Sodium Gradient and Renoprival Hypertension in the Rat

By SYDNEY M. FRIEDMAN, M.D., PH.D., CONSTANCE L. FRIEDMAN, PH.D., and MIYOSHI NAKASHIMA, B.SC.

Following nephrectomy in the rat blood pressure rises while the extracellular fluid volume increases, sodium concentration falls and potassium rises. These changes (without the potassium rise) can be mimicked by simple hyperosmotic loading while the reverse can be induced by dehydration. The rise in blood pressure is not due to either expansion of the extracellular space or the fall in sodium concentration alone but probably to the resultant decrease in the Na\textsubscript{i}/Na\textsubscript{o} gradient.

THE effects of renal extirpation have long been of critical importance to theories of the hypertensive process. Indeed, Goldblatt’s original thinking was conditioned by his failure to observe any rise in pressure in the nephrectomized dog.\textsuperscript{1} Later, however, Braun-Menendez and von Euler\textsuperscript{2} noted that blood pressure did in fact rise in the nephrectomized rat and subsequently, Grollman et al.\textsuperscript{3} showed that this was also true in the nephrectomized dog kept alive by peritoneal lavage. There is now no argument about the fact, but two opinions as to its explanation. One opinion is that the case for an antipressor function of the kidney in the hierarchy of renal pressor materials has been made.\textsuperscript{4} The other suggests that in the absence of renal regulation, salt and water undergo a basic redistribution which is causally related to the hypertension.\textsuperscript{5} As yet, no specific renal material has been isolated to prove the first case, nor has any electrolyte change been pinpointed to prove the latter.

Our immediate interest in the problem stems from the demonstration that smooth muscle tone in general and peripheral vascular tone in particular is directly related to the extra/intracellular gradient of sodium,\textsuperscript{6} a view also reached by Raab and co-workers,\textsuperscript{7} from different evidence. The sodium gradient is a dynamic equilibrium, or steady state, which can be altered in several basic ways, first and probably most simply by a shift of water between the cell and its environment in accord with osmotic requirements, second by an alteration in Donnan forces, third by a change in membrane permeability affecting either inward or outward movement of sodium or both, and fourth, by changes in the metabolically driven sodium transport (extrusion). Seemingly, no matter how caused, a fall in the gradient Na\textsubscript{i}/Na\textsubscript{o} results in an increase in tone.

In the present report the problem of renoprival hypertension has been restudied and evidence is presented to show that the rise in blood pressure is again a function of a fall in sodium gradient. The emphasis on sodium does not exclude potassium, calcium or other ions, but represents only our present limited point of attack.

METHODS

Adult male albino rats of an inbred Wistar strain were used throughout. The basic methods for deriving data concerning the gross extracellular distribution of Na, K and water have been described elsewhere.\textsuperscript{8} Briefly, inulin is injected intravenously in the bilaterally nephrectomized rat and allowed 2 hours for equilibration. An arterial (usually femoral) blood sample is then drawn and the concentrations of inulin, Na and K in the sample are measured. The product of the extracellular fluid volume (ECFV = volume distribution of inulin) and Na concentration yields a measure of total extracellular Na (EC Na) and ECK is similarly derived. In some experiments, a second procedure, e.g., infusion or gavage, was carried out at this time and a second blood sample taken after a measured interval in order to determine the degree and direction of changes. Groups of at least 8 animals

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Table 1. Effect of Nephrectomy on Blood Pressure and on Extracellular Fluid Volume, Na and K*

