primate to immersion, they do not traverse the vagus nerve. However, it is possible, as suggested some years ago by one of us, that cardiac sympathetic afferents may participate in the control of sodium excretion under conditions of central hypervolemia.\(^9\)

It should be noted that our conclusion is that vagal pathways are not necessary for the renal responses to immersion in the nonhuman primate and thus probably in man, rather than that vagal pathways do not contribute to the responses. Although the results are consistent with the latter possibility, the possibility exists that the first immersion (prevagotomy) predisposed the monkey to a potentiated response during the second immersion (post-vagotomy) which was not seen because the vagi were sectioned. That is to say, although the vagi are not necessary for the renal responses to immersion, they do contribute. Against this possibility are two qualitative observations: (1) The one monkey that was vagotomized before the first immersion showed a substantial natriuresis and diuresis (Fig. 1). (2) There tends in general to be a greater renal response to immersion following vagotomy (Table 1).

There is one aspect of the hemodynamic consequences of immersion that has been ignored by previous authors. This is the failure of the human\(^1\) and, indeed, of the monkey, to respond to immersion with a tachycardia despite a substantial increase in ventricular volume, central venous pressure, and, presumably, atrial pressure. It appears that, although a Bainbridge reflex is clearly demonstrable in the dog,\(^10\) it plays little or no physiological role in the primate.

**Acknowledgments**

The experiments were carried out with the assistance of Dr. M. Ellington and Phyllis Anding.

**References**


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**Failure of Left Atrial Distension to Alter Renal Function in the Nonhuman Primate**

JOSEPH P. GILMORE AND IRVING H. ZUCKER

**SUMMARY** Experiments were undertaken to determine the influence of increasing left atrial pressure on renal function in the nonhuman primate. Significant elevations of left atrial pressure, produced by using an intra-atrial balloon, had no effect on salt or water excretion, renal plasma flow, or glomerular filtration rate. There were no significant changes in heart rate or blood pressure. We conclude that, unlike those in the dog, atrial receptors in the nonhuman primate play little or no role in modulating salt and water excretion.

AS THE RESULT of the early studies of Henry et al.\(^1\) and the subsequent work of others,\(^2-5\) the concept that atrial stretch receptors play an important role in modulating water excretion has become firmly established in the literature. With few exceptions, these studies have used...
determine whether there is a smaller renal response to distension of the atrium in the nonhuman primate than in the dog.

**Methods**

The experiments were carried out with two *Macaca fasicularis* and three *Macaca mulata* monkeys ranging in weight from 2.8 to 5.8 kg. They were sedated with ketamine HCl (5 mg/kg) administered intramuscularly, followed by pentobarbital sodium, 30 mg/kg, administered intravenously and supplemented as needed throughout the experiment. A femoral vein was cannulated to administer solutions; one femoral artery was cannulated to obtain blood samples and the other to record arterial blood pressure with a transducer-tipped catheter. The ureters were approached through flank incisions and cannulated with polyethylene tubing. A tracheostomy was performed and the monkey was placed on positive-pressure ventilation with room air supplemented with 100% oxygen. The left chest was opened through the 4th intercostal space and the pericardium was incised. A number 8 Foley retention catheter was placed through the left atrial appendage into the atrium, and a transducer-tipped catheter was placed in the left atrium through a small pulmonary vein. The dynamic characteristics of this catheter system has been described by us previously. The chest was left open and covered with plastic wrapping. Rectal temperature was maintained at 37°C by a thermostatically controlled circulating hot-water pad on which the monkey lay. Blood gases (Pao2, Paco2, and pH) were monitored periodically throughout the experiment and kept within normal limits.

