Adrenergic Control of the Peripheral Circulation in Cardiomyopathic Hamsters with Heart Failure

By Allyn L. Mark, Howard E. Mayer, Phillip C. Schmid, Donald D. Heistad, and Francois M. Abboud

ABSTRACT

Adrenergic control of the peripheral circulation was studied in cardiomyopathic hamsters to determine if the functional status of terminal vascular sympathetic nerve endings is augmented in heart failure. Four groups of hamsters were studied: myopathic hamsters with heart failure (average age 296 days), myopathic hamsters without heart failure (average age 171 days), and two corresponding control groups of randomly bred hamsters matched for age. In hamsters with heart failure, the concentration of catecholamines in hearts, aortas, and femoral arteries was reduced compared with that in corresponding control hamsters. In myopathic hamsters without heart failure, the concentration of catecholamines was reduced in femoral arteries, but it was not reduced in hearts or aortas. Resting vascular resistance and vasoconstrictor responses to sympathetic nerve stimulation, norepinephrine, and angiotensin in the perfused hindquarters was reduced in hamsters with heart failure but not in myopathic hamsters without heart failure. These studies suggest that the functional status of terminal sympathetic nerve endings in blood vessels of the extremities is not augmented and may be reduced in this model of heart failure. Studies on other models of heart failure are needed to determine whether the absence of increased vascular catecholamines and the absence of augmented responses to sympathetic nerve stimulation are characteristic of heart failure in general or are unique to this model that has characteristics of high-output failure.

KEY WORDS

catecholamines  aorta  femoral artery
sympathetic nerve stimulation  norepinephrine  angiotensin

Myocardial norepinephrine stores are depleted and cardiac responses to sympathetic nerve stimulation are reduced in heart failure (1–5), but the status of sympathetic innervation of blood vessels in heart failure remains controversial. Several investigators have reported that reflex vasoconstrictor responses to exercise are increased in heart failure (6, 7), and Kramer et al. (8) have suggested that the amount of norepinephrine available for release from sympathetic nerve endings of resistance vessels in the extremities is augmented in heart failure. However, Hayduk and co-workers (9) have recently observed that the norepinephrine concentration of arteries is normal or decreased in heart failure. Also, Higgins et al. (10) have demonstrated that reflex increases in vascular resistance during bilateral carotid artery occlusion are reduced in dogs with experimental heart failure. These studies have raised questions about the sympathetic control of the peripheral circulation in heart failure. There have been no reports in which vascular responses to direct sympathetic nerve stimulation have been obtained in heart failure and correlated with measurements of catecholamines in blood vessels to assess the status of sympathetic innervation of blood vessels.

The present experiments were performed to study the adrenergic control of the peripheral circulation in the Syrian hamster (Mesocricetus auratus) with hereditary cardiomyopathy and congestive heart failure (11, 12). Specifically, these studies tested the hypothesis that the catecholamine concentration of blood vessels and the vasoconstrictor responses to direct sympathetic nerve stimulation are augmented by heart failure. We measured the concentration of catecholamine in hearts, aortas, and femoral arteries and obtained vascular responses to direct electrical sympathetic nerve stimulation, norepinephrine, and angiotensin.
Experiments were performed on four groups of hamsters: (1) myopathic hamsters (BIO 14.6 strain, Telaco, Inc.) with heart failure indicated by cardiomegaly, hepatomegaly, and anasarca (average age 296 days), (2) old control randomly bred hamsters (average age 308 days), (3) young hamsters with myopathy documented by histological examination but without heart failure (average age 171 days), and (4) young control randomly bred hamsters (average age 170 days). These studies were designed to separate the effects of heart failure from the effects of aging or myopathy. To separate the effects of aging, we compared hamsters in heart failure with old control hamsters. To separate the effects of myopathy without heart failure, we compared young myopathic hamsters without heart failure with young control hamsters or with hamsters with myopathy and heart failure.

