THE EFFECT OF HIGH AND LOW SODIUM DIETS UPON RENIN RELEASE AND BLOOD PRESSURE IN CHRONICALLY CANNULATED RABBITS DURING HEMORRHAGE AND VOLUME EXPANSION CONDITIONS

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ABSTRACT

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The Effect of High and Low Sodium Diets upon Renin Release and Blood Pressure in Chronically Cannulated Rabbits during Hemorrhage and Volume Expansion Conditions

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Two groups of male New Zealand white rabbits weighing 2.5-3.9 kg were maintained on high and low sodium diets for a period of 3 weeks. Urine samples were collected daily during the 3-week period from each rabbit and analyzed for sodium and potassium concentrations. A control group of rabbits was also maintained over a 3-week period, with daily urine collections. Each rabbit was anesthetized with sodium pentobarbital (35 mg/kg) via the marginal ear vein. Following the loss of consciousness, the right external jugular vein was cannulated in order to induce volume expansion and depletion. The left common carotid artery was also cannulated in order to monitor arterial blood pressure during the volume expanded and depleted procedures.

Urine from rabbits on the high sodium diet contained high concentrations of potassium and sodium, whereas urine
from rabbits on the low sodium diet had very low sodium and potassium levels as compared to control group readings. An elevated arterial blood pressure was observed in the high sodium rabbits and the low sodium rabbits had arterial blood pressures below control levels. Renin levels were slightly elevated during volume expansion in the high sodium rabbits but was significantly decreased in the low sodium and control groups. During volume depletion, renin levels were observed to decrease in the high sodium rabbits but increased significantly in the low sodium and control rabbits respectively.
ACKNOWLEDGMENTS

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CHAPTER I

INTRODUCTION

Variation in the intake of sodium has been shown to be inversely related to plasma renin and angiotensin activity (1). Such observations have led to correlations that indicate relationships between the renal hormonal system and the regulation of sodium balance. Excessive sodium ingestion or retention within the body seems to serve as a common denominator in renal or essential hypertension, indicating that sodium-exploited diets could result in higher blood pressure levels and decreased plasma renin activity (2,3).

Maintenance of blood volume is greatly dependent upon sodium levels within the circulatory and extracellular spaces (4,5). However, under sodium-loaded conditions, blood pressure is expected to rise above normal values, whereas in sodium-deprived conditions hypotensive levels may result from decreased plasma and extracellular fluid volumes. Thus, blood volume and blood pressure appear to be inversely related (6).

High renin levels are found to develop during decreased blood volume along with increased sodium retention (7,8). This is believed to cause the blood pressure to elevate toward normal values. This shared role could possibly illustrate the dual responsibility and balance between the renal hormonal system and extracellular sodium balances. It has been observed that the effects of volume expansion and hemorrhage on renal
hormonal and sodium and potassium levels might contribute to the quantitative analysis of the operations of components of the cardiovascular regulatory mechanism (9).

Volume expansion conditions produced through gradual perfusion of a plasma substitute tend to induce similar fluid balance problems for the animal system as that encountered during salt-loaded conditions. Renin values are expected to correspond similarly if all other parameters are controlled; however, high sodium levels tend to suppress renin release (3,8).

During volume depletion renin release seemed to increase (10,11) in order that blood pressure values might return to near normal averages, due to a low sodium diet which caused a decreased blood volume (12). Low sodium levels within the system, had little effect on repression of renin release and renin values were expected to rise, as would sodium retention, in order that some similarity between normal blood pressures and resultant pressures could be obtained.