The clearances of creatinine and para-aminom hippuric acid (PAH) were determined by the standard constant infusion technique. They were infused at the rate of 0.75 ml/min with the plasma creatinine concentration maintained between 10 and 15 mg/100 ml, and plasma PAH concentration maintained between 1 and 3 mg/100 ml. A 4-ml blood sample was obtained at the midpoints of the appropriate urine collections and, after the plasma was separated, the red cells were reconstituted with 6% dextran and then returned to the monkey intravenously. One hour after the completion of surgery and the beginning of the creatinine and PAH infusion, timed collection of urine samples was begun. After 30-40 minutes of relatively constant urine excretion, the balloon on the Foley catheter was inflated with 1-2 ml of saline in order to produce the largest elevation of left atrial pressure (LAP) that could be obtained with a minimal decrease in mean arterial pressure (MABP). After 30-40 minutes, the balloon was deflated, a new steady state achieved, and a second inflation carried out. The monkey was killed at the end of the experiment and the kidneys removed and weighed. Osmolality was determined by freezing point depression, sodium and potassium by flame photometry, and creatinine and PAH with an autoanalyzer. The paired t-test was employed for statistical analysis.

**Results**

The results of the experiments are shown in Table 1. The preinflation values represent the values obtained during the period that immediately precedes balloon inflation. The inflation values are those obtained during the period immediately prior to balloon deflation, whereas the postinflation values usually were obtained 20 minutes after balloon deflation. The control hemodynamic and renal data are in good agreement with those reported by others for both conscious and anesthetized *Macques.*

<table>
<thead>
<tr>
<th>Table 1 Effect of Inflation of a Balloon in the Left Atrium on Renal Function in the Nonhuman Primate</th>
</tr>
</thead>
<tbody>
<tr>
<td>V (ml/min)</td>
</tr>
<tr>
<td>(n = 10)</td>
</tr>
<tr>
<td>C_H2O (ml/min)</td>
</tr>
<tr>
<td>(n = 7)</td>
</tr>
<tr>
<td>C_Na (ml/min)</td>
</tr>
<tr>
<td>(n = 10)</td>
</tr>
<tr>
<td>C_K (mEq/l)</td>
</tr>
<tr>
<td>(n = 7)</td>
</tr>
<tr>
<td>C_HCO3 (mEq/l)</td>
</tr>
<tr>
<td>(n = 7)</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
</tr>
<tr>
<td>(n = 10)</td>
</tr>
</tbody>
</table>

In parentheses, n = number of balloon inflations.

* Significantly different from preinflation value (P < 0.005).
With the exception of LAP, inflation of the balloon had no significant effect on any of the measured parameters. Inflation of the balloon increased left atrial pressure by an average of 7.8 cm H$_2$O ($P < 0.005$). When atrial pressure increased, arterial pressure usually decreased initially but, shortly thereafter, returned to or toward the control level so that, in the new steady state, it was not significantly changed. Figure 1 shows results of an experiment in which inflation of the balloon had essentially no effect on blood pressure even though mean left atrial pressure was increased by 14.5 cm H$_2$O. No difference in response was observed between _M. fasicularis_ and _M. mullata_. The changes in urine flow were variable; it increased during five, decreased during four, and showed no change during one inflation. In addition, there was no relation between the extent of the increase in LAP and the change in urine flow (Table 2).

**Discussion**

The experiments reported here clearly demonstrate that alterations of left atrial pressure over a wide physiological range have no consistent influence on salt and water excretion in the nonhuman primate. These findings are in contrast with results of studies on the dog which have demonstrated a consistent diuresis, although inconsistent natriuresis, in response to left atrial distension. In order to demonstrate that, in our hands, distension of the dog atrium induces a significant diuresis, 19 left atrial balloon distensions were carried out in 8 normal dogs under the same experimental conditions used in the present study, i.e., thoracotomy, positive-pressure respiration, etc. (unpublished observations). When left atrial pressure was increased by 9.8 ± 0.87 cm H$_2$O, urine flow increased by 0.59 ± 0.19 ml/min ($P < 0.05$), and the latter change was due primarily to an increase in free-water clearance. This increase in atrial pressure in the dog was not significantly different from the increase in atrial pressure that was induced in the present experiments. It is important to note that our failure to find an increase in urine flow was not associated with a significant decrease in creatinine clearance or blood pressure, both of which could lead to a reduction in urinary excretion. In fact, in the dog, decreases in blood pressure of 20 mm Hg as a result of inflating a balloon in the left atrium are still associated with significant increases in urine flow.

