,38} ANF at low rates of infusion decreased plasma renin and plasma aldosterone levels. The decrease in plasma aldosterone may be due to the decrease in plasma renin and an inhibitory effect of ANF on the response of the adrenal glands to angiotensin II.\textsuperscript{39} Regarding the decrease in plasma renin, ANF apparently has no direct effect on the secretion of renin by the juxtaglomerular cells,\textsuperscript{40} and an indirect action, for example, through inhibiting renal sympathetic nerve activity\textsuperscript{34} may be involved.

Sodium nitroprusside is well established as a venoarterial vasodilator with no known direct effects on the autonomic nervous system.\textsuperscript{16} In the present study, two effects of sodium nitroprusside are obvious. Evidence for arterial vasodilation was obtained, with significant decreases in diastolic blood pressure, TPR, and forearm vascular resistance. TPR decreased by 15–25\%, but forearm vascular resistance decreased by 30–35\%, supporting previous studies showing that the effect of nitroprusside is not the same from one vascular bed to another.\textsuperscript{16,41} In addition to arterial vasodilation, sodium nitroprusside increased plasma norepinephrine associated with positive inotropic (pressure-volume ratio) and chronotropic responses; all these effects are more marked than those caused by ANF. These different autonomic effects may primarily relate to deactivation of not only low, but also high, pressure baroreceptors by sodium nitroprusside, resulting in larger increases in peripheral sympathetic activity and decreases in vagal activity than those caused by ANF. Left ventricular emptying (ejection fraction and fractional shortening) also improved, but this also relates to the significant decrease in afterload (left ventricular end-systolic stress) caused by sodium nitroprusside. Despite these stimulatory effects on the heart, cardiac output showed only a small increase of about 1 l/min after 1–2 hours of infusion. In contrast, the classic arterial vasodilator hydralazine causes similar increases in heart rate and plasma norepinephrine but a marked increase in cardiac output of 4 l/min.\textsuperscript{42} A comparison of changes in diastolic filling shows a small increase with hydralazine but a decrease in left ventricular end-diastolic volume with sodium nitroprusside, resulting in the absence of an increase in stroke volume after sodium nitroprusside and thus explaining the smaller increase in cardiac output. The present study does not provide direct evidence for venous effects of sodium nitroprusside, but from the comparison with hydralazine, it appears reasonable to conclude that venous effects of sodium nitroprusside, well established in studies in dogs,\textsuperscript{43,44} prevented the large increases in cardiac output that occur after administration of an arterial vasodilator.

The presence of cGMP in extracellular fluids is secondary to the egression of this nucleotide into the extracellular compartment. Both ANF and sodium nitroprusside appear to induce vasodilation by their potential to increase intracellular cGMP.\textsuperscript{45-48} However, taken together, previous studies in vitro\textsuperscript{49} and the present results in humans suggest that increases in plasma cGMP levels may not reflect effects on vascular smooth muscle but rather represent an ANF effect on endothelial cells. Although both ANF and sodium nitroprusside increase cGMP in smooth muscle cells,\textsuperscript{49} it is possible that this cyclic nucleotide cannot pass through the layer of endothelial cells. Therefore, the observed increase in plasma cGMP probably reflects an endothelial action of ANF rather than a vascular smooth muscle action. This observation should be kept in mind when using cGMP levels in the extracellular compartment as a marker for ANF action.

In conclusion, during infusion of sodium nitroprusside, evidence of arterial vasodilation (decreases in TPR, forearm vascular resistance, and diastolic blood pressure), with compensatory sympathetic hyperactivity (increases in plasma norepinephrine, heart rate, pressure-volume ratio, and cardiac index) and indirect evidence for venodilation (decrease in left-ventricular end-diastolic volume) was obtained. In contrast, at the doses used, ANF only decreased venous pressure (decreases in left ventricular end-diastolic volume, cardiac index, and systolic blood pressure). We conclude that, consistent with the primary stimulus for ANF release (atrial stretch), ANF at (high) physiologic concentrations primarily acts on the venous bed (and, thus, atrial stretch) and that higher concentrations may be needed for generalized arterial dilation.
Acknowledgments

We thank Ms. D. Holliswell, Mrs. R. Farkas, Ms. Suzanne Cossette, and Ms. Chantal Arquin for their technical assistance and Mrs. F. Browning for secretarial assistance.

References


**KEY WORDS** • heart • venous return • venodilation • arterial vasodilation • atrial natriuretic factor • sodium nitroprusside
Cardiac and vascular effects of atrial natriuretic factor and sodium nitroprusside in healthy men.
L F Roy, R I Ogilvie, P Larochelle, P Hamet and F H Leenen

doi: 10.1161/01.CIR.79.2.383
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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