Renal Responses of the Cardiac-Denervated Nonhuman Primate to Blood Volume Expansion

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SUMMARY. Experiments were performed to determine whether total, specific cardiac denervation affects the renal responses of the nonhuman primate to acute intravascular volume expansion. Adult male Macaca fascicularis monkeys underwent chronic intrapericardial cardiac denervation or sham surgery. After a 14- to 30-day recovery period, each animal was anesthetized with sodium pentobarbital and estimated blood volume was volume-expanded 20% with 6% dextran in isotonic saline. Control renal excretory function did not differ between the two groups, and both groups had similar increases in urine flow, sodium and potassium excretion, osmolar clearance, free water clearance, and renal plasma flow after volume expansion. The times to peak diuresis and natriuresis also were similar in both groups. These results demonstrate that the cardiac-denervated monkey shows unattenuated renal excretory responses to volume expansion. This could indicate that either cardiac receptors do not play a major role in eliciting these responses in the primate or that eliminating a role of cardiac afferents is compensated for by redundant afferents from arterial baroreceptors. (Circ Res 53: 24–32, 1983)

MECHANORECEPTORS located in the heart are believed to play an important role in controlling renal salt and water excretion, particularly during alterations in blood volume. Changes in cardiac receptor activity have effects on antidiuretic hormone and renin secretion and on efferent renal nerve activity, all of which can affect renal excretory function. However, most of the experimental evidence in support of this concept has come from studies using the dog as the experimental model (Gauer and Henry, 1976; Linden, 1976, Donald and Shepherd, 1978). Even so, the importance of these receptor mechanisms in this species has been questioned (Goetz, 1979).

Studies using the nonhuman primate as a model have, on the other hand, suggested that cardiac receptors may play little role in maintaining blood volume homeostasis in this species, particularly during hypervolemic interventions. For example, it has been demonstrated that atrial type B receptors are less sensitive in the monkey than in the dog, in that their discharge rate changes little with increases in atrial pressure (Zucker and Gilmore, 1975). Furthermore, localized increases in left atrial pressure or atrial stretch, induced by either inflation of a balloon in the left atrium or tightening of a mitral snare, leads to a diuresis and natriuresis in the dog (Gauer and Henry, 1976; Linden, 1976; Kaczmarczyk et al., 1981; Fater et al., 1982), but fails to elicit any renal effects in either the anesthetized (Gilmore and Zucker, 1978) or conscious monkey (Cornish and Gilmore, 1982).

With regard to the role of cardiac receptors in mediating the renal responses to outright volume expansion, it has been shown that cervical vagotomy, which interrupts vagally innervated cardiopulmonary receptor input to the central nervous system, attenuates the diuretic response to volume expansion in the dog (Atkins and Pearce, 1959; Gilmore and Weisfeldt, 1965), but fails to do so in the monkey (Gilmore et al., 1979). In addition, thoracic sympathectomy, which removes spinal sensory input from the cardiopulmonary region (Malliani, 1979), has no effect on the renal responses of the monkey to volume expansion (Cornish and Gilmore, 1983). However, neither of these denervations represents a total, specific denervation of the heart. Cervical vagotomy interrupts both pulmonary and cardiac vagal nerve fibers but leaves thoracic spinal afferents intact, whereas thoracic sympathectomy ablates the latter neural pathways but leaves vagal fibers intact. Therefore, with either of these denervations, the heart still remains partially innervated, and the failure to observe attenuated responses to volume expansion could be due to the presence of these remaining cardiac neural pathways.

The purpose of the present study, therefore, was to determine whether complete, selective cardiac denervation affects the renal responses of the monkey to volume expansion.

Methods

The experiments were performed on male Macaca fascicularis monkeys with a weight range of 4.4–6.5 kg. All animals were maintained on a standard monkey chow diet containing adequate amounts of sodium so that all animals were sodium-replete. Before each surgery or experiment, each animal was fasted overnight, but was allowed water ad libitum.
Surgical Preparation

The study involved the following two groups of animals.