This study was undertaken to reveal the effects of high, low and control sodium diets upon renin release and direct blood pressure in rabbits. Hemorrhage and volume expansion conditions were induced in order that comparative studies of their effects on renin release in the three dietary groups could be observed. Arterial blood pressure readings were compared to reveal dietary differences and increases or decreases of blood volume upon its levels. Urine sodium and potassium
levels were monitored to observe retention or expulsion during stress of the experimental and dietary conditions.
CHAPTER II

REVIEW OF LITERATURE

In recent years, studies have well established that the renin-angiotensin system plays a major role in the control and maintenance (homeostasis) of arterial blood pressure. This system has been shown by Page and Bumpus (13), and Peart (14) to react swiftly and consistently in correcting such adverse conditions as volume depletion or repletion. Studies by Mott (15,16) showed that blood pressure in humans, rabbits, kittens and cats is inversely related to blood volume. Arterial pressures were seen to fall proportionally with blood volume and following the completion of blood loss, were able to rise to steady levels somewhat below control values.

Huidobro et al. (17) showed that when blood pressure was lowered by hemorrhage or shock, renin was released by the intact kidney of anesthesized dogs. Similar results were found by Lever and Robertson (18) in rabbits. These findings suggested that the kidney participates in the regulation of arterial blood pressure and that renin appears to be the substance which the body uses to initiate some phases of homeostasis. Further studies by Hamilton and Collins (19) in dogs and Weber et al. (10) in rabbits corroborated these findings.

Bunag et al. (20) suggested that many factors are involved in the release of renin such as decreased blood volume
and changes in sodium balance. Studies performed by Brown et al. (8) showed that plasma volume in man and dogs is often reduced under certain conditions of sodium deprivation and as a result plasma renin concentration is increased. These findings were substantiated by studies in dogs performed by Bunag et al. (20) which showed consistent release of renin during hemorrhage in sodium-deprived animals. Brown et al. (8) found circulating renin levels in human patients following hemorrhage to be consistently greater than the normal mean values.

Pettinger et al. (2) and Miksche et al. (21) found that ingestion of a low sodium diet by rats elevated plasma renin activity, and that this elevation could be reversed or diminished by adding increments of sodium to the diet. These findings were substantiated in work performed by Gocke (1) in man, in which it was shown that plasma angiotensin levels are inversely related to sodium intake.

Investigations by Hodge et al. (7) in dogs revealed that renin is released during hemorrhagic shock and the concentration of angiotensin in the blood is increased during moderate hemorrhage. It was concluded that alterations of blood volume bring about changes in the rate of generation of angiotensin and demonstrates that the renin-angiotensin system is linked to the antihypertensive action of a normal kidney and acts synergistically with it. Tobian (22) indicated that the renin-angiotensin system is important in the hour to hour regulation of blood pressure, and that renin release is stimulated whenever
pressure is low at the terminal end of the arterioles.

Skinner et al. (23) found that renin secretion was increased during small reductions in renal perfusion pressure, and that this secretion is controlled by a pressure-dependent mechanism that responds rapidly to small changes in mean systemic arterial pressure. This suggests that renal baroreceptors might play an important role in the initiation of renin release. Studies by Korner et al. (24) in rabbits; Bunag et al. (19) and Vatner et al. (25) in dogs lend evidence to this suggestion and reveal an important role for baroreceptors in the homeostatic mechanism. Guyton et al. (5) found that the baroreceptor control system and the renin-angiotensin system have direct or indirect effects on different aspects of fluid balance and that they participate in controlling the long range level of arterial blood pressure.

Studies by Chalmers et al. (26) in rabbits further indicated that reflex autonomic effector activity minimizes circulatory effects caused by severe hemorrhage in rabbits. These studies illustrated the importance of baroreceptor mechanisms in volume related responses and their possible cooperation with the renin-angiotensin system. According to Hodge et al. (27) circulating angiotensin is reduced in dogs if renin secretion is lowered, which suggests that an increase in blood volume brings about a decrease in the output of renin from the kidneys. Further studies by Brown et al. (2) suggested that renin secretion might be controlled by changes in the
osmolarity of the tubular fluid in contact with the macula densa, since during sodium loading both the osmolarity of early distal tubular fluid and plasma renin concentration fall.