<table>
<thead>
<tr>
<th>Nephrectomy</th>
<th>Control</th>
<th>24 hrs</th>
<th>48 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct B.P., mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>systolic</td>
<td>94 ± 4</td>
<td>115 ± 4↑</td>
<td>127 ± 2↑</td>
</tr>
<tr>
<td>diastolic</td>
<td>56 ± 3</td>
<td>70 ± 3↑</td>
<td>88 ± 3↑</td>
</tr>
<tr>
<td>ECFV ml./100 Gm.</td>
<td>22.7 ± 0.7</td>
<td>24.4 ± 0.3↑</td>
<td>25.8 ± 0.4↑</td>
</tr>
<tr>
<td>Na conc., mEq./L.</td>
<td>144.4 ± 1.1</td>
<td>142.3 ± 1.5</td>
<td>135.4 ± 2.2↑</td>
</tr>
<tr>
<td>K conc., mEq./L.</td>
<td>4.17 ± 0.12</td>
<td>5.90 ± 0.16↑</td>
<td>7.62 ± 0.21↑</td>
</tr>
<tr>
<td>EC, Na, mEq./100 Gm.</td>
<td>3.27 ± 0.11</td>
<td>3.48 ± 0.06↑</td>
<td>3.49 ± 0.07↑</td>
</tr>
<tr>
<td>EC, K, mEq./100 Gm.</td>
<td>94 ± 4</td>
<td>144 ± 4↑</td>
<td>194 ± 0↑</td>
</tr>
<tr>
<td>Average body wt., Gm.</td>
<td>246 ± 3</td>
<td>241 ± 4</td>
<td>246 ± 5</td>
</tr>
<tr>
<td>No. of animals</td>
<td>9</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Water intake, ml./rat/24 hours</td>
<td>33 ± 3</td>
<td>8 ± 1</td>
<td>7 ± 1</td>
</tr>
<tr>
<td>Wt. change following nephrectomy, Gm.</td>
<td>-4 ± 1</td>
<td>0 ± 2</td>
<td>0 ± 2</td>
</tr>
<tr>
<td>Gk</td>
<td>6.8</td>
<td>0.5</td>
<td>0.0</td>
</tr>
<tr>
<td>G-approx</td>
<td>13.6</td>
<td>15.0</td>
<td>12.0</td>
</tr>
</tbody>
</table>

*± standard error.
↑p<0.02.
↑↑p<0.05.

were used throughout. All calculations were made separately for each animal and then averaged; this is particularly important in the case of the derived data. Inulin was determined by the method of Higashi and Peters, Na and K by flame photometry and blood pressure by direct electromanometry using either a Statham or Sanborn transducer. All operative procedures were performed under light ether anesthesia. Additional procedures are described as they arise.

The method used to estimate relative changes in Na gradient, shown in the tables as Gk and G-approx. will be discussed separately.

RESULTS

Experiment 1. Effect of Nephrectomy on Salt and Water Distribution and on Blood Pressure

This experiment is presented as typical of the changes that occur in the nephrectomized rat. Group 1 consisted of 9 animals serving as control, i.e., nephrectomized at the time of inulin injection 2 hours before blood sampling. Group 2 consisted of 14 rats nephrectomized 24 hours before inulin injection and the 14 animals of group 3 were nephrectomized 48 hours previously (table 1).

After nephrectomy, blood pressure increases steadily, accompanied by an increase in the extracellular fluid volume. There is frequently, as here, a small increase in total extracellular sodium which is probably real, but this is more than diluted out by the increase in fluid volume so that sodium concentration falls slightly at 24 hours, markedly at 48 hours. By contrast, there is a large increase in extracellular potassium which, doubling itself in 48 hours, is more than sufficient to offset the increase in fluid volume and hence K concentration rises steadily. These findings are in general agreement with those of other authors. They cannot be explained by fluid intake since the nephrectomized animals greatly reduced their water intake to just about match their insensible water loss and did not eat. There was a small loss of weight.

The calculated relative Na gradient decreased as blood pressure rose.

Experiment 2. Effect of Nephrectomy on Salt and Water Distribution in the Absence of Neurohypophyseal or Adrenal Function

Two experiments bearing on the problem of whether the neurohypophysis or adrenal play an active role in the changes in salt and water distribution following nephrectomy are pre-
sent here. In the first experiment 8 animals served as intact control and 10 as diabetes insipidus control, 2 parallel groups of 8 and 9 animals respectively being nephrectomized 24 hours before the experiment. Diabetes insipidus was produced and verified as previously described. The second experiment was similar except that adrenalectomy rather than diabetes insipidus was tested and all groups had 9 animals. Although the same measurements as in the first experiment were made, only the essential findings are summarized in figure 1 for direct comparison with those of the first experiment.

It is clear that the change in salt and water distribution which follows nephrectomy cannot be ascribed to any active role on the part of either the neurohypophysis or adrenal for it occurs equally well in the absence of these glands. The rat with diabetes insipidus ordinarily shows an increase in extracellular fluid volume and an increase in total sodium. The 24 hour adrenalectomized rat ordinarily shows a decrease in fluid volume, a minor decrease in Na and a clear rise in K concentration. The effects of nephrectomy appear superimposed on these expected changes. Thus the increase in fluid volume is accentuated in the rats with diabetes insipidus and the rise in K in the adrenalectomized animals.

