Reduced Baroreflex Sensitivity with Volume Loading in Conscious Dogs

By Stephen F. Vatner, Dedo H. Boettcher, Guy R. Heyndrickx, and Robert J. McRitchie

ABSTRACT

The Bainbridge reflex, i.e., the effect of rapid saline infusion (1.1 ± 0.1 liters) on heart rate and arterial and atrial blood pressures, was examined in 12 intact conscious dogs; mean arterial blood pressure rose by 33 ± 3 (SE) mm Hg, mean atrial pressure by 14 ± 1 mm Hg, and heart rate by 75 ± 9 beats/min. After beta-receptor blockade, heart rate rose slightly less (+49 ± 5 beats/min, P = 0.05). Cholinergic blockade, combined cholinergic and beta-receptor, or beta-receptor blockade after vagotomy blocked the heart rate response to the infusion. The rise in heart rate in the face of an increase in arterial blood pressure with volume loading suggested that the arterial baroreceptor reflex was not responding appropriately to the increase in arterial blood pressure. In conscious dogs after denervation of the arterial baroreceptors, the increase in heart rate with volume loading was no greater than that in those dogs with their arterial baroreceptors intact, suggesting that the baroreceptor reflex was not restraining heart rate in the normal response to volume loading. The relationship between the pulse interval (PI) and the systolic arterial blood pressure (SAP) following an intravenous injection of methoxamine was used to evaluate the sensitivity of the baroreceptor reflex in intact conscious dogs. After a mild amount of volume loading, when atrial pressure was 8 ± 2 mm Hg, the PI/SAP slope was significantly depressed from normal. When atrial pressure was elevated further to 28 ± 1 mm Hg by volume loading, the slope was further depressed. Thus, arterial baroreflex sensitivity is reduced progressively as atrial pressure is raised by volume loading, an observation that explains how heart rate can rise strikingly in the face of an elevated arterial blood pressure.

In 1915, Bainbridge (1) observed that a rapid infusion of saline or blood induces tachycardia, which is abolished by vagotomy; this response has been referred to as the Bainbridge reflex. The Bainbridge reflex is one of several physiological situations that does not follow Marey's law (2), which describes the inverse relationship between cardiac rate and arterial blood pressure, since volume loading results in an increase in both arterial blood pressure and cardiac rate. The infusion-induced elevation of arterial blood pressure would be expected to stimulate the arterial baroreceptors to reduce heart rate reflexly, unless a change in the gain of the reflex, the set point of the reflex, or both occurs (3). The goal of the present study was to evaluate the effects of acute volume loading on heart rate in the conscious dog and to examine the extent to which volume loading alters the properties of the arterial baroreceptor system.

Since one of the controversies concerning the Bainbridge reflex involves the questions of whether heart rate consistently rises with volume loading and to what extent the response is related to the initial heart rate prior to volume loading (4–6), the present study was conducted in conscious dogs in which resting heart rates were low and no anesthetic agent was present to affect reflex circulatory control (3, 7, 8). First, we determined the extent to which acute volume loading affects heart rate in healthy intact conscious dogs. Then, we analyzed the autonomic components of the reflex tachycardia in response to volume loading after beta-receptor blockade with propranolol and cholinergic blockade with atropine and after recovery from bilateral vagotomy. Finally, we evaluated the role of the arterial baroreceptors by examining (1) the effects of volume loading in conscious dogs after recovery from arterial baroreceptor denervation and (2) the sensitivity of the baroreflex system. Our measurement of baroreflex sensitivity involved a comparison of the effects of systolic arterial blood pressure rises induced by intravenous injections of a vasopressor agent on the subsequent pulse intervals in intact conscious dogs in the presence and the absence of volume loading (9).
BAROREFLEX SENSITIVITY WITH VOLUME LOADING

Methods

Sixteen mongrel dogs (25-35 kg) were anesthetized with sodium pentobarbital (30 mg/kg, iv), and heparin-filled Tygon catheters were placed in their aortas. In eight of these dogs catheters were advanced into the right atrium at the time of the experiment, and in the other eight dogs catheters were implanted in the left atrium at the time of the thoracotomy. Six of these dogs were studied before and 2 weeks after recovery from bilateral cervical section of the carotid sinus and aortic nerves, which was accomplished using sodium pentobarbital anesthesia and the technique of Edis and Shepherd (10, 11). The completeness of denervation was confirmed by the abolition of reflex heart rate changes in response to intravenous injections of methoxamine (50 μg/kg) and nitroglycerin (24 μg/kg) (11). Prior to denervation these doses of methoxamine and nitroglycerin produced 47 ± 5 and 97 ± 10 beats/min of bradycardia and tachycardia, respectively. Three additional dogs were studied 2-3 days after recovery from bilateral vagotomy.