A close relationship exists between sodium and body fluid volumes, especially extracellular fluid volume. According to Guyton et al. (5), any factor which alters fluid volume causes parallel and almost proportional changes in body sodium at the same time. Much evidence seems to point to excessive sodium ingestion or retention within the body as the common denominator of several forms of hypertension (Vander et al.). Studies by Vatner et al. (24) with dogs indicated that volume loading resulted in an increase in arterial blood pressure. This correlates with studies performed in rats by Gross (28) in which sodium was thought to play a permissive role due to constriction of one or both renal arteries. Brown et al. (2,8) in studies on man found that sodium rich diets produced no increase in the size and granularity of the juxtaglomerular cells, and thus renin levels were not elevated.

Studies performed with sheep by Norman (4) supported the concept that sodium retention causes hypertension almost entirely because of sodium induced expansion of the extracellular fluid volume. In both experimental animals and humans a prolonged increase in the total exchangeable sodium is usually associated with hypertension. Thus, it was concluded from these findings that increased sodium ion concentration has little, if
any, non-volume related effect on arterial pressure. On the other hand, sodium induced fluid volume expansion has a marked effect of elevating arterial pressure.

Investigations with dogs by Douglas et al. (3) revealed that increased salt intake resulted in arterial pressure increases to hypertensive levels. This was later corroborated by Vatner et al. (25) in dogs. Both studies revealed repressed renin levels similar to findings reported by Brown et al. (2,8) in man and dogs.
CHAPTER III

MATERIALS AND METHODS

Twenty-six male New Zealand white rabbits weighing 2.5-3.9 kg and obtained from a local breeding farm, were maintained on normal, high and low sodium diets for a period of 14 to 21 days. The normal and high sodium diets consisted of 150 g/day of Purina laboratory chow for rabbits (K⁺, 1.51 mEq/l; Na⁺, 0.40 mEq/l) whereas, the sodium deficient diet (150 g/day) was prepared by Teklad Test Diet Laboratories, Madison, Wisconsin. The diets were supplemented with 400 ml/day of distilled H₂O for the control and low sodium animals and with 1.5% saline solution for the high sodium diet group.

Urine samples were collected daily from each rabbit and later analyzed for sodium and potassium concentrations with an atomic absorption spectrophotometer (Model-107, Perkin-Elmer, Atlanta, Georgia). The rabbits were fasted for 24 hr prior to anesthetization with sodium pentobarbital. The injections were given via the marginal ear vein in concentration of 35 mg/kg body weight. The rabbits were allowed to lose consciousness and were restrained to a surgical board; then the ventral surface of the cervical area was shaved and prepared for surgery. Merthiolate (Tincture) was used to clean the shaved area. A 2 to 3 inch sagittal incision was made along the ventral midline of the cervical region. Using blunt forceps, superficial fascia and other connective tissue
were separated from the sternomastoid muscle along the ventrolateral surface of the neck. This technique freed the large external jugular vein. The left common carotid artery was found between the sternohyoideus, hyoideus and omohyoideus muscles. It was then freed from the surrounding tissue and adjacent vagus nerve. Approximately 3 to 5 cm of the vessels were exposed prior to cannulation. Ligatures were then placed upon each at the most accessible cephalad position. Rubber tipped forceps were then placed at the most posteriorly exposed portion of each vessel to impede blood flow through the isolated areas. The vessels were then stretched and a small incision, not greater than one-third of the vessel's diameter was made on the anteriorly exposed surface. The carotid cannula was placed 7.5 cm into the artery to reach the approximate level of the aorta. The jugular cannula was inserted approximately 9.0 cm into the vein to the level of the right auricle.

