THE RELATION OF THE ELECTROLYTE COMPOSITION
OF PLASMA AND SKELETAL MUSCLE*

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Darrow and his associates (1, 2) have recently obtained evidence that a
correlation exists between the concentration of serum bicarbonate, muscle
potassium, and intracellular sodium from a study on rats subjected to pro-
cedures designed to produce a deficit of one of the ions sodium, chloride, or
potassium. Thus, the serum bicarbonate concentration was found to vary
directly with the intracellular sodium and inversely with muscle potassium
when renal adjustment was attained in the presence of a deficiency of
sodium, chloride, or potassium. As an example, when a potassium de-
fi ciency was induced by maintaining rats on a diet low in potassium, or by
the repeated injection of desoxytocicosterone acetate (DCA), the loss of
muscle potassium and gain of intracellular sodium were found to be accom-
panied by an elevation of the serum bicarbonate concentration. In addi-
tion, the elevated serum bicarbonate concentration was found to be asso-
ciated with a decreased serum chloride concentration.

Several years ago one of the present authors (E. M.) and others (3) noted
that dogs subjected to repeated injections of DCA exhibited a striking re-
duction of muscle potassium, a gain of intracellular sodium, and a slight
decrease of the plasma chloride concentration. In this latter study there
was found to be a tendency toward an increased plasma bicarbonate con-
centration (not reported at the time, but see below); however, there
appeared to be no clear relationship between the changes of the muscle
sodium and potassium and the plasma bicarbonate level. In this respect
the observations on dogs with potassium deficiency differed from those
on rats.

The experiments included in this paper represent further studies on dogs
and rats with potassium deficiency induced by the administration of DCA
or by maintaining the animals on a diet low in potassium. They were
undertaken for the following purposes: (1) to observe and compare the
relationship of the electrolyte composition of plasma and skeletal muscle
of dogs and rats, and (2) to observe the influence of altering the dietary

* A preliminary report of this work was presented before the American Society of
Biological Chemists at Detroit, April 18, 1949 (Federation Proc., 8, 231 (1949)).
intake of sodium and chloride on the changes of the electrolyte composition of plasma and skeletal muscle of potassium-deficient animals.

Methods

In the experiments on dogs, young adult animals were placed on a constant diet (4) for at least 2 weeks before the experiments were undertaken. The animals which were maintained on the low potassium diet were given the basal diet without the daily supplement of potassium chloride. The dietary supply of sodium and chloride was altered by appropriate adjustment of the daily supplement of sodium citrate or sodium chloride. Certain of the animals received DCA\(^1\) (0.5 mg. per kilo of body weight) daily by subcutaneous injection for a period of 3 weeks.

In the experiments on rats, young adult males of the Wistar strain, of a uniform age and weight, were placed on a control diet for a period of 7 days. The control diet consisted of commercial casein 24 per cent, glucose 62 per cent, corn oil 8 per cent, and a salt mixture (5) 6 per cent. In addition all animals received daily (6 days a week) 2 drops of a vitamin supplement which furnished the following water-soluble vitamins in the amounts indicated: thiamine hydrochloride 25 \(\gamma\), riboflavin 30 \(\gamma\), nicotinamide 25 \(\gamma\), pyridoxine hydrochloride 25 \(\gamma\), calcium pantothenate 200 \(\gamma\), choline chloride 10 mg., and inositol 3 mg. Twice weekly all animals received 2 drops of a cod liver oil-vitamin E supplement which furnished 200 U. S. P. units of vitamin A, 20 U. S. P. units of vitamin D, and 1 mg. of \(\alpha\)-tocopherol. The salt mixture (5) of the diet was altered in composition with respect to sodium, potassium, and chloride when the rats were placed on experiment. Some of the animals received daily subcutaneous injections of DCA (2 mg. per day) for 14 days. The results of the analyses of the several diets employed are shown in Table I.