In the first series of experiments, we measured the catecholamine concentration of aortas, femoral arteries, and hearts from six hamsters in each group. The hamsters were killed by separation of the cervical vertebra. The vessels and heart were excised quickly, rinsed in cool saline, blotted, weighed, and frozen in liquid nitrogen. Each tissue sample was pulverized in a stainless steel apparatus which had been cooled in liquid nitrogen. The crushed frozen tissue was transferred to an ice-cold Potter-Elvehjem grinding tube containing 10 mg of sodium metabisulfite and was homogenized for 1 minute in 0.4N perchloric acid. Following centrifugation at 0°C for 20 minutes, the precipitate was washed with 0.4N HClO4 and recentrifuged. The supernatant fluids were combined, and catecholamines were extracted by the aluminum oxide absorption process of Anton and Sayre (13) and Mark et al. (14). The eluted catecholamines were analyzed using a modification of the fluorometric trihydroxyindole method of Haggendal (15). Faded tissue blanks and a series of standards were analyzed with each sample. Standards were prepared from pure l-norepinephrine HCl (Sigma Chemical Company). Fluorescence was measured with a spectrophotometer (Hitachi Perkin-Elmer MFP2A) equipped with a high-sensitivity cell holder and a recorder (Hitachi QPD33). Linear curves were obtained with standards ranging from 2.5 to 150.00 ng of norepinephrine. At high-sensitivity settings, 10 ng of norepinephrine gave full-scale readings. In fluorometric determinations on ten samples, the average recovery from the alumina extraction process was 94.3 ± 1.3% (SE). The data were not corrected for losses in the purification procedure.

The average weight of the segments of abdominal aorta from each hamster was 3.5 mg, and the average weight of the segments of femoral arteries was 2.5 mg. Because of the small sample weights, the segments of abdominal aorta from the six hamsters in each group were pooled for the determination. In addition, segments of femoral arteries from hamsters in each group were pooled for determination of catecholamines. Since values for concentration of catecholamines in vessels were obtained from determinations on pooled samples from hamsters in each group, the reproducibility of the method was tested. A series of determinations on several concentrations of standards and on six duplicate tissue samples run through the alumina extraction process and the fluorometric determination yielded a standard deviation of 4%. Determination of the catecholamine concentration and content of the heart was performed for each hamster. The catecholamine concentrations were expressed as nanograms per gram wet weight. Because the vessels were small, the entire sample was needed for determination of the catecholamine concentration. Therefore, dry weights and water content were not obtained on these specimens, but net weights were not significantly different in hamsters with heart failure and randomly bred hamsters. The water content of vessels (combined aorta and femoral arteries) and hearts was determined in five other hamsters with heart failure and in six other controls. After obtaining wet weights, the samples were freeze-dried. Dry weights were then obtained, and percent water was calculated.

In the second series of experiments, we measured vascular responses to direct sympathetic nerve stimulation and to close intra-arterial administration of norepinephrine and angiotensin in the perfused hindquarters of six or seven hamsters in each group. The hamsters were anesthetised with sodium pentobarbital, (20–40 mg, ip). A tracheotomy was performed, and the hamsters were ventilated artificially with air and supplemental oxygen. The abdominal aorta was cannulated with polyethylene tubing (PE 50), and the hindquarters were perfused at constant flow with heparinized arterial blood with a Holter model RL175 roller pump (Extracorporeal Medical Specialties, Inc.) while perfusion pressure was monitored. Initially a shunt was inserted in the perfusion tubing to bypass the Holter pump and to permit autoperfusion of the hindquarters, and 1.2 ml of 6% dextran in the perfusion tubing was added slowly to the perfusate by turning on the pump intermittently to minimize abrupt changes in hematocrit. The tubing was primed with dextran instead of the hamster's blood, because preliminary studies indicated that this procedure was necessary to prevent hypovolemia and hypotension in these small hamsters. After the equilibration period, the shunt was removed. Flow to the hindquarter was adjusted initially so that perfusion pressure approximated arterial blood pressure. Flow then was kept constant (0.9–1.3 ml/min) so that changes in perfusion pressure reflected changes in hindquarter vascular resistance. Systemic arterial blood pressure was measured frequently by turning off the pump and recording pressure upstream from the pump.

Direct nerve stimulation was produced with a small platinum electrode placed around the lumbar sympathetic chain that was crushed proximally. The chain was stimulated at supramaximal voltage with 4-msec pulses at variable frequency for 15 seconds. l-Norepinephrine bitartrate and 5-Val-angiotensin II amide were injected into the perfusion tubing upstream from...
from the pump in 2.5-20.0 mliters of saline; injection of these volumes of saline alone had no effect. Doses of norepinephrine are expressed in terms of base. We obtained pressure-flow curves for the perfused hindquarters before and after sectioning the lumbar sympathetic chains in individual hamsters with heart failure and in old control hamsters. These studies were carried out to compare the resting vascular resistance in the two groups in the innervated state and after denervation. Before the chains were cut the sympathetic chains were identified by obtaining vasoconstrictor responses to electrical stimulation.