No attempt was made to compare effects on blood pressure in these 2 experiments. Since both glands are active in the normal maintenance of the blood pressure the effect of nephrectomy could only be studied in therapeutically maintained animals.

A series of experiments not reported here, aldosterone and pitressin alone or in various combinations did not reverse the salt and water redistribution following nephrectomy.

**Experiment 3. Effect of Simple Dehydration on Salt and Water Distribution and on Blood Pressure**

The possibility that the increase in blood pressure following nephrectomy is a direct outcome of the alteration in fluid and salt balance was next explored. In seeking information on this point we attempted to determine the effects on blood pressure of controlled alterations in salt and water distribution in the normal rat. In the first of these experiments 4 groups of 8 animals were used, the first group serving as control, the others deprived of water for 24, 48 or 72 hours. The findings are shown in table 2 and are in general agreement with known facts.
TABLE 3.—Effect of an Oral Hyperosmotic Glucose Load on Blood Pressure and on Extracellular Fluid Volume, Na and K

<table>
<thead>
<tr>
<th>Control</th>
<th>Hydrated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct  B.P., mm. Hg</td>
<td></td>
</tr>
<tr>
<td>systolic</td>
<td>112 ± 6</td>
</tr>
<tr>
<td>diastolic</td>
<td>66 ± 5</td>
</tr>
<tr>
<td>mean</td>
<td>83 ± 5</td>
</tr>
<tr>
<td>ECFV ml./100 Gm.</td>
<td>21.7 ± 0.3</td>
</tr>
<tr>
<td>Na conc., mEq./L.</td>
<td>146.1 ± 1.1</td>
</tr>
<tr>
<td>K conc., mEq./L.</td>
<td>3.64 ± 0.09</td>
</tr>
<tr>
<td>EC Na, mEq./100 Gm.</td>
<td>3.16 ± 0.05</td>
</tr>
<tr>
<td>EC K, mEq./100 Gm.</td>
<td>79 ± 2</td>
</tr>
<tr>
<td>Average body wt., Gm.</td>
<td>264 ± 6</td>
</tr>
<tr>
<td>No. of animals</td>
<td>10</td>
</tr>
</tbody>
</table>

*p<0.02.

served as control while the animals of group 2 were given 5 per cent glucose in saline by stomach tube in an amount equal to 5 per cent of their body weight. Half of this was given at the time of insulin injection and half one hour later (table 3).

Blood pressure rose in the hyperhydrated group. This observation has been repeated and is in general agreement with the findings of others. The rise in blood pressure is accompanied by an increase in fluid volume. Total extracellular sodium is usually increased, as in this experiment, but this is more than diluted out so that sodium concentration falls. Although there is no rise in plasma K the diluting effect of the increase in fluid volume is obviated by a real increase in ECK. The picture is remarkably similar to that observed following nephrectomy.

It would thus be anticipated that the administration of a hyperosmotic load to the nephrectomized rat would accentuate whatever rise of pressure might already have occurred. This was readily demonstrated by giving the load as described above to 48 hour nephrectomized rats with the well defined results shown in figure 2 and agrees with the findings in the dog.14

The relative change in gradient cannot be
Table 4.—Effect of an Intravenous Hyperosmotic Glucose Load on Blood Pressure and on Extracellular Fluid Volume, Na and K in Normal and Dehydrated Rats