Blood from dogs was withdrawn under oil by direct puncture of the femoral artery, placed under oil in a special centrifuge tube containing heparin ("liquaemin," Organon, Inc.) to prevent clotting, and centrifuged at once for the plasma analyses. Skeletal muscle (lumbar portion, sacrospinalis) was obtained under sodium pentobarbital anesthesia as quickly as possible following the collection of the blood and sampled for the several analyses in the manner previously described (6). The rats were placed under sodium pentobarbital anesthesia and arterial blood was collected under oil by direct puncture of the left ventricle. The gastrocnemius muscles were then removed. In order to provide adequate samples for the several analyses, equal aliquots of plasma separated under oil from two rats in the same group (control or experimental) were combined under oil.

\(^1\) We are indebted to the Ciba Pharmaceutical Products, Inc., for the generous supply of "percorten" which was employed in these experiments.
The gastrocnemius muscles from the two rats were also combined and sampled. In presenting the results of the analysis of plasma and muscle of rats, therefore, the designation in Table II of the number of animals employed in a given experiment represents the number of animal "pairs."

The following determinations were made on the plasma: water, sodium, potassium, chloride, and total CO₂; on the muscle, water, chloride, sodium, potassium, and total fat. The chemical methods for the analysis of plasma obtained from both dogs and rats were the same as those employed in previous studies (7), with the exception that the plasma for the determinations of sodium and potassium was ashed as described by Eichelberger and Roma (8). Chlorides were determined on dog muscle by the wet ashing method described by Hastings and Eichelberger (9). The ashing procedure described by Eichelberger (10) was employed for the determination of sodium and potassium in dog muscle. All of the other procedures on dog muscle were the same as those employed in previous studies (7). The chemical determinations on rat muscle were carried out on the dry fat-free tissue remaining after the determinations of water and fat content. This residue was finely ground with a Wiley laboratory mill, intermediate model, with 20 mesh sieve, and kept in a weighing bottle. Before sampling, the powder was dried to a constant weight at 100–105°. Chlorides were determined on weighed aliquots of the powder according to the method of Eichelberger and Bibler (11). For the determinations of sodium and potassium weighed aliquots of the powder were first ashed as described by Eichelberger and Bibler (11). The ash was dissolved in 5 cc. of 1 N HCl and transferred to a 25 cc. volumetric flask with hot redistilled water, and then treated in the same manner as the solution of the ash obtained from dog muscle.

The data obtained on plasma are expressed in terms of 1000 gm. of

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Table I

<table>
<thead>
<tr>
<th>Type of diet</th>
<th>Na((\text{mM}))</th>
<th>K((\text{mM}))</th>
<th>Cl((\text{mM}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>32</td>
<td>11.5</td>
<td>27</td>
</tr>
<tr>
<td>Low potassium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal Na and Cl</td>
<td>32</td>
<td>14</td>
<td>63</td>
</tr>
<tr>
<td>&quot; &quot; high Cl</td>
<td>32</td>
<td>0.1</td>
<td>27</td>
</tr>
<tr>
<td>&quot; &quot; low Cl</td>
<td>32</td>
<td>0.1</td>
<td>3</td>
</tr>
<tr>
<td>Low Na, high Cl</td>
<td>14</td>
<td>0.1</td>
<td>43</td>
</tr>
</tbody>
</table>

plasma water. The plasma bicarbonate was calculated from the figure for plasma total CO$_2$ by the Henderson-Hasselbalch equation, assuming a constant pH of 7.4. The data obtained on muscle are presented in terms of 100 gm. of fat-free solids. For comparative purposes the intracellular sodium of both dog and rat muscle was calculated in the manner described by Darrow et al. (2) for rat muscle, as follows:

\[
\frac{(Cl)_m - 1}{[Cl]_e} = (H_2O)_e
\]

\[
(Na)_m - (H_2O)[Na]_e = (Na)_i
\]

in which (Cl)$_m$ and (Na)$_m$ are, respectively, total tissue chloride and sodium per 100 gm. of fat-free solids, (H$_2$O)$_e$ is the extracellular water per 100 gm. of fat-free solids, and (Na)$_i$ is the intracellular sodium per 100 gm. of fat-free solids. [Cl]$_e$ and [Na]$_e$ are, respectively, the concentrations of chloride and sodium in an ultrafiltrate of plasma, calculated from their corresponding plasma concentrations per 1000 gm. of plasma water and an average Donnan factor of 0.96. The constant, 1, appearing in the first equation is an average correction for chloride that apparently does not react like extracellular chloride (12).