While the 12 trained, unsedated dogs rested quietly, 2-3 liters of saline (38°C) was infused through two peripheral veins over a 3-15-minute period until arterial pressure exceeded 20 mm Hg; the rates of infusion varied from 0.2 to 0.5 liters/min. Infusions were terminated when the dogs either became restless or began to hyperventilate. Up to this point the trained dogs rested quietly. Since the maximum increase in right atrial pressure (+27 ± 2 mm Hg) was not significantly different from the maximum increment in left atrial pressure (+25 ± 2 mm Hg), the left and right atrial pressure values were pooled. The same volume of saline was infused into 6 of these dogs on separate days after beta-receptor blockade with propranolol (1-2 mg/kg), cholinergic blockade with atropine (0.1-0.2 mg/kg), or combined beta-receptor and cholinergic blockade. On a separate day, in 10 conscious dogs, the effects of raising arterial blood pressure by an infusion of a vasoconstrictor on the responses of atrial pressure and heart rate were examined. In these experiments, methoxamine (5-50 μg/kg min⁻¹) was infused over a time period similar to that used for the saline infusion. The goal of these experiments was to compare the responses of heart rate when arterial blood pressure was elevated equivalent amounts by a vasoconstrictor and by volume loading.

To test baroreflex sensitivity, injections of methoxamine (50 μg/kg, iv) were administered to six intact conscious dogs on three separate days in the control state at rest, after mild volume loading (saline infusion = 0.5 ± 0.1 liters), and after maximum volume loading (saline infusion = 2.6 ± 0.2 liters). In eight additional dogs, methoxamine (200 μg/kg, iv) was administered to produce a massive stimulus to the arterial baroreceptors on separate days at rest and after maximum volume loading. The results from two of these dogs had to be discarded, since arrhythmias developed following the administration of this larger dose. In six dogs, the injections of methoxamine were repeated after beta-receptor blockade and cholinergic blockade on separate days. The sensitivity of the arterial baroreceptor reflex was determined by plotting the pulse interval (PI) in msec of each beat against the peak systolic arterial blood pressure (SAP) in mm Hg of each preceding beat (9) until peak systolic arterial blood pressure began to fall.

This relationship, PI/SAP (msec/mm Hg), was treated as a linear function, the slope (regression coefficient) was taken as a measure of baroreceptor sensitivity and calculated by the method of least squares. The significance of the difference between slopes was tested by use of the analysis of variance (12).

In four dogs, nitroglycerin (150-200 μg/kg min⁻¹, iv) was infused to induce a tachycardia similar to that occurring with volume loading. During the steady state of hypotension and tachycardia, methoxamine (50 μg/kg, iv) was administered as a bolus, and the PI/SAP slopes were compared with those that occurred when methoxamine was administered in the presence of the tachycardia induced by saline infusion.

Arterial and atrial pressures were measured with Statham P23Db transducers. Electronic resistance-capacitance filters with 2-second time constants were used to derive mean arterial and atrial pressures. Lead II of the electrocardiogram was monitored to detect arrhythmias. Data were recorded on a multichannel tape recorder and played back on a direct-writing oscillograph. Averages ± SE were calculated, and groups were compared using the paired t-test (13).

Results

Heart rate and arterial blood pressure data were calculated after mean atrial pressure rose to 15 mm Hg, which will be termed moderate volume loading, and at the point just before the dogs became restless (atrial pressure = 27.5 ± 1.2 mm Hg), which will be termed maximum volume loading.