Because the myopathic hamsters were anemic, we decreased hematocrit in three randomly bred hamsters by exchanging 0.8 ml of 6% dextran (molecular weight 89,000) for 0.8 ml of blood in increments of 0.1 ml and measured resting hindquarter perfusion pressures and responses to norepinephrine before and during anemia.

Because the doses of the drugs were the same in all groups and because the flows were on the average 30% lower in control hamsters, the concentration of the drugs were on the average 30% higher in the controls. Therefore, in five experiments on randomly bred controls we compared responses to 25 and 50 ng of norepinephrine with responses to doses that were 30% lower, 17.5 and 35 ng.

Statistical analyses were performed with analysis of variance (16).

Results

Anatomical measurements in the four groups are shown in Table 1. Body, heart, and liver weights of hamsters with heart failure were greater than those weights of control hamsters of similar age. Hematocrit was lower in myopathic hamsters with and without heart failure than it was in corresponding control hamsters. In addition, hematocrit was lower in hamsters with failure than it was in myopathic hamsters without failure.

Catecholamine Concentration.—In hamsters with heart failure, the concentration of catecholamine in heart, aorta, and femoral arteries was reduced compared with that in corresponding control hamsters (Table 2). In myopathic hamsters without heart failure, the catecholamine concentrations of heart and aorta were similar to those in age-matched controls (Table 2). Femoral artery catecholamines were reduced in myopathic hamsters without heart failure, but the reduction was not as great as that in the hamsters with heart failure (Table 2). Specifically, femoral artery catecholamines were 369 ng/g wet weight or 57% lower in hamsters with heart failure than they were in old controls but were only 268 ng/g wet weight or 37% lower in myopathic hamsters without heart failure than they were in young controls.

In the randomly bred control hamsters, cardiac and aortic catecholamines were 118 and 102% higher in the old hamsters than they were in the young hamsters (Table 2). In the myopathic hamsters, cardiac and aortic catecholamines were only 27 and 9% higher in the old hamsters with heart failure than they were in the young hamsters without heart failure (Table 2). With aging, femoral artery catecholamines decreased 9% in control hamsters and 38% in myopathic hamsters (Table 2).

Water content of the blood vessels in hamsters with heart failure and in control hamsters averaged 72 ± 1.3 (se) and 72 ± 1.0%, respectively.

### Table 1

**Anatomical Measurements**

<table>
<thead>
<tr>
<th></th>
<th>Myopathic hamsters with heart failure (n = 12)</th>
<th>Old randomly bred controls (n = 13)</th>
<th>Myopathic hamsters without heart failure (n = 12)</th>
<th>Young randomly bred controls (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (days)</td>
<td>296 ± 10</td>
<td>308 ± 8</td>
<td>171 ± 6</td>
<td>170 ± 5</td>
</tr>
<tr>
<td>Body weight (g)</td>
<td>150 ± 6</td>
<td>126 ± 3</td>
<td>109 ± 6</td>
<td>109 ± 2</td>
</tr>
<tr>
<td>Heart weight (mg)</td>
<td>534 ± 32*</td>
<td>405 ± 12</td>
<td>373 ± 38</td>
<td>324 ± 16</td>
</tr>
<tr>
<td>% of body wt</td>
<td>0.38 ± 0.03</td>
<td>0.32 ± 0.01</td>
<td>0.33 ± 0.02</td>
<td>0.30 ± 0.01</td>
</tr>
<tr>
<td>Liver weight (g)</td>
<td>10.5 ± 1.9*</td>
<td>5.2 ± 0.3</td>
<td>4.2 ± 0.6</td>
<td>4.4 ± 0.2</td>
</tr>
<tr>
<td>% of body wt</td>
<td>7.1 ± 0.7*</td>
<td>4.1 ± 0.2</td>
<td>3.6 ± 0.3</td>
<td>4.0 ± 0.1</td>
</tr>
<tr>
<td>Venous hematocrit †(%)</td>
<td>33.0 ± 4.4*</td>
<td>46.6 ± 1.4</td>
<td>41.5 ± 4.1†</td>
<td>50.5 ± 1.4</td>
</tr>
</tbody>
</table>

All values are means ± se. Measurements were obtained after the hamsters had been killed with the exception of venous hematocrit which was measured at the start of the studies of vascular reactivity.

*Values in myopathic hamsters with heart failure that are significantly different (P < 0.05) from values in old randomly bred controls.