Results

Electrolyte Content of Plasma and Skeletal Muscle of Rats with Potassium Deficiency

The results of the analysis of plasma and skeletal muscle of rats maintained on the control diet and on a diet low in potassium (Group I) and of rats receiving DCA (Group II) are presented in Table II. It will be seen that in each subgroup of the animals placed on the potassium-deficient diet for a period of 5 weeks there was a loss of muscle potassium and a gain of intracellular sodium. Further, the changes in muscle composition were accompanied by an elevated plasma bicarbonate concentration and by a fall of the plasma chloride. It should be pointed out that the altered plasma composition occurred in the presence of adequate dietary sodium and chloride. On the other hand, it will be noted that, while the loss of muscle potassium was similar in the several subgroups of animals, the gain of intracellular sodium was somewhat less in those animals receiving diets containing chloride in excess of sodium. In addition, the average increase of the plasma bicarbonate concentration and the fall of plasma chloride were also found to be less in these same animals.

The results of the analysis of plasma and muscle obtained from rats receiving DCA for a period of 14 days revealed changes similar to those encountered in animals maintained on a potassium-deficient diet. Thus, a
plasma bicarbonate increase and a plasma chloride decrease were found to accompany the deficit of muscle potassium and gain of intracellular sodium.

The observation of an increased plasma bicarbonate concentration in the presence of a loss of muscle potassium and a gain of intracellular sodium in potassium-deficient rats is in agreement with the finding of Darrow and his coworkers (2).

### Table II

**Average Electrolyte Content of Plasma and Skeletal Muscle of Rats Maintained on Diets Deficient in Potassium and of Rats Receiving Desoxycorticosterone Acetate**

<table>
<thead>
<tr>
<th></th>
<th>Plasma per kilo water</th>
<th>Muscle per 100 gm. fat-free solids</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Na</td>
<td>K</td>
</tr>
<tr>
<td>Control diet (3) *</td>
<td>156.1</td>
<td>4.1</td>
</tr>
<tr>
<td>Low potassium diet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal Na, normal Cl (3)</td>
<td>158.4</td>
<td>2.1</td>
</tr>
<tr>
<td>&quot; &quot; high Cl (3)</td>
<td>157.1</td>
<td>2.2</td>
</tr>
<tr>
<td>&quot; &quot; low Cl (3)</td>
<td>154.0</td>
<td>2.1</td>
</tr>
<tr>
<td>Low Na, high Cl (3)</td>
<td>156.3</td>
<td>2.5</td>
</tr>
</tbody>
</table>

**Group I. Control and low K diets for 5 wk. period**

**Group II. Control and low K diets, DCA† administration for 2 wk. period**

<table>
<thead>
<tr>
<th></th>
<th>m.eq.</th>
<th>m.eq.</th>
<th>m.eq.</th>
<th>m.eq.</th>
<th>gm.</th>
<th>m.eq.</th>
<th>m.eq.</th>
<th>m.eq.</th>
<th>m.eq.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control diet (2)</td>
<td>152.3</td>
<td>4.5</td>
<td>29.8</td>
<td>103.7</td>
<td>324.7</td>
<td>5.6</td>
<td>8.9</td>
<td>45.3</td>
<td>2.7</td>
</tr>
<tr>
<td>&quot; &quot; + DCA (2)</td>
<td>158.1</td>
<td>3.4</td>
<td>42.4</td>
<td>91.3</td>
<td>317.0</td>
<td>5.5</td>
<td>15.7</td>
<td>35.1</td>
<td>8.6</td>
</tr>
<tr>
<td>Low potassium‡ (2)</td>
<td>155.6</td>
<td>3.1</td>
<td>33.0</td>
<td>102.5</td>
<td>314.0</td>
<td>5.7</td>
<td>12.9</td>
<td>38.0</td>
<td>6.3</td>
</tr>
<tr>
<td>&quot; &quot; ‡ + DCA (2)</td>
<td>158.8</td>
<td>2.7</td>
<td>45.1</td>
<td>90.5</td>
<td>316.5</td>
<td>5.6</td>
<td>16.8</td>
<td>33.1</td>
<td>9.3</td>
</tr>
</tbody>
</table>