<table>
<thead>
<tr>
<th></th>
<th>Normal Preinfusion</th>
<th>Normal Postinfusion</th>
<th>Change</th>
<th>Dehydrated Preinfusion</th>
<th>Dehydrated Postinfusion</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct B.P., mm. Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>systolic</td>
<td>91 ± 8</td>
<td>104 ± 7</td>
<td>+13*</td>
<td>58 ± 4</td>
<td>82 ± 3</td>
<td>+24*</td>
</tr>
<tr>
<td>diastolic</td>
<td>55 ± 4</td>
<td>60 ± 4</td>
<td>+ 5*</td>
<td>37 ± 3</td>
<td>42 ± 2</td>
<td>+ 5*</td>
</tr>
<tr>
<td>ECFV ml./100 Gm.</td>
<td>20.7 ± 0.6</td>
<td>24.1 ± 0.5*</td>
<td>+ 3.3*</td>
<td>17.7 ± 0.4</td>
<td>20.6 ± 0.4*</td>
<td>+ 2.9*</td>
</tr>
<tr>
<td>Na conc., mEq./L</td>
<td>144.3 ± 1.3</td>
<td>127.6 ± 2.4*</td>
<td>−16.7*</td>
<td>151.6 ± 2.8</td>
<td>134.8 ± 1.6*</td>
<td>−16.8*</td>
</tr>
<tr>
<td>K conc., mEq./L</td>
<td>3.29 ± 0.08</td>
<td>3.33 ± 0.06</td>
<td>+ 0.04</td>
<td>3.29 ± 0.03</td>
<td>3.27 ± 0.08</td>
<td>− 0.02</td>
</tr>
<tr>
<td>EC Na, mEq./100 Gm.</td>
<td>2.90 ± 0.06</td>
<td>3.07 ± 0.05</td>
<td>+ 0.08</td>
<td>2.65 ± 0.06</td>
<td>2.77 ± 0.05</td>
<td>+ 0.11</td>
</tr>
<tr>
<td>EC K, mEq./100 Gm.</td>
<td>68 ± 1</td>
<td>80 ± 2*</td>
<td>+12*</td>
<td>58 ± 1</td>
<td>68 ± 2*</td>
<td>+ 8*</td>
</tr>
<tr>
<td>Average body wt., Gm.</td>
<td>275 ± 7</td>
<td>303 ± 5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of animals</td>
<td>8</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gk</td>
<td>7.1</td>
<td>6.0</td>
<td></td>
<td>7.9</td>
<td>6.8</td>
<td></td>
</tr>
<tr>
<td>G-approx</td>
<td>14.2</td>
<td>12.0</td>
<td></td>
<td>15.8</td>
<td>13.6</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.02.

calculated without knowing how much fluid was actually absorbed from the load.

Experiment 5. Effect of an Intravenous Hyperosmotic Load on Salt and Water Distribution and on Blood Pressure

This experiment was arranged to provide data for estimating gradient change by injecting the load as a measured volume of warmed 5 per cent glucose in saline intravenously. The continuous infusion syringe delivered 3.7 ml. in 2 min. The experiment was internally controlled and made use of 2 basic types of experiment animal, the first fully nourished, the second deprived of water for 72 hours. Two groups of 8 rats each were thus used. Basal measurements were made as usual after 2 hours of inulin equilibration, the 2 min. infusion was then given and a second sample taken less than 30 sec. after it was completed (table 4).

The initial measurements are as reported in experiment 3. Thus, in the dehydrated group, extracellular fluid is reduced and Na concentration increased. This is accompanied by a lower blood pressure and higher relative gradient than in the normal.

The infusion in both groups caused an increase in extracellular fluid greater than the amount actually injected as is expected with a hyperosmotic infusion. Sodium concentration fell in proportion to the dilution while K concentration remained unchanged. The gradient was reduced and blood pressure rose, moderately, but in every animal.

Experiment 6. Effect of Sodium on the Blood Pressure Response to an Expansion of the Extracellular Fluid Volume

While it is apparent from the preceding results that the response to hyperosmotic loading is similar to that which follows nephrectomy, the expansion of the extracellular space might perhaps be considered the basic change in both. Equally well, the fall in sodium concentration might be considered the important factor. Two experiments can be presented to demonstrate that neither of these interpretations alone is valid. In these, the effect of fluid volume expansion on the sodium concentration was balanced off by using an intravenous infusion of NaCl, slightly hypotonic in the one, 100 mEq./L., and slightly hypertonic in the other, 200 mEq./L. In each case 7 rats nephrectomized for 48 hours were available. The initial measurements were made as usual 2 hours after inulin injection and, following this, the NaCl solution, warmed, was infused at the rate of 2 ml./100 Gm. The second blood sample was taken 5 min. after the start of the infusion (table 5).
Both infusions increased the extracellular fluid volume, neither caused a rise in blood pressure. Further, while hypotonic infusion lowered the plasma sodium concentration, blood pressure remained unchanged. Hyperosmotic infusion in this case raised the concentration and caused a fall in blood pressure.

The calculation of relative change in gradient in these experiments (described later) allows for the added sodium and water in both cases. Gradient, like blood pressure, was essentially unchanged by the hypotonic infusion. In the case of the hyperosmotic infusion gradient rose and blood pressure fell.

The specific effect of the sodium ion is implicit in the fact that the infusion of a glucose solution of comparable osmotic activity (compare experiment 5) raised the blood pressure.