†n = 6-7 for determinations of venous hematocrit.

‡Values in myopathic hamsters without failure that are significantly different (P < 0.05) from values in young controls.
TABLE 2

Myocardial and Vascular Catecholamine Concentration

<table>
<thead>
<tr>
<th></th>
<th>Myopathic hamsters with heart failure (n = 6)</th>
<th>Old randomly bred controls (n = 6)</th>
<th>Myopathic hamsters without heart failure (n = 6)</th>
<th>Young randomly bred controls (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart (ng/g wet wt)</td>
<td>433 ± 72*</td>
<td>718 ± 65</td>
<td>340 ± 35</td>
<td>330 ± 16</td>
</tr>
<tr>
<td>Aorta (ng/g wet wt)</td>
<td>277</td>
<td>458</td>
<td>209</td>
<td>227</td>
</tr>
<tr>
<td>Femoral artery (ng/g wet wt)</td>
<td>279</td>
<td>648</td>
<td>447</td>
<td>715</td>
</tr>
</tbody>
</table>

All values for the heart are means ± SE. Values for the aorta and the femoral artery were determined on the pooled samples of the hamsters in each group. See description of methods for discussion of the reproducibility of measurements of catecholamines.

*The catecholamine concentration of hearts was significantly lower (P < 0.05) in hamsters with heart failure than it was in old randomly bred controls. In addition, myocardial catecholamine content also was significantly lower (P < 0.05) averaging 190 ± 32 ng in hamsters with heart failure and 270 ± 26 ng in control hamsters.

(P > 0.05). The water content of hearts in the two groups averaged 77 ± 1.0 and 79 ± 1.0%, respectively (P > 0.05).

Vascular Reactivity.—Base-line observations are shown in Table 3. In hamsters with heart failure, resting hindquarter vascular resistance was about 43% lower than that in old control hamsters and about 52% lower than that in myopathic hamsters without heart failure (Table 3). Resting vascular resistance was not reduced in myopathic hamsters compared with young control hamsters (Table 3). Sectioning the lumbar sympathetic chains did not produce significant decreases in resistance in either myopathic hamsters with heart failure or in old controls, and the difference in resting resistance between the two groups persisted after sectioning the chains (Table 4).

Vasoconstrictor responses to sympathetic nerve stimulation, norepinephrine, and angiotensin were reduced (P < 0.05) in hamsters with heart failure compared with old controls (Figs. 1 and 2). Responses to nerve stimulation tended to be reduced to a greater extent than responses to norepinephrine and angiotensin (Fig. 3).

In three randomly bred hamsters, decreases in hematocrit from 45 ± 3.0% to 36 ± 3.5% were not associated with decreases in resting hindquarter perfusion pressure or responses to norepinephrine. Resting perfusion pressure averaged 87 ± 13.3 mm Hg before and 90 ± 12.2 mm Hg during anemia (P > 0.05). Increases in perfusion pressure with 25 and 50 ng of norepinephrine averaged 22 ± 3.1 and 33 ± 6.7 mm Hg before and 25 ± 4.0 and 40 ± 5.4 mm Hg during anemia (P > 0.05).

In five control hamsters, responses to 25 and 17.5 ng of norepinephrine averaged 11.2 ±1.4 and 9.5 ±2.2 mm Hg, respectively (P > 0.05).

TABLE 3

Base-Line Observations in Studies of Vascular Reactivity

<table>
<thead>
<tr>
<th></th>
<th>Myopathic hamsters with heart failure (n = 6)</th>
<th>Old randomly bred controls (n = 7)</th>
<th>Myopathic hamsters without heart failure (n = 6)</th>
<th>Young randomly bred controls (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial blood pressure (mm Hg)</td>
<td>79.8 ± 8.9</td>
<td>91.3 ± 13.0</td>
<td>92.8 ± 7.4</td>
<td>112.0 ± 7.7</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>290 ± 37*</td>
<td>374 ± 10</td>
<td>272 ± 25</td>
<td>332 ± 19</td>
</tr>
<tr>
<td>Hindquarters flow (ml/min)</td>
<td>1.3 ± 0.1</td>
<td>1.0 ± 0.1</td>
<td>0.9 ± 0.1</td>
<td>0.9 ± 0.1</td>
</tr>
<tr>
<td>Perfusion pressure (mm Hg)</td>
<td>70.8 ± 5.4</td>
<td>94.3 ± 11.2</td>
<td>90.5 ± 10.5</td>
<td>90.0 ± 9.0</td>
</tr>
<tr>
<td>Hindquarter vascular resistance (units)</td>
<td>55.0 ± 5.0*</td>
<td>97.1 ± 11.2</td>
<td>115.8 ± 30.3</td>
<td>108.3 ± 15.9</td>
</tr>
</tbody>
</table>

All values are means ± se. Base-line observations were taken just before responses to the vasoconstrictor stimuli were obtained. None of the values in the myopathic hamsters without failure was significantly different from values in the young control hamsters.