Dow-Corning medical grade silastic tubing, selected because of its non-reactivity in tissue (# 602-205, .04 in. I. D. x .085 in. O. D.) was used for the jugular vein and (# 602-135, .02 in. I. D. x .037 in. O. D.) carotid artery intubation. The tubing was prepared for cannulation through washing with soapy water (non-oily base) and rinsing several times with distilled water. The tubing was stored in Zepharin chloride (Benzalkonium chloride antiseptic, 1:1000 dilution) until approximately 1 hr prior to surgery, then rinsed in a
sterile physiological saline solution. To prevent dislodging, both cannulas were anchored in position through the use of a 1.5 cm² (0.3 in thick) patch of Dow-Corning (#501-5) silastic sheeting. These anchors were attached to the cannulas with Dow-Corning (#891) medical adhesive.

Ligatures were then loosely tied around the inserted cannulas to prevent incidental loss of blood. The cannulas were tested for patency and flushed with a heparin-saline solution (0.9%). Starting at the site of the initial ventral skin incision a 3 to 4 cm pouch was made in the subcutaneous layer to the middle of the neck over the spine. A small incision was then made and the catheters exteriorated through the opening. The ventral skin incision was then closed with suture. Following a recovery period of about 1 hr, the initial (control) blood sample (2 ml) was collected from each rabbit into a heparinated tube via the carotid cannula. The samples were centrifuged and the plasma was collected and stored for later analysis.

The carotid cannula was then attached to a pressure transducer (Narco-Bio Systems Inc., Houston Texas) via a three way stopcock valve and to a heparinated syringe for cannula flushing. The transducer was attached via a strain gage preamplifier (Model 312, Narco-Bio Systems Inc., Houston, Texas) to a desk model Physiograph (DMP-4B, Narco-Bio Systems Inc., Houston, Texas). This arrangement allowed for the direct measurement of carotid artery pressure.
The venous cannula was attached directly to an infusion-withdrawal pump (Harvard Apparatus) in order to volume expand and hemorrhage the rabbits. Control blood pressure was monitored for 15 to 20 min or until the blood pressure stabilized. Volume expansion was effected through the venous infusion of 25 ml of a protein-buffered saline perfusate (37 C) at a rate of 1.15 M Na₂HPO₄ solution (pH 7.4), 4-6 mEq/l of potassium and 10 g/200 ml sterile physiological saline of human serum protein albumin (Lot #400601; Calbio Chem., San Diego, California). Upon the completion of infusion a 2 ml blood sample (post-expansion) was collected via the arterial cannula, and stored for future analysis. A 5 min period was allowed to elapse which provided an interval for pressure stabilization by the rabbits.

Fifty ml of blood was removed from the rabbits system via the jugular cannula at a rate of 0.21 ml/min for 4 hr. Following the completion of hemorrhage a 2 ml blood sample was collected and stored. Plasma was obtained from each blood sample and analyzed for sodium and potassium concentrations using Moni-Trol I standard (Dade Division, American Hospital Supply Corp., Miami, Florida) on the atomic absorption spectrophotometer. The sodium and potassium readings obtained for each group were evaluated using an Olivetti P-652 microcomputer and graphed to illustrate dietary influences on plasma ion concentrations. Plasma renin activity was also determined for each plasma sample by incubating 1.0
ml of the sample with 0.2 M maleate buffer (pH 6.0), 10 ml of Dimercaprol and 10 ml of hydroxyquinoline. A 1.0 ml aliquot of this sample incubation mixture was incubated for 1.0 hr at 37 C and another 1.0 ml sample incubated at 4 C. The amount of angiotensin I formed in each incubation tube was measured by radioimmunoassay (RIA) using the New England Nuclear Kit (Angiotensin I, RIA Kit, NEA-022).

A Beckman LS-230 liquid scintillation system with teletype was used to record the angiotensin I levels in each plasma sample. The data were then used with the Olivetti renin assay program (Olivetti P-652 Microcomputer; LN-20 Tape system) to determine plasma renin activity. The values obtained from this procedure revealed renin activity in all phases of the experiment, illustrating dietary influences and volume variations upon plasma concentrations.
CHAPTER IV

EXPERIMENTAL RESULTS

Statistical analysis of standard deviation, plasma renin, sodium and potassium levels, as well as urine sodium and potassium levels, were computed using the Olivetti P-652 Microcomputer and LN-20 Tape System. Further statistical and analytical data were computed and compiled at the Atlanta University Computer Center, Atlanta, Georgia.