**DISCUSSION**

We have presented evidence elsewhere to show that the sodium gradient, that is, the relation of extracellular to intracellular sodium, is itself a determinant of the tone of smooth muscle in general and of the peripheral vasculature in particular. This view is in general harmony with concepts of the role of sodium in excitable tissues but differs in ascribing for smooth muscle less importance to acute depolarization and repolarization and more importance to the steady or equilibrium state.

The general factors involved in determining the sodium gradient may be formulated:

Let

- $c_i = \text{intracellular concentration of Na}$
- $c_e = \text{extracellular concentration of Na}$
- $v_i = \text{intracellular fluid volume}$
- $v_e = \text{extracellular fluid volume}$

Then

- $c_i v_i = \text{total effective intracellular Na} = n_i$
- $c_e v_e = \text{total effective extracellular Na} = n_e$

Total body fluid

$V = v_i + v_e$

Total body Na

$N = n_i + n_e + n_s$

where $n_s$ represents slowly mobilizable stones.

By direct transposition

$$c_i = \frac{n_i}{v_i} = \frac{N_i - n_e - n_s}{V_i - v_e} = \frac{N_i - c_e v_e - n_s}{V_i - v_e}$$

and the gradient

$$G = \frac{c_e}{c_i} = \frac{c_i (V_i - v_e)}{N_i - c_e v_e - n_s} \quad (1)$$

This formulation implies that whatever fluid or sodium moves out of one compartment is necessarily found in the other. This is true for sudden permeability changes where $V_i, N_i$ and $n_e$ are all unchanged. Here the gradient change depends on changes in $c_e v_e$. Since a decrease of this product in the numerator also increases the denominator...
small changes in permeability obviously have large effects on the gradient. This fits our data for acute pressor and depressor agents very well\textsuperscript{15, 16} and explains why our best correlation was between blood pressure and the product $c_e v_c$.

As is well known, however, the effective intracellular sodium is relatively quite a small quantity and where there is no abrupt change in permeability cannot be expected to change very much. In brief, the denominator in equation (1) $N_t - c_e v_c - n_s$ which is the expanded expression for $n_1$, is in effect a constant so that the equation reduces to

$$G = \frac{c_e (V_c - v_c)}{k}$$

This equation would apply to slowly developing equilibrium states such as follow nephrectomy and dehydration, assuming $V_t$ is either unchanged or known. The relative gradient, $G_k$, where $k$ is unresolved, was calculated for our data in these two states (experiments 1 and 2) using values for $V_t$ taken from the data of Aach, Rolf and White\textsuperscript{17} although the results in these cases are similar if $V_t$ is taken as unchanged. In both these experiments the blood pressure is inversely related to the direction of gradient shift. A numerical approximation of $G$ can be made by setting $k$ equal to 0.5 mEq./100 Gm. based on 50 ml. of intracellular water/100 Gm. containing sodium at an average concentration of 10 mEq./L. This value is shown in the tables as $G$-approx.

It is possible to estimate the direction of gradient change in loading experiments only when the load is given directly into the circulation so that the added amounts are known as in experiments 5 and 6. In these experiments, $n_1$ cannot be assumed to be constant since sodium may be forced to shift to satisfy acutely imposed forces and presumably stored sodium cannot alone account for changes in the extracellular space. Accordingly, the longer form of equation (1) was used with $n_s$ considered to remain unchanged in the 5 min. of the actual experiment. Both $V_t$ and, where sodium is given, $N_t$ are increased after infusion by the amount administered. Body fluid is taken as 70 ml. and intracellular sodium as 0.5 mEq./100 Gm. in the derivation of $G$-approx. Here again, the direction of change of blood pressure is inverse to that of the sodium gradient.

In the rat, then, it seems fair to say that the redistribution in salt and water following nephrectomy is itself sufficient cause for the progressive rise in blood pressure as was first argued by Braun-Menendez.\textsuperscript{18} Presumably the steady accumulation of metabolites alters the osmotic and hydrogen ion equilibrium and leads to a shift of water from cells to environment. This lowers external sodium concentration relative to internal which in turn results in an increase in vascular tone. Some additional sodium appears to be mobilized from the stores so that the total extracellular sodium is increased, but this is apparently insufficient to compensate for the basic derangement. The kidney may be said to have an antihypertensive function, if by this one refers simply to its regulation of the internal environment.