EFFECTS OF MODERATE VOLUME LOADING (ATRIAL PRESSURE = 15 mm Hg)

In normal conscious dogs, a saline infusion of 1.1 ± 0.1 liters increased mean arterial blood pressure from 94 ± 3 to 127 ± 6 mm Hg and heart rate from 73 ± 3 to 148 ± 11 beats/min (Table 1). The rise in heart rate that occurred along with the increases in arterial and atrial pressures is depicted in Figure 1. After beta-receptor blockade, moderate volume loading caused slightly less tachycardia (P = 0.05). After cholinergic or combined beta-receptor and cholinergic blockade, no tachycardia was observed. After recovery from arterial baroreceptor denervation, heart rate increased in response to moderate volume loading to 147 ± 9 beats/min, a level almost identical to that observed after volume loading in the intact dogs (Table 1). After recovery from bilateral vagotomy and propranolol administration in three dogs, heart rate remained constant at 114 ± 3 beats/min with moderate volume loading.

EFFECTS OF MAXIMUM VOLUME LOADING

In normal conscious dogs, an infusion of 2.6 ± 0.2 liters of saline increased heart rate to 178 ± 5 beats/min and mean atrial pressure to 27.5 ± 1.2 mm Hg (Table 1). After beta-receptor blockade, heart rate rose significantly less (P < 0.01). After atropine administration alone or after combined administration of propranolol and atropine, heart rate was 144 ± 3 beats/min.
TABLE 1

Effects of Saline Infusion on Heart Rate, Mean Atrial Pressure, and Mean Arterial Blood Pressure

<table>
<thead>
<tr>
<th></th>
<th>Heart rate (beats/min)</th>
<th>Atrial pressure (mm Hg)</th>
<th>Arterial pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preinfusion</td>
<td>Postinfusion</td>
<td>Moderate</td>
</tr>
<tr>
<td>Normal conscious dogs (n = 12)</td>
<td>73 ± 3</td>
<td>148 ± 11*</td>
<td>178 ± 5*</td>
</tr>
<tr>
<td>β-receptor blockade (n = 6)</td>
<td>83 ± 2</td>
<td>122 ± 7*</td>
<td>144 ± 8*</td>
</tr>
<tr>
<td>Cholinergic blockade (n = 6)</td>
<td>186 ± 13</td>
<td>184 ± 10</td>
<td>178 ± 10</td>
</tr>
<tr>
<td>β-receptor and cholinergic blockade (n = 6)</td>
<td>156 ± 7</td>
<td>156 ± 6</td>
<td>156 ± 6</td>
</tr>
<tr>
<td>Denervated conscious dogs (n = 6)</td>
<td>103 ± 11</td>
<td>147 ± 9†</td>
<td>150 ± 9†</td>
</tr>
<tr>
<td>Vagotomy and β-receptor blockade (n = 3)</td>
<td>114 ± 3†</td>
<td>114 ± 3†</td>
<td>114 ± 3†</td>
</tr>
</tbody>
</table>

All values are means ± se. The moderate infusion consisted of 1.1 ± 0.1 liters of saline delivered over 2-10 minutes; the maximum infusion consisted of 2.6 ± 0.2 liters of saline delivered over 3-15 minutes. The volumes and the rates of infusion were not significantly different in the different groups of dogs for either the moderate or the maximum infusion.

* Postinfusion response significantly different from the preinfusion control response, P < 0.01.
† Postinfusion response significantly different from the postinfusion response in the control state, P < 0.01.
‡ Postinfusion response significantly different from the preinfusion control response, P < 0.05.
§ Postinfusion response significantly different from the postinfusion response in the control state, P < 0.05.

Effects of Methoxamine

Injection - In contrast to the slight bradycardia that resulted from methoxamine (30 μg/kg) delivered in an intravenous bolus injection, a rapid rise in arterial blood pressure and a striking bradycardia could be observed when methoxamine (300 μg/kg) was infused into the less intense bradyarrhythmia observed when methoxamine was infused to induce a similar rise in mean arterial blood pressure. The injection of methoxamine at a rate of 30 μg/kg decreased the heart rate abruptly from 81 ± 4 to 55 ± 5 beats/min. In conscious dogs without volume loading, the injection of methoxamine at a rate of 30 μg/kg decreased the heart rate abruptly from 81 ± 4 to 55 ± 5 beats/min. In these two situations equivalent increases in arterial blood pressure were less following injection of methoxamine. In conscious dogs without volume loading, the injection of methoxamine at a rate of 30 μg/kg decreased, the heart rate fell from 88 ± 3 to 69 ± 3 beats/min (P < 0.01) (Fig. 2). Decrease in heart rate were more pronounced with lower infusion rates, while the heart rate was more rapid with higher infusion rates. When methoxamine was infused to produce a rise in mean arterial pressure similar to that observed with volume loading, the heart rate fell from 88 ± 2 to 69 ± 3 beats/min (P < 0.01) (Fig. 2). The heart rate fell from 88 ± 2 to 69 ± 3 beats/min (P < 0.01) (Fig. 2).