*Values in myopathic hamsters with heart failure that are significantly different (P < 0.05) from values in the old randomly bred controls. Abelmann et al. (18) have also observed that heart rate is slower in hamsters with heart failure than it is in control hamsters of similar age.
TABLE 4
Pressure-Flow Curves before and after Sectioning the Lumbar Sympathetic Chain

<table>
<thead>
<tr>
<th>Hamster</th>
<th>Before</th>
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<th>Before</th>
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<td>1</td>
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<td>54</td>
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<td>67</td>
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<tr>
<td><strong>MEAN ± SE</strong></td>
<td><strong>73 ± 8</strong></td>
<td><strong>71 ± 8</strong></td>
<td><strong>87 ± 7</strong></td>
<td><strong>84 ± 10</strong></td>
<td><strong>96 ± 7</strong></td>
<td><strong>93 ± 10</strong></td>
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</table>

**Old Randomly Bred Controls**

**Myopathic Hamsters with Heart Failure**

<table>
<thead>
<tr>
<th>Hamster</th>
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<tbody>
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<td>35</td>
<td>36</td>
</tr>
<tr>
<td><strong>MEAN ± SE</strong></td>
<td><strong>32 ± 6</strong></td>
<td><strong>27 ± 3</strong></td>
<td><strong>39 ± 6</strong></td>
<td><strong>34 ± 2</strong></td>
<td><strong>45 ± 6</strong></td>
<td><strong>37 ± 2</strong></td>
</tr>
</tbody>
</table>

Sectioning the chains did not significantly alter the pressure-flow relationships in either group (P > 0.05).

Discussion

In this model of heart failure, i.e., the Syrian hamster with hereditary myopathy and congestive heart failure, the functional status of terminal sympathetic nerve endings of blood vessels to the extremities was not augmented. Also, the data suggest that the functional status might be reduced.

In hamsters with heart failure, the concentration of catecholamines in the femoral arteries and the aorta was reduced rather than increased (Table 2). These decreases in catecholamine concentration did not result from increased water content since the water content of vessels did not differ in hamsters with and without heart failure. These data on water content are consistent with reports on two other models of heart failure (9, 17).

In addition to the decreases in catecholamine concentration, vasoconstrictor responses to direct sympathetic nerve stimulation were also reduced in hamsters with heart failure (Figs. 1 and 2). Although responses to norepinephrine, the adrenergic neurotransmitter, and to angiotensin were decreased in hamsters with heart failure, responses to sympathetic nerve stimulation (SNS) at 4, 8, 16, and 32 Hz were lower in the hamsters with heart failure than they were in the control hamsters by 50, 63, 65, and 65%, respectively. Responses to 12.5, 25, 50, and 100 ng of norepinephrine were lower in hamsters with heart failure by 42, 47, 51, and 52%, respectively. Responses to 25 and 50 ng of angiotensin were 44 and 47% lower in the group with heart failure.
ADRENERGIC CONTROL IN HEART FAILURE

FIGURE 3
Responses in hamsters with heart failure compared with those in the hamsters with myopathy without heart failure. After onset of heart failure, responses to nerve stimulation at 4, 8, 16, and 32 Hz were lower by 62, 73, 64, and 61%, respectively. Responses to the four doses of norepinephrine were lower by 44, 50, 46, and 45%, and responses to the two doses of angiotensin were lower by 43 and 44% after onset of heart failure.