It seems likely that a similar explanation is true for renalprival hypertension in the dog. Here the problem is complicated by the fact that the animal is usually maintained in approximate balance by one or another type of vivadialysis. Nonetheless, several investigators have felt that the rise in blood pressure did in fact depend on some masked alteration in salt and water balance.\textsuperscript{14} Causal emphasis was at first placed on an expanded plasma volume and later on an expansion of the extracellular fluid volume. The demonstration that blood pressure rises even if plasma volume is held constant made this explanation doubtful. A rise in plasma sodium concentration has been looked for since this has been considered of possible importance in hypertensive states, but definitive evidence has been presented to show that blood pressure rises even if sodium does not rise. In point of fact, these same experiments usually show a fall in plasma sodium, as might be expected from the preceding analysis. Orbison et al.\textsuperscript{5} have
emphasized, however, that a tenous equilibrium does exist even where the dog is in apparent balance, by showing that an extreme pressor response may be obtained by expanding the extracellular space. This tallies with our findings in the rat. The claim that implanting the ureters into the vena cava does not raise blood pressure is not convincing since a small rise in pressure is shown and the toxic nature of the procedure is acknowledged.3

Although our analysis of gradient changes is in the early stages of development and is necessarily crude, it does demonstrate that 3 important quantities at least—body water, freely mobile sodium and stored sodium—each of which may vary independently, are involved. The rise of blood pressure which follows nephrectomy can easily be mimicked in the rat by a simple hyperosmotic load which decreases plasma sodium and increases extracellular fluid. It has also been shown, however, that the rise in blood pressure is not related to any of these quantities considered alone, but rather to their interrelation as defined by the sodium gradient.

These experiments suggest that renoprival hypertension can be explained on the same basis as other pressor and depressor phenomena which we have studied. In this case no specific hormone alters permeability or ion binding or metabolism. Instead, the accumulation of unexcreted metabolites tends to shift water out of the cells and to lower the sodium gradient. In the general sense of a final common pathway, renoprival hypertension is pertinent to the problem of essential hypertension. Etiologically, it does not seem to have common ground.

**Summary**

The rise in blood pressure following nephrectomy in the rat is accompanied by an increase in extracellular fluid volume and, despite a small increase in extracellular sodium, a fall in sodium concentration in the plasma. There is also a marked increase in extracellular potassium which more than offsets the diluting effect of the increase in fluid volume so that plasma potassium rises. The basic pattern of salt and water shift following nephrectomy is not due to active intervention on the part of either the neurohypophysis or adrenal glands since it occurs equally well in the absence of both these functions.

An orally or intravenously administered hyperosmotic load mimics the effects of nephrectomy insofar as extracellular fluid volume, sodium and blood pressure are concerned. Water deprivation produces the reverse patterns accompanied by a fall in blood pressure. In both cases the blood pressure is inversely related to the \( \frac{Na_0}{Na_1} \) gradient, which is a direct determinant of smooth muscle tone. Since the accumulation of metabolites following nephrectomy is analogous to the introduction of an hyperosmotic load, this alone is sufficient cause for the postnephrectomy rise in blood pressure.

A basic formulation of the factors involved in the sodium gradient is presented.

**SUUMARIO IN INTERLINGUA**

Le augmento del tension de sanguine post nephrectomia in rattos es accompaniate de un augmento del volumine de liquido extracellulare e—in despecto de un leve augmento del natrium extracellulare—de un reduction del concentration de natrium in le plasma. Il occurre etiam un marcate augmento del kalium extracellulare que non solmente compensa le effecto dilutori del augmentate volumine de liquido sed de facto effectua un augmento del nivello de kalium in le plasma. Le configuration fundamental del migration de sal e aqua post nephrectomia non resulta de un intervention active per le neurohypohysse o per le corpore suprarenal, proque illo remane sin alteration quando iste duo functiones es eliminate.

Un carga hyperosmotic administrate per via oral o intravenose imita le effectos de nephrectomia con respecto al volumine de liquido extracellulare, al concentration de natrium, e al tension de sanguine. Depriva-
tion de aqua produce un configuration contrari, accompaniate de un reduction del tension de sanguine. In ambe casos le tension de sanguine es relationate inversemente al gradiente $Na_{1}/Na_{2}$, le qual es un determinante directe del tono de musculo lisie. Viste que le accumulation de metabolitos post nephrectomia es analoge al introduction de un carga liyperosmotie, isto per se es sufficiente pro causar le augmento post-nephrectomie in le tension de sanguine.

Es presentate un formulation fundamental del factores que es interessate in le gradiente de natrium.

REFERENCES
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