In conscious dogs without volume loading, the injection of methoxamine at a rate of 30 μg/kg decreased, the heart rate fell from 88 ± 3 to 69 ± 3 beats/min (P < 0.01) (Fig. 2). The heart rate fell from 88 ± 2 to 69 ± 3 beats/min (P < 0.01) (Fig. 2).
and increased mean arterial blood pressure from 91 ± 2 to 108 ± 3 mm Hg (Fig. 3). In contrast, after an infusion of saline, a 50-µg/kg dose of methoxamine administered as an intravenous bolus increased arterial blood pressure from 126 ± 2 to 154 ± 3 mm Hg while heart rate fell from 178 ± 11 to 155 ± 14 beats/min. The increase in pressure induced by methoxamine following volume loading, was significantly greater (P < 0.02) than that prior to volume loading and the reflex bradycardia was significantly less (P < 0.01). Atropine nearly abolished the bradycardia both in the presence and the absence of volume loading, but propranolol had little effect in either instance.

PI/SAP Slopes.—In the absence of volume loading, when control atrial pressure averaged 2 ± 1 mm Hg, the average PI/SAP slope determined following a bolus injection of methoxamine of either 50 or 200 µg/kg was relatively steep (Fig. 4, Table 2). In contrast, the PI/SAP slopes obtained with methoxamine after maximum volume loading, when atrial pressure averaged 26 ± 1 mm Hg, were relatively flat and significantly different in each case from the normal slopes (P < 0.001) (Table 2). After mild volume loading, when atrial pressure averaged 8 ± 2 mm Hg, methoxamine

Comparison of the effects of saline infusion (2.6 ± 0.2 liters, 11 dogs) (circles), methoxamine infusion (50 µg/kg min⁻¹, 7 dogs) (squares), and methoxamine administered by intravenous injection (200 µg/kg min⁻¹, 1 dog) (triangles) on heart rate and mean atrial pressure, which are both plotted against mean arterial blood pressure. A striking bradycardia occurred with the rise in arterial blood pressure induced by the bolus injection of methoxamine, and a slight but still significant bradycardia occurred with the infusion of the drug. In contrast, for similar increases in arterial blood pressure induced by saline infusion, substantial tachycardia resulted.

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Comparison of the pulse interval (PI)/systolic arterial blood pressure (SAP) slopes in response to 50 µg/kg of methoxamine (MX) in the same dog studied on three separate days (left) and in response to 200 µg/kg of methoxamine in another dog studied on three separate days (right). Slopes were determined on different days when atrial pressure was low, i.e., no infusion (circles), during partial volume loading (triangles), and after maximum volume loading (squares). The control atrial pressures prior to the methoxamine injections are shown at the top of each section. The asterisks denote statistically different slopes (P < 0.001). Note the similarity of slopes for each of the three atrial pressure levels in response to the two different doses of methoxamine.
TABLE 2

PI/SAP Slopes in Response to Methoxamine in Conscious Dogs with and without Volume Loading

<table>
<thead>
<tr>
<th>Dog</th>
<th>Atrial pressure (mm Hg)</th>
<th>PI/SAP slope (msec/mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Infusion</td>
</tr>
<tr>
<td>1</td>
<td>0.5</td>
<td>8.5</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>5.0</td>
</tr>
<tr>
<td>3</td>
<td>2.0</td>
<td>9.5</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>5.5</td>
</tr>
<tr>
<td>5</td>
<td>5.0</td>
<td>14.5</td>
</tr>
<tr>
<td>6</td>
<td>4.5</td>
<td>5.0</td>
</tr>
<tr>
<td>MEAN ± SE</td>
<td>2.0 ± 1.0</td>
<td>8.0 ± 1.5</td>
</tr>
</tbody>
</table>

**Methoxamine (50 µg/kg)**

<table>
<thead>
<tr>
<th>Dog</th>
<th>Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>6.0</td>
</tr>
<tr>
<td>8</td>
<td>4.0</td>
</tr>
<tr>
<td>9</td>
<td>1.0</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>3.0</td>
</tr>
<tr>
<td>12</td>
<td>2.0</td>
</tr>
<tr>
<td>MEAN ± SE</td>
<td>2.7 ± 0.9</td>
</tr>
</tbody>
</table>

