**Effect of Potassium Administration on (1) Peripheral Vascular Reactivity and (2) Blood Pressure of the Potassium-Deficient Rat**

**By Meyer Friedman, M.D., S. Charles Freed, M.D., and Ray H. Rosenman, M.D.**

One hour after administration of potassium chloride to potassium-deficient rats, the depressed peripheral vascular response to pressor substances was significantly elevated. Administration of potassium chloride to potassium-deficient rats also returned to higher levels the lowered blood pressure of previously normotensive, as well as hypertensive rats. It appears that the depressor effect of potassium deprivation is due to the loss of peripheral vascular reactivity, both of which are rapidly restored by potassium administration specifically.

PREVIOUS studies from our laboratory have shown that potassium deprivation has a significant depressor effect in the normotensive\(^1,2\) and a profound effect in the hypertensive rat.\(^3\) Although various lesions usually were found in both the heart and kidneys of these animals, we were not able to find any correlation between their severity and the degree of hypotension observed. Finally, it was found\(^4\) that these same rats exhibited a marked decrease in their peripheral vascular reactivity as judged by their pressor response to the predominantly peripherally acting substances, norepinephrine, angiotonin and renin. This last, of course, suggested that the depressor response observed in the potassium-deficient rat was not due to some structural defect in the heart or kidney but to a functional one in the peripheral arteriole, occasioned by potassium deficit.

If this latter concept were correct, then administration of potassium to a rat previously deprived of potassium should result in (1) an increase in peripheral vascular reactivity, and (2) an increase in the blood pressure occurring *pari passu* with the former. The present report, detailing the effects of potassium administration on the peripheral vascular reactivity and blood pressure of the potassium-deficient rat indicate that the above concept is probably correct.

**Part I**

**Effect of Potassium Replacement on Peripheral Vascular Reactivity**

**Methods**

Twenty-one Long-Evans rats (6 weeks old) were deprived of adequate potassium for 10 weeks by the ingestion of a diet containing 0.006 per cent potassium and 0.38 per cent sodium.\(^3\) A control group of 14 rats was given the same diet except that its potassium content was 0.4 per cent.

The effect of potassium upon the peripheral vascular reactivity of the group of 21 potassium-deficient rats was determined by a modification of the technic developed by Page and Taylor for dogs\(^5\) and adapted for study of vascular reactivity in the rat by Masson, Page, and Corcoran.\(^6\) First, the pressor responses of 9 of the 21 rats were observed after the intravenous injection of norepinephrine, angiotonin, and renin, according to previously described methods.\(^6\) Similar studies were done on 6 of the 14 control rats. Then, the same vasoconstrictor drugs\(^*\) were tested in the remaining potassium-deficient and control rats after they had received a subcutaneous injection of 10 cc. of isotonic potassium chloride solution (155 mEq. per liter) one hour before.

*We wish to express our appreciation to Dr. Arthur C. Corcoran and Dr. Kenneth Savard of the Cleveland Clinic for the generous supplies of angiotonin and renin which they placed at our disposal for these studies.*
EFFECT OF POTASSIUM ADMINISTRATION

Results

The pressor responses which occurred are presented in table 1 and the average responses are depicted in figure 1. It can readily be seen that the administration of potassium to the rats previously deprived of it consistently increased his mean pressor response to each of the three substances administered. Thus, the average pressor response of the deficient rat to each of the test substances was approximately doubled. On the other hand (see fig. 1), no significant increase in pressor response was noted in the control animals after similar potassium injection.

<table>
<thead>
<tr>
<th>Type of Rat</th>
<th>No. of Rats</th>
<th>Average Blood Pressure Responses After Intravenous Injection of Pressor Substances (mm Hg)</th>
<th>Norepinephrine</th>
<th>Angiotonin</th>
<th>Renin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Initial Peak Increase</td>
<td>Initial Peak Increase</td>
<td>Initial Peak Increase</td>
<td></td>
</tr>
<tr>
<td>Potassium-deficient</td>
<td>9</td>
<td>76 (40-104)* 84 (62-108) ±4.8 ±1.4</td>
<td>73 (40-100) 98 (82-120) ±6.2 ±4.8</td>
<td>72 (56-96) 80 (72-110) ±4.7 ±4.2</td>
<td>+17</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>±8 (2-16)</td>
<td>(10-56)</td>
<td>±4.8</td>
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<tr>
<td></td>
<td>12</td>
<td>85 (40-104) 102 (54-128) ±5.5 ±1.6</td>
<td>88 (46-104) 140 (72-168) ±6.2 ±8.3</td>
<td>91 (80-110) 119 (104-170) ±4.9 ±7.4</td>
<td>±28</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>±17 (10-26)</td>
<td>(26-74)</td>
<td>±4.7</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>68 (52-84) 90 (72-104) ±5.9 ±3.5</td>
<td>73 (50-90) 141 (94-162) ±5.2 ±9.9</td>
<td>83 (56-102) 129 (88-144) ±6.2 ±7.0</td>
<td>±46</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>±22 (16-26)</td>
<td>(44-90)</td>
<td>±5.4</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>78 (44-100) 104 (60-124) ±7.5 ±3.0</td>
<td>83 (44-106) 149 (92-190) ±8.4 ±12.0</td>
<td>82 (44-108) 127 (62-176) ±8.9 ±16.0</td>
<td>±45</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>±26 (16-36)</td>
<td>(46-80)</td>
<td>±4.9</td>
</tr>
</tbody>
</table>

* Figures in parentheses refer to range of values obtained.  
† Standard error of the mean.  
‡ 10 ml. isotonic potassium chloride injected subcutaneously one hour before beginning of experiment.