* The numbers within parentheses indicate the number of pairs of rats.
† Daily subcutaneous injection of 2 mg. per rat.
‡ Low potassium and normal sodium and chloride diet.

**Electrolyte Content of Plasma and Skeletal Muscle of Dogs with Potassium Deficiency**

Following Administration of Desoxycorticosterone Acetate—Table III presents the results of the analysis of plasma and muscle obtained from dogs following the injection of DCA (1 mg. per kilo of body weight daily) for a period of 14 days and from animals 14 days after the administration of DCA had been discontinued. These data, with the exception of the values for the plasma bicarbonate concentration, were included in a previous study (3). In comparison with the control values, it will be seen that following the administration of DCA the decrease of muscle potassium and the gain of intracellular sodium were accompanied by an average decrease of the
plasma chloride concentration of 4.3 m.eq. per kilo of water and by an average increase of the plasma bicarbonate concentration of 3.2 m.eq. per kilo of water. The maximum plasma bicarbonate concentration encountered in this group of animals was found to be 29.8 m.eq. per kilo of water and was accompanied by a muscle potassium of 21.0 m.eq. per 100 gm. of fat-free solids (a minimum value for the group) and by an intracellular sodium of 12.4 m.eq. On the other hand, the minimum plasma bicarbonate concentration was 20.3 m.eq. per kilo of water and was associated with a muscle potassium of 29.2 m.eq. per 100 gm. of fat-free solids and with an intracellular sodium of 9.9 m.eq.

The data presented in Table III reveal that a marked alteration of the

<table>
<thead>
<tr>
<th>Table III</th>
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<tbody>
<tr>
<td>Average Electrolyte Content of Plasma and Skeletal Muscle of Dogs Following Administration of Desoxycorticosterone Acetate and after Its Discontinuance*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Plasm per kilo water</th>
<th>Skeletal muscle per 100 gm. fat-free solids</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Na</td>
</tr>
<tr>
<td></td>
<td>m.eq.</td>
</tr>
<tr>
<td>Controls (40)</td>
<td>156.0</td>
</tr>
<tr>
<td>S.d.</td>
<td>2.8</td>
</tr>
<tr>
<td>Following DCA (9)</td>
<td>156.5</td>
</tr>
<tr>
<td>S.d.</td>
<td>3.1</td>
</tr>
<tr>
<td>After DCA discontinuance (5)†</td>
<td>159.2</td>
</tr>
<tr>
<td>After DCA discontinuance (5)‡</td>
<td>156.3</td>
</tr>
<tr>
<td></td>
<td>156.3</td>
</tr>
</tbody>
</table>

* 2 week periods. 1 mg. per kilo of body weight of DCA was administered daily.
† High sodium and low potassium diet.
‡ Low sodium and moderately high potassium diet.

The muscle composition with respect to potassium and sodium continued to be present in the dogs observed 14 days after the administration of the DCA had been discontinued. On the other hand, the average plasma bicarbonate and chloride concentrations were found to approach the corresponding control values.

The results of these experiments indicated, therefore, that potassium deficiency induced by the administration of DCA to dogs maintained on a low potassium diet is accompanied by a tendency toward an increased plasma bicarbonate concentration. However, when compared with the change observed in rats, the average increase of the plasma bicarbonate concentration was found to be relatively small. In addition, the level of
plasma bicarbonate appeared to bear no clear relationship to the changes of muscle potassium and intracellular sodium.