Responses to nerve stimulation tended to be reduced to a greater extent than responses to norepinephrine and angiotensin (Figs. 1 and 3). These abnormalities apparently did not result from aging or from myopathy, since similar changes were not seen in control hamsters of similar age or in young myopathic hamsters of the same strain but without heart failure (Figs. 1 and 3). In addition, the decreased vasoconstrictor responses probably did not result from the altered resting pressure-flow relationship (low resting vascular resistance) in the hamsters with heart failure, since four of the hamsters from the control groups also had low resting vascular resistance but did not have decreased vasoconstrictor responses. This observation suggests that the altered resting pressure-flow relationships in the hamsters with heart failure do not explain the decreased vasoconstrictor responses. Moreover, these results suggest that the amount of norepinephrine available for release from sympathetic nerve endings in blood vessels of the extremities is reduced by heart failure in this model. The observations do not support previous suggestions that the activity of terminal sympathetic nerve endings of vessels to the extremities is augmented in heart failure (8).

Since flow to the hindquarters averaged 30% more in the hamsters with heart failure (Table 3) and the doses of norepinephrine and angiotensin were the same in the various groups, the concentration of drugs was slightly lower in heart failure. Several observations indicate that this concentration difference does not detract from the conclusions. First, inspection of the dose-response curves (Figs. 1 and 3) indicates that these small differences in concentration could not account for the large differences in the relative potency of the drugs in the heart failure and control groups. This situation was also considered by calculating the relative potency of each drug in the old randomly bred controls vs. that in the hamsters with heart failure by assuming equal doses or by assuming that the doses, i.e., concentration, were 30% less in the hamsters with heart failure. The relative potency of norepinephrine in control hamsters compared with hamsters with heart failure was 2.85 using both methods although the relative potency for angiotensin was 2.33 by assuming equal doses and 1.88 by assuming the doses were 30% less in hamsters with heart failure. Therefore, with either method there was a noticeable, significant difference in the relative potency of the drugs in the control hamsters and the hamsters with heart failure. Second, in the additional experiments in which we compared responses to the original doses (25 and 50 ng) of norepinephrine and to doses which were 30% lower (17.5 and 35 ng), the responses to the lower doses were somewhat less. Therefore, if we had given the lower doses to the control hamsters to achieve the same concentrations of drugs as in the heart failure hamsters, there would have been less difference in responses to the drugs in the control and heart failure groups. Consequently, the differences in responses to nerve stimulation between control and heart failure groups would have been more selective. This phenomenon would strengthen, rather than weaken, the conclusion that the functional status of vascular sympathetic nerve
endings may be reduced by this model of heart failure.

Studies by Abelmann et al. (18-19) suggest that cardiomyopathy in the Syrian hamster initially causes a hypokinetic circulatory state, but subsequently the development of heart failure is associated with a hyperkinetic circulatory state. Our observation that vascular resistance was reduced in hamsters with heart failure but not in hamsters with myopathy alone is consistent with this suggestion and presents the possibility that absence of augmented activity of terminal vascular sympathetic nerve endings may be characteristic of this model of heart failure or various other models of "high-output" failure but not of the more common forms of "low-output" failure with high vascular resistance. However, several observations in other models of heart failure make this possibility unlikely. Hayduk et al. (9) have reported that in dogs with low-output failure produced by tricuspid avulsion the norepinephrine content of arteries is normal or decreased. Furthermore, recent studies by Schmid et al. (20) have indicated that resting sympathetic tone of blood vessels in the extremity is normal in dogs with heart failure and that responses to direct nerve stimulation are normal or reduced. Finally, administration of ganglionic blocking agents or phentolamine to patients with heart failure has not demonstrated increased resting neurogenic tone of resistance and capacitance vessels in the extremities (6, 21, 22).

The mechanism of the reduced vascular resistance during heart failure in the myopathic hamster is not clear. It apparently does not result from decreased sympathetic neurogenic tone, since vascular resistance remained considerably higher in the control hamsters than it did in the hamsters with heart failure after the lumbar sympathetic chains were cut (Fig. 2). Decreases in hematocrit in the myopathic hamster, which also have been observed by Abelmann and co-workers (19), may have contributed to decreased resistance by lowering viscosity, but a reduction in hematocrit in hamsters with myopathy alone was not associated with a decrease in vascular resistance. In addition, vascular resistance was low (43 units) in one of the hamsters with heart failure that had a normal hematocrit (45%), and acute decreases in hematocrit in three control hamsters did not decrease resting perfusion pressures or responses to norepinephrine. These observations suggest that anemia does not completely explain the reduced vascular resistance. Involvement of vascular smooth muscle by the myopathy could contribute to decreased resistance, but it probably does not because the histological studies did not reveal changes in vascular smooth muscle and because vascular resistance was not decreased in myopathic hamsters without heart failure. We postulate that the decrease in resting vascular resistance was caused largely by local metabolic or humoral factors.

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References

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