Cardiac-Denervated (n = 5)

Each animal was sedated with ketamine HCl (5 mg/kg) administered intramuscularly, followed by anesthetization with sodium pentobarbital (20 mg/kg) administered through an intracath inserted into an antecubital vein. A cuffed endotracheal tube was inserted, and each animal was artificially ventilated with a Harvard respirator.

The method used for cardiac denervation was the one-stage intrapericardial technique of Randall et al. (1980), as described for the dog, but with modifications for the monkey. In brief, using aseptic technique, we performed a left thoracotomy through the 4th intercostal space. The left thoracic vagus nerve (LTV), right thoracic vagus nerve (RTV), left stellate ganglion (LS), and right stellate ganglion (RS) were isolated. The pericardium was opened, a pericardial cradle formed, and a Walton-Brodie strain gauge arch sutured to the base of the left ventricle. The latter was used to record left ventricular contractile force (LVCF) which was displayed on a Beckman Dynograph recorder. The output of the LVCF channel was used to trigger a tachograph for recording heart rate. After all recordings were stable, the LTV, RTV, LS, and RS each were stimulated separately with a stainless steel electrode and Grass S9 square-wave stimulator. Stimulus parameters were 5 msec duration, 10/sec frequency, and voltages of 4–6 V for the vagus nerves and 8–10 V for the stellate ganglia. Typical predenervation inotropic and chronotropic responses are shown in the upper tracings in Figure 1. After these responses had been obtained, all cardiac nerves were surgically ablated within the pericardium. This procedure involved a careful transection around the complete circumference of the superior vena cava, with ligation and division of the azygos vein. The dissection was continued medially from the superior vena cava across the superior surfaces of the right and left atria and pulmonary veins. All nervous and connective tissue was removed from the area between the roots of the pulmonary artery and the ascending aorta. The adventitia was also removed from the complete circumference of the pulmonary artery, approximately 5 mm distal to the pulmonary valve annulus. After performing these procedures, we again stimulated the LTV, RTV, LS, and RS. The lower tracings in Figure 1 show the absence of any inotropic and chronotropic responses after denervation. If any residual response remained, further dissection was performed until the responses to stimulation were abolished. When total denervation was assured, the strain gauge arch was removed, the pericardium closed, and the chest closed in layers and evacuated. Each animal was allowed to recover and was treated with benzathine penicillin G-procaine penicillin G (Longicil, 300,000 U/day) for 2 days.

Sham-Operated Controls (n = 5)

The animals in this group underwent the same thoracotomy procedure as the denervated animals but no cardiac nerves were severed. The LTV, RTV, LS, and RS were isolated but not stimulated. The pericardium was also opened, and a strain gauge arch was sutured to the base of the left ventricle. Each animal remained on the operating table with its chest open the same length of time as did the animals in the denervation group. The strain gauge then was removed, pericardium closed, and chest closed and evacuated. Each animal was allowed to recover and underwent the same antibiotic regimen as the denervated animals.

Experimental Procedure

The volume expansion experiment was performed no sooner than 14 days or later than 30 days after the cardiac

![Figure 1](https://example.com/figure1.png)

**Figure 1.** Typical cardiac responses of a monkey to cardiac nerve stimulation before and after cardiac denervation. HR = heart rate, LVCF = left ventricular contractile force, LTV = left thoracic vagus, RTV = right thoracic vagus, LS = left stellate ganglion and RS = right stellate ganglion.
denervation or sham denervation surgery. At this time, each animal was again sedated with ketamine HCl and anesthetized with sodium pentobarbital, as described earlier. To measure arterial blood pressure (ABP), a polyethylene catheter was inserted into a femoral artery, advanced into the aorta, and connected to a Statham transducer (P23ID). Central venous pressure (CVP) was measured by means of a similar catheter inserted into a femoral vein and advanced into the thoracic inferior vena cava. All pressures were monitored continuously with a Grass model 7D Polygraph, and heart rate was calculated from a fast trace of the blood pressure recording. The other femoral artery and vein were cannulated for withdrawing arterial blood samples and infusing solutions, respectively. Both ureters were exposed through bilateral flank incisions and cannulated with polyethylene tubing. All incisions were closed with surgical clips.