Control Sodium Group

The blood pressure of the control group rabbits during short term volume expansion (1.16 ml/min for 10.5 min) was seen to decrease (Fig. 1) from a normal value of 70 to 62 mmHg. The decreasing blood pressure reversed after 6 ml of the perfusate had been infused and an increase was recorded. A near normal value of 67 mmHg was attained following the infusion of 9 ml of the perfusate. The return to near normal pressure values required approximately 7.5 min and was maintained throughout the infusion.

The average pressure of the control rabbits decreased from 62 to 54 mmHg (Fig. 2) following a volume depletion of 3 ml. The arterial pressure then increased to 58 mmHg at 6 ml of hemorrhage and established the highest pressure reading attained by the group during volume depletion. A steady decline in pressure was observed until a hemorrhage volume of 21 ml and an arterial pressure of 44 mmHg was reached. A
slight increase in pressure to 48 mmHg occurred at the completion (24 ml) of hemorrhage.

Plasma renin values (Fig. 3) decreased during volume expansion (5.2 to 1.9 ng/ml/hr). Following infusion a mean value of 62 mmHg was maintained by the control sodium animals and hemorrhage (1.9 ml/min for 12 min) was begun. Plasma renin levels (Fig. 3) increased during volume depletion (1.9 to 7.9 ng/ml/hr) and a slight rise in arterial pressure (43 to 49 mmHg) was recorded.

Long term volume expansion (0.21 ml/min for 2.0 hr) resulted in a gradual decrease in the pressure (Fig. 4) of the control rabbits from 71 to 67 mmHg after 15 ml of the perfusate had been infused. The average arterial pressure then rose to 69 mmHg following the infusion of 20 ml of the perfusate. The arterial pressure then decreased during the final 5 ml infusion from 69 to 59 mmHg.

Long term volume depletion (0.21 ml/min) was accomplished over a four hour period in which the arterial pressure of the control group (Fig. 5) remained relatively stable until a hemorrhage volume of 5 ml had been reached. A sharp decrease in pressure from 51 to 44 mmHg occurred at a hemorrhage volume of 10 ml and was maintained until a volume of 15 ml had been removed from the system. The arterial pressure then increased to 53 mmHg, which was slightly higher than normal pressure, and gradually decreased to 48 mmHg. The arterial pressure remained relatively stable until 35 ml hemorrhage had been
accomplished. At 40 ml the highest arterial pressure was attained by the control group (64 mmHg). The arterial pressure gradually declined as the hemorrhage volume reached 45 ml, and reached its lowest value following a total hemorrhage volume of 50 ml.

The control plasma renin values (Fig. 6) were seen to decrease during volume expansion (4.8 to 2.6 ng/ml/hr) and rise during hemorrhage (2.6 to 9.1 ng/ml/hr). Plasma sodium levels (Fig. 7) increased from their initial value of 71 to 73 mEq/l following the volume expansion period. This value increased to 84 mEq/l following the completion of volume depletion. Potassium values (Fig. 8) decreased from initial readings of 6.3 to 6.2 mEq/l in the post-volume expansion period. The decline reversed and a value of 8.3 mEq/l was observed in the post-hemorrhage plasma.

Urine sodium values (Fig. 9) in the group remained relatively stable throughout the dietary period. An average value of 98 mEq/l was maintained. Urine potassium levels (Fig. 10) fluctuated throughout the dietary period, reaching a high value of 10.3 mEq/l and a low value of 4.0 mEq/l.