From the data presented in Table II it is seen that with rats the rise of the plasma bicarbonate concentration was associated with a more or less equivalent but reciprocal change of the plasma chloride concentration. With dogs, the plasma bicarbonate and chloride concentrations were altered in a similar manner, but the magnitudes of the changes were less. These observations suggest the possibility that the increase of the plasma bicarbonate concentration is dependent upon the extent of the plasma chloride decrease and, further, that the plasma chloride concentration can be better maintained in dogs than in rats. It was of interest, therefore, to carry out additional experiments on dogs. In one experiment, in order to confirm the previous findings on dogs, a group of animals was maintained on a low potassium and a normal or high sodium chloride diet and DCA was given (0.5 mg. per kilo of body weight daily) for a period of 3 weeks. In a second experiment, the effect of restricting the intake of chloride as well as potassium was observed. For the latter purpose two dogs were placed on a diet low in potassium and chloride but normal with respect to sodium, and DCA was administered in the same amount and for the same period of time as with the other animals.

From the data presented in Table IV, it will be seen that the average changes of the electrolyte composition of the plasma and muscle encountered in the group of eleven dogs receiving DCA for a period of 21 days were similar to those observed in the animals reported above. An examination of the data obtained from dogs treated in this manner revealed that the changes in muscle composition with respect to potassium and intracellular sodium were of a magnitude similar to those observed in rats. On the other hand, the results of the analysis of the plasma obtained from these dogs gave ample evidence that the changes of the bicarbonate and chloride concentration were less pronounced than those encountered in rats. In this connection, the results obtained on the two dogs which received DCA while restricted in their dietary intake of potassium and chloride are of special interest. From the data obtained on these animals, presented in Table IV, it will be seen that the average plasma bicarbonate concentration was increased to 41.3 m.eq. and was accompanied by a fall of the plasma chloride to 97.1 m.eq. per kilo of water. The chemical analysis of muscle revealed that the potassium was reduced to an average value of 25.1 m.eq. and that the intracellular sodium was increased to an average value of 17.1 m.eq. per 100 gm. of fat-free solids. Thus, with a dietary restriction of chloride as well as of potassium, the administration of DCA led to a marked alteration of the electrolyte composition of muscle and to changes of the plasma bicarbonate and chloride concentration which were of magnitudes even greater than those observed in potassium-deficient rats.
Following Dietary Restriction of Potassium—In commenting on the data presented in Table II, it was pointed out that with rats placed on a low potassium diet for a period of 5 weeks there occurred an increase of the plasma bicarbonate concentration and a fall of plasma chloride, even though the animals' diet was normal with respect to sodium and chloride. From other experiments it was found that a rise of the plasma bicarbonate concentration and a fall of plasma chloride could be demonstrated with rats on the same dietary regimen for as short a period as 7 days. On the other hand, it has been our experience that the electrolyte composition of muscle and plasma of dogs receiving a low potassium and a normal or high sodium chloride diet for a period of 21 days shows relatively little alteration from the normal.

In Table IV are presented the results of the analysis of plasma and muscle of dogs maintained on a diet low in potassium and chloride but normal in

| Table IV |

Average Electrolyte Content of Plasma and Skeletal Muscle of Dogs Maintained on Diets Deficient in Potassium and of Dogs Receiving Desoxycorticosterone Acetate