**Methoxamine (200 µg/kg)**

<table>
<thead>
<tr>
<th>Dog</th>
<th>Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>30.5</td>
</tr>
<tr>
<td>8</td>
<td>33.0</td>
</tr>
<tr>
<td>9</td>
<td>35.0</td>
</tr>
<tr>
<td>10</td>
<td>20.0</td>
</tr>
<tr>
<td>11</td>
<td>27.0</td>
</tr>
<tr>
<td>12</td>
<td>27.0</td>
</tr>
<tr>
<td>MEAN ± SE</td>
<td>28.8 ± 2.2</td>
</tr>
</tbody>
</table>

Mild infusion = 0.5 ± 0.1 liters delivered over 1–7 minutes; maximum infusion = 2.6 ± 0.2 liters delivered over 3–15 minutes. *P* values compare slopes during mild infusion with control and then between maximum and mild infusion for dogs 1–6. *P* values compare maximum infusion slopes with control for dogs 7–12.

produced intermediate slopes (Fig. 4) that were significantly less than those that occurred without volume loading but significantly greater than those that occurred with maximum volume loading in each instance except one (Table 2). The PI/SAP slopes were measured from the point at which the systolic arterial blood pressure (SAP) began to rise following methoxamine administration to the point at which SAP began to fall. The fact that the average SAP values tended to be higher in the dogs after volume loading did not influence the results significantly; specifically, after volume loading the PI/SAP slopes were flat regardless of whether the control SAP was 120 mm Hg or 160 mm Hg.

The PI/SAP slopes were examined in four dogs after intravenous administration of a 50-µg/kg bolus of methoxamine during a nitroglycerin infusion at a time when heart rate was elevated to an average of 145 ± 10 beats/min to determine if a flat PI/SAP slope like that which occurred during volume loading would result when the tachycardia was of a different origin. In these dogs, the average PI/SAP slope obtained with methoxamine was 30.3 ± 3.7 msec/mm Hg, which was significantly steeper (*P < 0.01*) than the slope obtained with methoxamine during volume loading, which averaged 21.0 ± 0.4 msec/mm Hg.

**Discussion**

It is clear from the results of the present study and the study of Horwitz and Bishop (14) that the Bainbridge reflex can be demonstrated consistently in the conscious dog; striking tachycardia occurs in response to volume loading. However, the afferent and efferent pathways of this reflex have not been established. Bainbridge suggested, and it is possible, that low-pressure receptors including atrial receptors are responsible for the origin of the afferent limb of the reflex (1, 15, 16). These studies as well as that of Hakumaki (17), which showed increases in sympathetic and decreases in parasympathetic activity with volume loading, support the concept that the tachycardia is mediated by a reflex. Moreover, it has been shown by Linden (16) that atrial receptor activity increases with volume loading. Further support for the concept that the tachycardia is reflex in origin can be gathered from the experiments after autonomic blockades conducted by Horwitz and Bishop (14) and from the current study. For example, we found that heart rate still increased with volume loading after simple beta-receptor blockade but not after combined beta-receptor and cholinergic blockade or after cholinergic blockade alone. Although it has been suggested that volume loading induces a direct
positive chronotropic effect (18–20), the data obtained in the present study in the dogs studied several days after recovery from bilateral vagotomy indicate that this mechanism, if present, must be minor, since heart rate failed to rise with volume loading in these dogs even though control rates were only 114 ± 3 beats/min, a level considerably less than that observed with either moderate volume loading (148 ± 11 beats/min) or maximum volume loading (178 ± 5 beats/min) in the intact conscious dogs.

Acute volume loading in the present study increased heart rate and mean arterial blood pressure. In the face of a rise in arterial blood pressure, the arterial baroreceptor reflex would be expected to restrain heart rate, as it did in response to an equivalent pressure rise during an infusion of methoxamine (Fig. 2). If the arterial baroreceptor reflex had responded appropriately to the increased blood pressure with volume loading, then the tachycardia would have been expected to be even greater in the conscious dogs with denervated arterial baroreceptors since this restraining influence was absent. In fact, however, the maximum heart rate attained in dogs with denervated baroreceptors was not greater than that in intact dogs, indicating that tachycardia due to volume loading occurs in the absence of arterial baroreceptors. This finding suggests that the arterial baroreceptor reflex exerts different effects on the control of cardiac rate depending on the level of atrial pressure.