After these preparations were completed and blood pressure had stabilized, each animal was given a priming dose of creatinine (33 mg/kg) and p-aminohippurate (PAH) (8 mg/kg), followed by a sustaining infusion (0.75 ml/min) containing 1.6 g/liter of both creatinine and PAH in 0.6% NaCl solution. An hour later, timed urine samples consisting of continuous 10-minute collection periods were started. At the midpoint of alternate urine collection periods, 4-ml arterial blood samples were taken for later chemical analysis. After centrifugation and decanting of the plasma, the blood cells were resuspended in 6% dextran in isotonic saline and returned to the animal at the time of the next blood sample. After 3-4 periods of relatively constant urine flow, each animal was volume-expanded 20% of estimated blood volume with 6% high molecular weight dextran in isotonic saline (6% Gentran 75, Travenol), the volume being infused by hand over a 5- to 6-minute period. Blood volume was estimated as 6% of body weight (Billman et al., 1983). The experiment was continued until urine flow declined to a value at least one-half of its peak diuresis value, or no sooner than 120 minutes post expansion.

At the end of the experiment, each animal was subjected to a number of interventions so that we might further verify cardiac denervation. These included the heart rate and arterial pressure responses to vena caval injections of phenylephrine (200 μg) and veratrine (20 μg), left atrial injections of veratrine (20 μg), and bilateral carotid occlusion. All drugs were dissolved in isotonic saline and their injections preceded by injections of saline vehicle. Responses were determined during the 15-second period after injection. The vena caval injections were given through the CVP catheter. A left thoracotomy was performed and left atrial injections were given through a catheter inserted directly into the left atrium via a pulmonary vein. A midline neck incision was made and both carotid arteries isolated and occluded for at least 20 seconds.

Analyses

Plasma and urine concentrations of creatinine and PAH were determined, using the methods described by Smith (1960), and creatinine and PAH clearances were calculated to estimate glomerular filtration rate and effective renal plasma flow, respectively. Sodium and potassium concentrations were determined by flame photometry (Instrumentation Laboratories 643) and osmolalities by freezing point depression (Advanced Instruments 3D II). These data were used to compute basic renal functions.

Since this study consisted of repeated measurements of each variable, changes within each group were evaluated statistically by using a single-factor analysis of variance with repeated measures design and the Newman-Keuls multiple range test. Comparisons between groups were assessed with the unpaired t-test. Probability values of less than 0.05 were considered statistically significant. All tests were from Winer (1962).

**RESULTS**

**Renal Responses**

The renal excretory responses to volume expansion in both the sham-operated and cardiac-denervated animals are shown in Figures 2 and 3. For convenience, “control” values referred to in this section represent the mean of the two control periods immediately preceding volume expansion.

Volume expansion effects on urine flow, sodium excretion, and the filtered load of sodium excreted are shown in Figure 2. Control values for these parameters did not differ between the two groups of animals.

In the sham-operated group, urine flow increased from 0.26 ± 0.05 to a peak value of 1.40 ± 0.29 ml/min, whereas, in the cardiac-denervated group, it increased from 0.38 ± 0.06 to 1.38 ± 0.27 ml/min. These urine flow responses and the mean times to

![Figure 2](image-url)
peak diuresis, 80.0 ± 16.8 and 98.0 ± 21.6 minutes in the sham-operated and cardiac-denervated animals, respectively, did not differ between the two groups. Sodium excretion increased from 24.5 ± 5.1 to a peak value of 125.3 ± 40.8 μEq/min in the sham-operated group and from 36.8 ± 9.3 to 131.2 ± 21.8 μEq/min in the cardiac-denervated group. These increases also did not differ significantly between the two groups. Furthermore, the mean times to peak natriuresis, 86.0 ± 18.8 and 108.0 ± 20.9 minutes in the sham-operated and cardiac-denervated animals, respectively, did not differ. The filtered load of sodium excreted also showed similar group responses, in that it increased from 1.59 ± 0.90 to 6.15 ± 2.32% in the sham-operated group and from 1.62 ± 0.50 to 5.30 ± 1.16% in the cardiac-denervated group.