Low Sodium Group

Volume expansion (Fig. 4) resulted in an initial increase in arterial pressure of the sodium deprived rabbits. An increase in the initial average (54 to 63 mmHg) was recorded. The rise in pressure occurred following an infusion of 5 ml of the plasma protein perfusate and became the highest arterial
Fig. 6  Plasma renin activity of control (●), low sodium (○) and high sodium (□) diet rabbits during long term volume expansion and hemorrhage. Infusion rate was 0.21 ml/min for 2.0 hr, and hemorrhage rate 0.21 ml/min for 4.0 hr. N = 7 for control rabbits; N = 8 for high sodium rabbits; N = 6 for low sodium rabbits.
Fig. 7 Plasma sodium levels of control (●), low sodium (○) and high sodium (□) diet rabbits following long term volume expansion and hemorrhage. N = 7 for control rabbits; N = 8 for high sodium rabbits; N = 6 for low sodium rabbits.
Fig. 8  Plasma potassium levels of control (●), low sodium (○) and high sodium (□) diet rabbits following long term volume expansion and hemorrhage. N = 7 for control rabbits; N = 8 for high sodium rabbits; N = 6 for low sodium rabbits.
Fig. 9 Urine sodium levels of control (●), low sodium (○) and high sodium (□) diet rabbits during a 22 day dietary period. 
N = 7 for control rabbits; N = 8 for high sodium rabbits; N = 6 for low sodium rabbits.
Fig. 10 Urine potassium levels of control (●), low sodium (○) and high sodium (□) diet rabbits during a 22 day dietary period. N = 7 for control rabbits; N = 8 for high sodium rabbits; N = 6 for low sodium rabbits.
pressure value attained by the group throughout infusion. The average pressure of the group gradually declined from its highest value of 63 to 40 mmHg at the completion of volume expansion. There appeared to be an attempt at normalization of pressure after 20 ml of perfusate had been infused but the pressure continued to gradually decrease.

The arterial pressure of the low sodium group (Fig. 5) decreased slightly following a hemorrhage volume of 5 ml, then rose from 34 to 44 mmHg. A gradual decrease was observed as the hemorrhage volume increased from 10 to 35 ml. The arterial pressure was observed to increase to its highest level (47 mmHg) following 45 ml of hemorrhage and remain at this level until hemorrhage was completed.

The plasma renin levels (Fig. 6) of the low sodium rabbits decreased during volume expansion from an initial value of 9.2 to 3.8 ng/ml/hr. This decreasing trend reversed during hemorrhage and plasma renin activity was observed to rise significantly from 3.8 to 9.8 ng/ml/hr. Plasma sodium levels increased from an initial value of 100 to 110 mEq/l following volume depletion. The plasma potassium levels (Fig. 8) increased (6.9 to 7.4 mEq/l) following volume expansion. The increase in plasma potassium levels continued throughout volume depletion, reaching its highest recorded value (8.8 mEq/l) at the completion of the 4 hr hemorrhage period. Potassium levels (Fig. 10) also decreased greatly from an initial value (7.4 mEq/l) to their lowest value of 2.3 mEq/l on day 8 of
the diet. The potassium level then slowly rose to a new value of 7.2 mEq/l on day 18 of the diet. A decrease in urine potassium level was then recorded until the completion of the dietary period, at which time a value of 4.2 mEq/l was reached.

High Sodium Group

The arterial pressure of the elevated sodium rabbits (Fig. 4) was observed to decrease from its initial control value (84 to 78 mmHg) following the infusion of 25 ml of the plasma perfusate. The average arterial pressure for the elevated sodium groups (Fig. 5) was observed to rise from 72 to 77 mmHg following a hemorrhage volume of 20 ml. The pressure was then observed to decrease until a volume of 40 ml was removed from the arterial system. A gradual rise to its highest pressure of 79 mmHg occurred at a hemorrhage volume of 50 ml.