To evaluate the sensitivity of the arterial baroreceptor reflex more precisely, the method of Smyth et al. (9) was employed. The slope of pulse interval vs. systolic arterial blood pressure plots was determined in response to an intravenous bolus dose of methoxamine. In normal conscious dogs, the PI/SAP slope was steep, reflecting the intense reflex cardiac slowing that is observed in response to the rise in arterial blood pressure. In contrast, after volume loading the PI/SAP slope was depressed markedly and was actually almost flat. An intermediate slope was observed following methoxamine injection after partial volume loading when atrial pressure was at an intermediate level (8 ± 2 mm Hg) (Fig. 4).

Several criticisms can be leveled against the method of Smyth et al. (9) for assessing baroreflex sensitivity. First, this method is better suited to identifying rapid, vagally mediated bradycardia than it is to the bradycardia mediated more slowly by the withdrawal of sympathetic tone. This fact did not constitute a major problem, since studies after sympathetic blockade failed to demonstrate a difference in early and later components of the reflex bradycardia either before or after volume loading. This finding is consistent with those of other studies demonstrating that reflex bradycardia in response to arterial baroreceptor hypertension is almost entirely due to enhanced vagal restraint (7, 21). Second, the injection of a vasoconstrictor may have effects other than a simple rise in arterial blood pressure and is therefore not as pure a baroreceptor stimulus as, for instance, raising the blood pressure mechanically. This fact did not constitute a major problem either, since dogs with denervated arterial baroreceptors responded to methoxamine-induced hypertension with no heart rate change. If a methoxamine injection elicited effects on cardiac rate through mechanisms other than arterial baroreceptor stimulation, then a change in heart rate would have been observed in the dogs with denervated arterial baroreceptors. Another possible source of error was that the PI/SAP responses to methoxamine were different solely because of the presence of tachycardia and not because of the elevated atrial pressure. To investigate this possibility, the same dose of methoxamine was administered after heart rate had been elevated by an infusion of nitroglycerin. In these cases, although the heart rates were similar to those during volume loading, the PI/SAP slopes were significantly greater than those that occurred after volume loading, indicating that the depressed PI/SAP slope observed after volume loading could not be explained by the presence of tachycardia per se. In summary, the technique of Smyth et al. (9) was chosen because it is generally accepted as quantitative and because reproducible responses were found in this study when PI/SAP slopes were determined under the same conditions on separate days.

The results of the present study suggest that the sensitivity of the arterial baroreceptor reflex is reduced or that the set point of the reflex, the gain of the reflex, or both are altered during acute volume loading. The exact mechanism by which this reflex is reset or overridden was not determined. Possibilities include either peripheral resetting or central resetting (3, 22); the latter involves alterations in the integration of the nerve traffic in the central nervous system. As discussed by Korner (3) and by Korner et al. (22), inputs from all cardiovascular receptor areas are integrated in the central nervous system. The extent to which each individual input induces reflex changes depends in part on the inputs from each of the other afferents.
In this study, it appeared that the input from low-pressure receptors in the cardiopulmonary area may have modified the expected arterial baroreceptor reflex heart rate responses to the rise in arterial blood pressure that occurred; thus, the arterial baroreceptor reflex failed to counteract the positive chronotropic effects induced by the volume loading.

Finally, the sensitivity of the baroreceptor reflex is reduced in man (21) and experimental animals (23) with chronic heart failure, which might be considered to be analogous to a state of chronic volume loading. In this connection, it is interesting to note that patients with heart failure as well as normal subjects after volume loading exhibit attenuated reflex tachycardia in response to orthostatic stress (24). Thus, the mechanism of the altered baroreflex sensitivity in heart failure as well as in exercise could be due to the concomitant volume expansion and the overriding influence of low-pressure reflexes.

Acknowledgment

We acknowledge the technical assistance of T. Manders, R. Peters, and P. Quinn, the help in the preparation of the manuscript from V. Fowler, and the supply of propranolol by Ayerst Laboratories. We are also grateful for the encouragement and support from Dr. E. Braunwald.

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Circ Res. 1975;37:236-242
doi: 10.1161/01.RES.37.2.236

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

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