Potassium excretion, osmolar clearance, and free water clearance responses to volume expansion are shown in Figure 3. Control values for these parameters also did not differ between the two groups.

In both groups of animals, potassium excretion showed a variable response in that it was significantly increased from control only during certain volume expansion periods. In the sham-operated animals, potassium excretion increased from 12.4 ± 2.0 to a peak value of 16.9 ± 4.5 μEq/min and, in the cardiac-denervated animals, from 12.5 ± 2.7 to 16.0 ± 3.1 μEq/min. These increases did not differ significantly from each other. Osmolar and free water clearance also increased similar amounts in each group. Osmolar clearance increased from 0.39 ± 0.04 to a peak of 1.07 ± 0.32 ml/min in the sham-operated animals and from 0.48 ± 0.09 to 1.05 ± 0.21 ml/min in the cardiac-denervated animals. Free water clearance increased from −0.13 ± 0.06 to 0.34 ± 0.17 ml/min in the sham-operated group and from −0.08 ± 0.04 to 0.44 ± 0.14 ml/min in the cardiac-denervated group.

Figures 2 and 3 also show that there were no group differences with respect to the time of onset of the renal excretory responses or pattern of the responses.

**Hemodynamic Responses**

The effects of volume expansion on mean arterial blood pressure, heart rate, and central venous pressure in both groups of animals are shown in Figure 4. Control values for arterial pressure and heart rate did not differ between the groups, but control central venous pressure was significantly lower in the cardiac-denervated animals. However, this difference may be due to the closeness of the individual values and subsequent small standard error in this group, and not of physiological significance.

Arterial pressure did not change with volume
expansion in the sham-operated group. In the cardiac-denervated group, arterial pressure did not change within the first 70 minutes after the volume was infused, but after that time, was slightly, but significantly, greater than control. There were, however, no significant group differences at any time period. Heart rate did not change in either group during the early volume expansion periods, but was significantly decreased in both groups during the latter periods of the experiment. Central venous pressure increased markedly in both groups immediately after the volume expansion. In the sham-operated animals, it increased from 6.6 ± 1.1 to 14.9 ± 1.7 cm H₂O and, in the cardiac-denervated animals, from 4.0 ± 0.2 to 12.1 ± 1.2 cm H₂O. Both of these increases were similar in magnitude. As the experiment progressed, this parameter slowly decreased back to control.

Figure 5 shows the effects of volume expansion on creatinine clearance, PAH clearance and filtration fraction. Control values for these parameters also did not differ between the two groups.

In both groups, creatinine clearance showed some tendency to increase after volume expansion, but this did not reach statistical significance at any time period (0.05 < p < 0.1). PAH clearance increased significantly, greater than control. There were, however, no significant group differences as indicated at P < 0.05. PAH clearance increased similar amounts in both groups of animals, first attaining statistical significance at 20–30 minutes. In the sham-operated animals, this parameter increased from 94.3 ± 18.9 to a peak value of 144.9 ± 24.8 ml/min, and in the cardiac-denervated animals, from 122.6 ± 10.2 to 163.0 ± 16.2 ml/min. Sixty minutes after the volume was infused, PAH clearance had returned to control in both groups. However, during the last three time periods of the experiment, this parameter was significantly higher in the cardiac-denervated animals than in the sham-operated animals. These volume expansion-induced increases in PAH clearance, unaccompanied by significant increases in creatinine clearance, were reflected by a decreased filtration fraction in both groups of animals. In the sham-operated group, filtration fraction maximally decreased from 0.17 ± 0.03 to 0.12 ± 0.03 and, in the cardiac-denervated group, from 0.13 ± 0.02 to 0.09 ± 0.01. Both of these changes were of similar magnitude.