Plasma renin levels (Fig. 6) for the elevated sodium group rose from an initial value of 4.4 to their highest value of 6.0 ng/ml/hr following volume expansion. However, the elevated plasma renin level decreased during volume depletion to 3.8 ng/ml/hr. Plasma sodium levels (Fig. 7) in the high sodium group were observed to rise from their initial value of 102 to 104 mEq/l following the completion of volume expansion and decline to 98 mEq/l following the completion of volume depletion. The plasma potassium levels (Fig. 8) decreased from a value of 8.0 to 7.3 mEq/l in the
post volume expansion period and finally reached their lowest value of 7.0 mEq/l in the post hemorrhage period.

Urine sodium levels (Fig. 9) increased from an initial value of 150 to 305 mEq/l on day 14 of the high sodium diet. The urine sodium level at that time was observed to decrease slightly and began to increase to near its highest value by attaining a level of 300 mEq/l following day 22 of the diet. Urine potassium levels (Fig. 10) were initially seen to decrease until day 4 of the diet. Then a gradual increase was observed from day 4 to day 8 of the diet (3.3 to 12.4 mEq/l). The potassium levels decreased to 7.6 mEq/l at the end of the dietary period.

Group Weights

The average weights (Table 1) of the low sodium rabbits decreased over the dietary period (2.95 to 2.80 kg). The high sodium animals were observed to increase in weight (3.0 to 3.45 kg) and the control rabbits increased slightly (2.95 to 3.05 kg) in weight over initial control values.
Table 1. A summary of rabbit weights illustrating variations during dietary sodium difference.

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Pre-diet weight (kg)</th>
<th>Post-diet weight (kg)</th>
<th>Total days</th>
</tr>
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<tr>
<td>Control</td>
<td>7</td>
<td>2.95</td>
<td>3.05</td>
<td>22</td>
</tr>
<tr>
<td>High Na</td>
<td>8</td>
<td>3.00</td>
<td>3.45</td>
<td>22</td>
</tr>
<tr>
<td>Low Na</td>
<td>6</td>
<td>2.95</td>
<td>2.80</td>
<td>22</td>
</tr>
</tbody>
</table>
CHAPTER V

DISCUSSION

Short and long term volume expansion in rabbits maintained on control and low sodium diets resulted in similar reductions in plasma renin activity. The low sodium animals revealed the highest initial plasma renin activity, indicating that renin was the major factor in the maintenance of arterial pressure in the group (2,10,29). The control rabbits revealed a significantly lower initial plasma renin level, which indicated that its participation in arterial pressure maintenance was lower than that being required for the low sodium rabbits (18,21,25,30).

Rabbits maintained on high sodium diets revealed the lowest initial plasma renin activity, indicating the suppressive role played by high plasma sodium osmolarity on renin release (1,2,25,30,31,32). Upon completion of volume loading, the high sodium rabbits revealed an increase in plasma renin activity. The levels of activity seen in hypertensive rabbits could have represented quantities which have immediate pressor effect or are necessary for hypertension development (18).

Rabbits maintained on high sodium diet yielded the highest recorded arterial pressure throughout the volume expansion period. The control animals remained slightly above the low sodium group average. High and control sodium groups recorded losses in arterial pressure which implied that the duration
of systemic shock related to arterial pressure tends to dilate peripheral vessels (7). Systemic dilation allows mean arterial pressure to remain at near normal values, pending the onset of angiotensin activity (12). Control rabbits revealed an increase in arterial pressure near the completion of volume expansion which probably resulted from vasodilator dilution caused by continued infusion (12,22,25).

Arterial pressure among the high sodium rabbits declined slightly throughout the infusion period. Autoregulation of the kidneys to reduce renal perfusion pressure caused by an expanded blood volume, and renin suppression caused by high plasma sodium concentrations, possibly are factors which in addition to reaction of present renin amounts contribute to the declining pressure (12,23,26,28). Volume expansion of the low sodium diet animals resulted in an initial rise in arterial pressure which probably developed from an expanded blood volume (4,15,22,25). The arterial pressure began to decline following the initial rise and at one other point in volume expansion a rise in pressure was recorded.