To demonstrate that the monkey was capable of responding to an intervention which increases salt and water excretion, two additional monkeys were studied under the following conditions. They were prepared as described above for atrial balloon inflations, and the chest was closed. They were then put into a tank in the seated position for subsequent water immersion to the neck. We have found that this latter procedure induces a consistent and significant increase in central venous pressure and urine flow, as it does in man. The monkeys then were immersed and the changes in urine flow and left atrial pressure noted. The tank was then emptied, a new steady state achieved, and the left atrial balloon inflated until LAP increased by approximately the same amount as during immersion. The results were as follows. During immersion, left atrial pressure increased by 13.0 cm H$_2$O, urine flow by 200%, and sodium excretion by 500%. In contrast, left atrial balloon inflation increased atrial pressure by 9.5 cm H$_2$O, urine flow by 25%, and sodium excretion by 10%.

Our failure to find consistent or significant increases in urine flow in the monkeys in response to significant elevations in LAP is consistent with our previous finding that atrial receptors in the monkey are substantially less sensitive than those in the dog. In that study we found that, under resting conditions, the discharge of atrial receptors/cm H$_2$O LAP is significantly less in the monkey than in the dog. In addition, an increase in LAP of 5 cm H$_2$O increased atrial receptor discharge in the monkey by only four impulses/cycle, whereas, in the dog, discharge increased by 20 impulses/cycle.

In addition to producing a consistent diuresis, atrial distension also has been shown to produce a consistent tachycardia in the dog.  The failure to show elevations in heart rate in response to atrial distension in the present study is in accord with our previous studies in which

**Table 2**  Relationship between the Change in Left Atrial Pressure and Urine Flow in the Nonhuman Primate in Response to Left Atrial Distension

<table>
<thead>
<tr>
<th>Δ LAP (cm H$_2$O)</th>
<th>Δ V (ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.0</td>
<td>+0.005</td>
</tr>
<tr>
<td>7.0</td>
<td>+0.020</td>
</tr>
<tr>
<td>10.0</td>
<td>+0.410</td>
</tr>
<tr>
<td>5.5</td>
<td>+0.030</td>
</tr>
<tr>
<td>5.0</td>
<td>+0.065</td>
</tr>
<tr>
<td>3.5</td>
<td>-0.070</td>
</tr>
<tr>
<td>12.5</td>
<td>+0.065</td>
</tr>
<tr>
<td>9.0</td>
<td>0.00</td>
</tr>
<tr>
<td>14.5</td>
<td>-0.03</td>
</tr>
</tbody>
</table>

**Figure 1**  Influence of inflating a balloon in the left atrium of a monkey on left atrial pressure (LAP) and mean arterial pressure (AP). Upward deflection of respiration is inspiration. Fast tracings at 25 mm/sec and slow tracings at 1 mm/sec. Horizontal arrow denotes the time it took for the left atrial balloon to be inflated with 1 ml of saline.
elevations of LAP induced by volume expansion in the nonhuman primate were not associated with a tachycardia. In this regard, it is of interest that during immersion of man or the nonhuman primate, heart rate changes little or not at all, despite substantial elevations of central venous pressure.

As we have suggested previously, this difference in atrial receptor sensitivity between the dog and primate may be related to the evolution of an upright or semiupright posture of the latter. If we assume that the primate is in an upright to semiupright posture a greater proportion of the time than the dog, a highly sensitive atrial stretch receptor mechanism would be homeostatically inappropriate because wide fluctuations in ADH release and renal sympathetic tone could result. Since there is no evidence that atrial stretch receptors adapt under normal conditions, prolonged recumbency could lead to a substantial inhibition of ADH release and a diuresis in the primate if sensitivity were the same as in the dog. This hypothesis is supported by the work of Goetz et al. who failed to observe a change in plasma ADH levels in humans undergoing a nonhypotensive hemorrhage, whereas this maneuver has been shown to elevate plasma ADH substantially in dogs. These differences between the dog and the primate raise questions as to the usefulness of the dog as a model for man for studying the neurohumoral control of blood volume. Further, our results obtained from the nonhuman primate suggest that left atrial distension may have little influence on salt and water excretion or heart rate in man.

Acknowledgments

The experiments were carried out with the excellent assistance of Dr. Morris Ellington, Phillis Anding, and John Dietz.

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J P Gilmore and I H Zucker

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