Verification of Cardiac Denervation

As described in Methods, in addition to the verification of denervation by nerve stimulation at the time of surgery, further verification was obtained after the volume expansion experiment by determining the arterial pressure and heart rate responses of both groups of animals to injections of veratrine and phenylephrine and carotid occlusion. The results of these interventions are presented in Table 1.

Veratrine was used to test for afferent cardiac and pulmonary innervation since the veratrum alkaloids stimulate chemoreceptors in these areas which leads to a reflex decrease in blood pressure and heart rate (Dawes, 1947). Left atrial injection of veratrine caused significant decreases in blood pressure and heart rate in the sham-operated group but had no effect in the cardiac-denervated animals. Vena caval injection of veratrine also decreased blood pressure and heart rate in the intact animals. In the denervated group, this latter intervention caused a small, but still significant, decrease in blood pressure, but had no effect on heart rate. In these denervated animals, the slight depressor response obtained when veratrine is given close to the right side of the heart probably reflects veratrum-stimulating pulmonary chemoreceptors (Dawes, 1947) since the intrapericardial denervation technique (Randall et al., 1980) does not include this area.

Vena caval injection of phenylephrine and bilateral carotid artery occlusion were used to test for efferent innervation. Phenylephrine, an α-agonist, increased blood pressure in both groups of animals, but only the intact group showed the typical reflex bradycardia. Heart rate failed to change in the denervated group. Carotid occlusion, due to “unloading” of the carotid baroreceptors, increased blood pressure in both groups, but only the intact group responded with an increase in heart rate.

Injections of isotonic saline vehicle had no effect in either group.
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**TABLE 1**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Change in blood pressure (mm Hg)</th>
<th>Change in heart rate (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intact</td>
<td>Denervated</td>
</tr>
<tr>
<td>Veratrine (20 μg) Left atrium</td>
<td>-18.69 ± 3.83*</td>
<td>-1.56 ± 1.56†</td>
</tr>
<tr>
<td>Veratrine (20 μg) Vena cava</td>
<td>-24.31 ± 2.59*</td>
<td>-6.28 ± 1.20†</td>
</tr>
<tr>
<td>Phenylephrine (200 μg) Vena cava</td>
<td>+38.36 ± 5.40*</td>
<td>+53.00 ± 7.51*</td>
</tr>
<tr>
<td>Bilateral carotid artery occlusion</td>
<td>+32.66 ± 3.87*</td>
<td>+25.18 ± 5.63*</td>
</tr>
</tbody>
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Values are means ± SE.
* Indicates change is statistically significant (P < 0.05).
† Indicates significant group differences (P < 0.05).

**Discussion**

The results of the present study have demonstrated that, in the nonhuman primate, chronic cardiac denervation does not attenuate the renal excretory or hemodynamic responses to an acute blood volume expansion. However, it could be argued that the similar responses of our cardiac-denervated and sham-operated animals were because the thoracotomy procedure led to a change in compliance of the cardiac chambers such that cardiac receptors in the latter animals became less sensitive to volume changes. We do not feel this possibility is likely, however, since both groups of animals had responses that were similar in magnitude to those we have previously reported in nonthoracotomized intact monkeys (Peterson et al., 1983). Therefore, our results indicate that cardiac receptors are not necessary for eliciting the renal responses to hypervolemia in this species.

Evidence from previous studies has also suggested that cardiac or low pressure receptors may not play a major role in controlling renal salt and water excretion in the nonhuman primate. As mentioned previously, left atrial stretch receptors have been shown to have a low sensitivity in the monkey (Zucker and Gilmore, 1975), and localized stimulation of these receptors in either the anesthetized (Gilmore and Zucker, 1978) or conscious monkey (Cornish and Gilmore, 1982) fails to affect renal excretory function.