Table 1. Changes in Mean Blood Pressure following Intravenous Injection of Pressor Substances into Potassium-Deficient Rats before and after the Administration of Potassium

Part II

EFFECT OF POTASSIUM REPLACEMENT ON BLOOD PRESSURE

Methods

The preceding observations indicated that parenteral administration of potassium rapidly improved the peripheral vascular deficiency occurring in the potassium-deficient rat. Moreover, the rapidity of recovery strongly indicated that the defect itself was not only reversible but probably functional in nature.

In order to determine whether potassium replacement also would restore the lowered blood pressure of deficient rats to the normotensive level existing before the deprivation of this cation, 10 initially normotensive rats were deprived of dietary potassium for 10 weeks. A control group of 10 rats was maintained on the same diet but also containing adequate potassium (0.4 per cent). After this preliminary period, the deficient and control rats were given a subcutaneous injection of 10 cc. of isotonic potassium chloride (155 mEq per liter), and later potassium chloride solution (1 per cent) in lieu of drinking water. Blood pressures were taken on these rats before and 1 and 24 hours after the subcutaneous administration of potassium, by means of the microphonic manometer. Food was withheld from all rats during this 24 hour interval.

In order to determine whether potassium replacement would restore the blood pressure of a group of deficient rats, previously hypertensive (that is, before
the dietary restriction of potassium), the following experiment was done. Five hypertensive rats\(^4\) were placed on the potassium-deficient diet (0.006 per cent potassium). At the end of eight weeks, these five rats exhibited a marked decrease in systolic blood pressures, compared with the control hypertensive rats. They were then fed the identical diet except that the potassium content was increased (0.4 per cent potassium) and their blood pressures, together with those of the original controls, were followed weekly. The control rats were fed the latter diet (0.4 per cent potassium) throughout the experiment.

**Results**

### A. Upon Previously Normotensive Rats

The average systolic blood pressure of the 10 rats given the potassium-deficient diet for 10 weeks was 82 mm. Hg (range: 56 to 100 mm. Hg; S.E. mean: ±2.9). These findings confirmed our earlier observations of the hypotensive effect of potassium restriction.\(^1\)\(^-\)\(^2\) As figure 2 depicts, parenteral, and later oral, administration of potassium to 10 of these rats was followed by a marked rise in their pressure as early as 60 minutes after the injection. At this time the average systolic pressure had risen to 102 mm. Hg (range: 96–122; S.E. mean: ±2.6), a rise of 29 mm. in a single day. Administration of the same amount of potassium to the control normotensive rats had no significant effect. (See fig. 2.) In the latter, the average initial pressure of 125 mm. Hg (range: 100 to 140; S.E. mean: ±5.3) decreased to 118 mm. Hg (range: 96 to 144; S.E. mean: ±4.7), and 24 hours after injection of potassium, the average pressure was 112 mm. Hg (range: 80 to 144; S.E. mean: ±5.8).

### B. Upon Previously Hypertensive Rats

Reinforcement of potassium in previously hypertensive but now normotensive potassium-deficient rats was found to lead to a return of the hypertension (see fig. 3). Thus, the average blood pressure of the five hypertensive rats fell to 136 mm. Hg (range: 122 to 160; S.E. mean: ±7.0) after eight weeks of potassium deprivation, in contrast to the average pressure of 188 mm. Hg (range: 146 to 240; S.E. mean: ±10.3) observed in the controls. However, when the deficient rats were again fed the same diet but with adequate potassium, a rise in pressure was noted within a week. As figure 3 illustrates, this rise continued until the animals once again became significantly hypertensive, the average systolic pressure rising to 180 mm. Hg (range: 120 to 230; S.E. mean: ±19.6) at the eighth week. In the control group, the average pressure increased slightly during this interval to 194 mm. Hg (range: 142 to 240; S.E. mean: ±23.2).

**Discussion**

In a previous study\(^4\) it was found that the reactivity of the peripheral vasculature was depressed markedly by potassium deprivation. The restoration of this peripheral vascular re-
activity (as measured by the pressor response of the animal to vasoconstrictor substances) in potassium-deficient rats, after administration of potassium, strongly suggests that the original decrease in reactivity was due to a specific deficiency of this same cation. In view of the fact that a generalized decrease in the tone of smooth muscle of the gastrointestinal and genitourinary systems has been found in the potassium-deficient animals, it seems possible that the peripheral vascular defect herein noted may well be due to a decrease in the tone of arteriolar musculature.

The present results also indicate that the fall in blood pressure occurring in both the normotensive and hypertensive rat subjected to potassium deprivation can be quickly reversed by the administration of potassium. This increase in pressure after potassium administration moreover, appears to take place, pari passu, with the return of peripheral vascular reactivity. This rapid and concomitant rate of return of both reactivity and blood pressure after administration of potassium not only suggests that both the decrease in reactivity and pressure are specifically due to the absence of this cation, but also that the two processes are causally related. In other words, the changes of blood pressure noted in the rat after potassium deprivation appear to be due to the changes produced by the latter in the peripheral vasculature, changes which are functional in nature and quickly reversible after administration of potassium alone.

SUMMARY

Administration of potassium was found to effect a rapid restoration of the decreased peripheral vascular reactivity found in the potassium-deficient rat. Administration of the same cation also was observed to restore the blood pressure of previously normotensive and hypertensive rats to the levels present before deficiency of potassium had been accomplished. The relationship of the decrease in the peripheral vascular reactivity and the blood pressure in the potassium-deficient rat was discussed.

REFERENCES

Effect of Potassium Administration on (1) Peripheral Vascular Reactivity and (2) Blood Pressure of the Potassium-Deficient Rat
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