The low sodium and control rabbits yielded marked increases in plasma renin activity following volume depletion. Low sodium rabbits achieved the highest recorded renin level of the three dietary groups. Increases recorded by the low sodium and control rabbits indicated that renin is released in large quantities during volume depleted conditions in order to return and maintain arterial pressure to near normal
values (1,7,10,15,17,18,20,21,26,32).

Plasma renin activity among high sodium rabbits was seen to decline below initial levels to the lowest recorded value, indicating that high plasma sodium concentration had successfully suppressed renin release (1,8,20,21,32). Arterial pressure of control and low sodium rabbits showed an average increase during volume depletion (15,16,19,22,26). Low sodium animals were able to maintain an arterial pressure above their average recorded value prior to the initiation of hemorrhage, indicating the vasoconstrictive activity of angiotensin in blood pressure maintenance during hemorrhage in volume depleted rabbits (7,15,16,17,22,26). The control sodium rabbits revealed a decline in arterial pressure near completion of hemorrhage which could be due to severe blood loss and resultant cardiovascular collapse (12,19). The high sodium rabbits showed an increase in arterial pressure during volume depletion. However, plasma renin levels decreased during the depletion period. The arterial pressure of rabbits is believed to be directly effected by serotonin, vasopressin or prostaglandins, which are known to have different or indirect effects on the fluid balance system and play positive roles in the maintenance and elevation of arterial pressure (5,7,20,24,25,26).

Rabbit plasma sodium for control rabbits showed the lowest initial value as compared to the readings of low and high sodium diet rabbits. High sodium diets apparently
elevated plasma sodium levels far above control levels and the low sodium diet elevated sodium levels through active retention in an effort to elevate blood volume and arterial pressure (4,7,9).

A close relationship exists between sodium and body fluid volume, especially extracellular fluid volume. Any factor which alters fluid volume causes parallel and almost proportional changes in body sodium at the same time (5). During volume expansion the plasma sodium levels were elevated in all three dietary groups, apparently in an attempt to maintain body fluid volume equilibrium (9,12). During volume depletion the plasma sodium levels continued to increase in low and control sodium rabbits, whereas high sodium animals showed a slight decrease.

Plasma potassium values for control and low sodium rabbits increased throughout volume expansion and depletion; however, high sodium groups decreased from initial elevated levels. These potassium values imply that plasma levels evidently play a more significant role in blood volume maintenance in control and low sodium rabbits than in high sodium diet rabbits (33).

Urine sodium values recorded during the duration of the diets revealed increasing values for the high sodium animals and very reduced levels among the low sodium animals. The control group maintained a steady value throughout the dietary period. These values indicated sodium conservation among
the low sodium group and increased sodium expulsion among the high sodium group (9,12).

Urine potassium values fluctuated greatly among the three dietary groups, with low sodium rabbits conserving and high sodium diet rabbits expelling large quantities of potassium. Control rabbits exhibited variations in potassium conservation during the dietary period, suggesting apparent fluctuations in body potassium values.

The body weights of the rabbits increased while maintained on the high sodium diet. This was probably due to increased blood and extracellular fluid volume accompanying sodium retention. Low sodium animals exhibited a loss in weight which probably resulted from a depleted extracellular fluid and blood volume (9,12). Control rabbits were able to maintain their body weight at near initial values with a slight increase in body weight which was obviously due to body growth.
CHAPTER VI

SUMMARY

1. A high sodium diet in male New Zealand white rabbits suppressed renin release during volume depletion, elevated mean arterial pressure and increased plasma and urine potassium and sodium levels. Plasma renin levels were increased during volume expansion and arterial pressure decreased slightly.

2. A low sodium diet in male New Zealand white rabbits elevated initial plasma renin levels and increased renin release during volume depletion. Plasma sodium and potassium levels were increased and urine sodium and potassium levels as well as arterial pressure decreased.

3. Control and low sodium diets in male New Zealand white rabbits resulted in similarly reduced and increased plasma renin levels during volume expansion and volume depletion, respectively, as well as a slight increase in mean arterial pressure.
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