Studies examining the volumetric control of antidiuretic hormone (ADH) and renin secretion in the primate have also questioned the sensitivity of cardiopulmonary receptors. Nonhypotensive hemorrhage, a slow withdrawal of blood such that atrial pressure falls but arterial pressure remains fairly constant, markedly increases ADH and renin secretion in the dog (Gauer and Henry, 1976; Share, 1976), even with blood losses as low as 2.6% of blood volume (Claybaugh and Share, 1973). This type of hemorrhage is believed to primarily "unload" cardiopulmonary receptors rather than aortic and carotid sinus baroreceptors. In contrast, hemorrhage in the monkey of as much as 10% of blood volume fails to increase ADH unless arterial pressure falls (Arnauld et al., 1977). A similar low sensitivity for the volumetric control of ADH and renin during hemorrhage has also been demonstrated in humans (Brown et al., 1966; Hesse et al., 1968; Robertson and Mahr, 1972; Goetz, et al., 1974). In addition, lower body negative pressure (LBNP) at a level which markedly decreases central venous pressure fails to increase plasma ADH (Goldsmith et al., 1982) or renin levels (Mark et al., 1978) in man unless arterial pressure falls.

Studies determining ADH and renin changes during hypervolemia in the primate have been less conclusive. In the monkey, Gilmore et al. (1980) found that ADH fails to change when blood volume is expanded 30% whereas Billman et al. (1983) have recently reported that ADH and renin decrease with a 25% blood volume expansion. Experiments in humans using head-out water immersion, a hypervolemic stimulus in which blood is translocated to expand the cardiopulmonary blood volume and elicits a marked diuresis, have also been inconclusive in that both decreases (Epstein et al., 1980) and increases (Kravik et al., 1982) in ADH levels have been reported. However, none of the above-mentioned studies used a graded hypervolemic stimulus, so it is difficult to evaluate these results with regard to the sensitivity of the system. Although we did not measure ADH in the present experiments, both our cardiac-denervated and sham-operated monkeys showed similar increases in free water clearance with volume expansion. However, this does not necessarily mean that similar, if any, decreases in ADH occurred in both groups, since the macaque monkey does show vasopressin-resistant hyposthenuria when solute excretion rates are high (Tisher et al., 1972).
Even though a possible explanation for our results could be the low sensitivity of cardiac receptors in the primate, the possibility remains that the renal responses to the particular hypervolemic stimulus used in our study had no relationship to cardiac receptor sensitivity. Since a comparable study has never before been performed in the primate, our only evidence to support this latter possibility must come from previous studies on the dog, a species where cardiac receptors are quite sensitive to blood volume changes. However, mixed results have been reported in the dog, possibly because of differences in cardiac denervation techniques or volume expansion protocols. When comparing our results only with studies that also utilized an intrapericardial surgical denervation it appears that, even in the dog, cardiac receptors are not necessary for eliciting the renal responses to volume expansion. Kaczmarczyk et al. (1981) and Fater et al. (1982) both demonstrated that cardiac denervation abolished the diuretic and natriuretic responses to localized atrial stretch but did not affect the responses to volume expansion. In contrast, Mulcahy et al. (1973, 1975), in two separate studies, reported that volume expansion caused an exaggerated diuresis (Mulcahy et al., 1973) and natriuresis (Mulcahy et al., 1975) in cardiac-denervated dogs. These latter authors concluded that their results were consistent with the hypothesis that cardiac afferent nerves play a role in controlling renal excretion. However, their results do not agree with the prevailing opinion that stimulation of canine cardiac receptors activates mechanisms to increase salt and water excretion (Gauer and Henry, 1976; Linden, 1976), since they would imply that the opposite occurs. However, their results may be partially explained by the fact that the denervated dogs in one of their studies (Mulcahy et al., 1973) had elevated plasma volumes and baseline urine flows, which may have accounted for the exaggerated renal responses to volume expansion.

Since our results have shown that receptors in the heart are not necessary for eliciting the renal responses to volume expansion in the monkey, the question arises as to which regions of the vasculature, if any, function as "blood volume receptors" in this species. The previously mentioned observations of Arnauld et al. (1977), Mark et al. (1978), and Goldsmith et al. (1982) that volumetric control of ADH and renin secretion in the primate seem to depend more on arterial pressure changes than central venous pressure changes would imply that the link between blood volume and release of these hormones is through high pressure baroreceptors in the aortic arch and carotid sinuses. Furthermore, Echtenkamp et al. (1980) have shown that vagotomized monkeys still show decreases in efferent renal nerve activity with volume expansion, a response which was abolished when these animals were subsequently sinoaortic denervated. However, in our animals, the resting level of renal efferent nerve activity may have been so low that volume expansion decreases in this activity may be insignificant with respect to effects on renal excretion. In fact, Gagnon et al. (1982) has recently suggested that renal nerve activity may be depressed by barbiturate anesthesia, which could account for the higher baseline sodium excretion seen in our animals compared with the conscious monkeys in the study of Cornish and Gilmore (1982). Nevertheless, the unattenuated renal responses to volume expansion in our cardiac-denervated monkeys could be due to the fact that their high pressure baroreceptor mechanisms remained intact, and mechanisms other then the renal nerves caused the responses. However, assessing the relative importance of a particular group of intravascular receptors may be more complex than this, in that Gilmore et al. (1979) has shown that vagotomy and sinoaortic denervation does not affect the renal responses of the monkey to volume expansion, thus suggesting that vagal and high pressure baroreceptor pathways are not necessary for eliciting the responses either. We have, however, recently reported that an extensive cardiopulmonary receptor denervation and baroreceptor denervation consisting of bilateral cervical vagotomy, sinoaortic denervation, and thoracic dorsal rhizotomy does blunt the renal excretory responses to dextran volume expansion in the monkey (Peterson et al., 1983). When this latter finding is considered, along with the results of the present study, the vagotomy-sinoaortic denervation study of Gilmore et al. (1979), and the thoracic sympathectomy study of Cornish and Gilmore (1983), it appears that, in the monkey, selective denervation of certain intravascular receptors has no effect on the volume expansion responses, whereas a more extensive denervation does. This would suggest that the monkeys possesses functionally redundant volume receptor mechanisms. That is, with ablation of either cardiac, vagal-sinoaortic, or thoracic spinal neural pathways, the remaining, intact receptor mechanisms can fully compensate for removal of the latter and elicit unattenuated responses to volume expansion. This means, however, that with volume expansion as the volume stimulus, it may be impossible to determine whether one particular group of intravascular receptors has greater relative importance.

It should be also noted that the purpose of the present study was quite specific, to determine if cardiac receptors are necessary for eliciting normal renal responses to an acute hypervolemic stimulus. Even though our results were negative, this does not necessarily imply that these receptors do not play a role in the primate in the maintenance of long-term body fluid or circulatory homeostasis. In this regard, Willman et al. (1965) reported elevated blood volumes in cardiac autotransplanted male baboons. Since we did not measure these volumes, we do not know whether they were elevated in our denervated animals, although the recovery time after denervation (14–30 days) may have been too short to detect any differences. Furthermore, there is evi-
dence to suggest that cardiopulmonary receptors do have effects on peripheral blood flow in man (Abboud and Mark, 1979; Walker et al., 1980). With respect to this point, the previously cited studies of Mark et al. (1977) and Goldsmith et al. (1983) are of interest. As discussed earlier, these investigators reported that low levels of LBNP decreased central venous pressure, but had no effect on plasma renin and ADH levels, respectively, unless the stimulus caused arterial pressure to decrease. However, fore-

arm blood flow decreased (Mark et al., 1978) and plasma norepinephrine rose (Goldsmith et al., 1982) at all levels of LBNP. This suggests that, in humans, cardiopulmonary receptor control of vascular resistance and adrenal medullary secretion are quite sensitive, even though control of renin and ADH release may not be. Since, in the monkey, this particular area has not been studied, future work seems warranted, particularly because of the nonhuman primate's potential for invasive studies.

In conclusion, the results of the present study have shown that the cardiac-denervated nonhuman primate does not show attenuated renal responses to an acute blood volume expansion. This indicates that the renal effects of this hypervolemic stimulus do not depend on innervated cardiac receptors, at least when other intravascular receptor pathways remain intact. Future work in this area is needed to determine whether cardiac receptors in this species play any role in the long-term maintenance of body fluid homeostasis or control of peripheral blood flow.

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