<table>
<thead>
<tr>
<th>Days on diet</th>
<th>Plasma per kilo water</th>
<th>Skeletal muscle per 100 gm. fat-free solids</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Na m.eq.</td>
<td>K m.eq.</td>
</tr>
<tr>
<td>Normal diet (5)*</td>
<td>21</td>
<td>156.8</td>
</tr>
<tr>
<td>Low potassium + DOA†</td>
<td>21</td>
<td>161.1</td>
</tr>
<tr>
<td>S.d.</td>
<td>3.2</td>
<td>0.6</td>
</tr>
<tr>
<td>Low potassium-low chloride, normal sodium (2)</td>
<td>21</td>
<td>153.4</td>
</tr>
<tr>
<td>Same + DCA† (2)</td>
<td>21</td>
<td>155.1</td>
</tr>
<tr>
<td>Low potassium-low chloride, normal sodium (2)</td>
<td>84</td>
<td>159.3</td>
</tr>
<tr>
<td>Same (1)</td>
<td>84</td>
<td>3.7</td>
</tr>
<tr>
<td>After NaCl intake‡</td>
<td>84</td>
<td>163.8</td>
</tr>
<tr>
<td>Low potassium-low chloride, normal sodium (2)</td>
<td>84</td>
<td>162.2</td>
</tr>
<tr>
<td>After NaCl and KCl intake§</td>
<td>84</td>
<td>164.3</td>
</tr>
</tbody>
</table>

* The numbers within the parentheses indicate the number of animals.
† 0.5 mg. per kilo of body weight of DCA was administered daily.
‡ Diet supplemented with 1 gm. of NaCl per kilo of body weight per day for 3 days.
§ Diet supplemented with 0.1 gm. of NaCl and 0.69 gm. of KCl per kilo of body weight per day for 3 days.

concentration and a fall of the plasma chloride could be demonstrated with rats on the same dietary regimen for as short a period as 7 days. On the other hand, it has been our experience that the electrolyte composition of muscle and plasma of dogs receiving a low potassium and a normal or high sodium chloride diet for a period of 21 days shows relatively little alteration from the normal.
sodium content for periods of 21 and 84 days. It will be seen that the two dogs which received the diet for 21 days exhibited an average loss in muscle potassium of 4.3 m.eq. and an average gain in intracellular sodium of 1.4 m.eq. per 100 gm. of fat-free solids when compared with the corresponding average control values. The average values for potassium and intracellular sodium of muscle from the two dogs placed on the same diet for 84 days revealed deviations from the normal which approximated those observed in the animals above. A similar comparison of the plasma composition revealed that both the plasma bicarbonate and chloride were reduced slightly following the shorter dietary period. On the other hand, with the more prolonged dietary restriction of potassium and chloride there was a definite tendency toward a reduction of the plasma chloride concentration and an increase of the plasma bicarbonate.

The changes of the electrolyte composition of plasma and muscle exhibited by the dogs following the prolonged dietary deficiency of potassium and chloride were similar in direction to those observed in rats when placed on a low potassium diet, but were of a smaller magnitude. In order to observe the effect on the plasma and muscle of supplementing the diet with sodium and potassium chloride, additional experiments were carried out on dogs after they had been maintained on the diet low in potassium and chloride for a period of 84 days. For this purpose the diet of one dog was supplemented with 1 gm. of sodium chloride per kilo of body weight per day for 3 days, and the diet of two other dogs was supplemented with 0.4 gm. of sodium chloride and 0.69 gm. of potassium chloride per kilo of body weight daily for 3 days. From the data presented in Table IV, it will be seen that the supplementation of the diet with sodium chloride resulted in an increase of the plasma chloride from 98.0 to 120.7 m.eq. and a fall of the plasma bicarbonate from 25.3 to 18.7 m.eq. per kilo of water. On the other hand, the levels for muscle potassium and intracellular sodium apparently underwent no change, since these values were found to approximate those observed in the animals studied at the close of the dietary period. In the two dogs whose diet was supplemented with sodium chloride and potassium chloride there was also found to be a prompt increase of the plasma chloride from an average of 104.7 to 115.3 m.eq. and a fall of the plasma bicarbonate concentration from an average of 31.9 to 20.1 m.eq. per kilo of water. In this case the chemical analysis of the muscle revealed a tendency toward restoration of normal levels of potassium and intracellular sodium.

The results of these experiments indicate that with dogs subjected to rather prolonged periods of dietary restriction of potassium and chloride there is a resistance to marked alterations of the electrolyte composition of plasma and muscle. Under the latter experimental conditions, there was found to be a tendency toward a loss of muscle potassium and a gain of
intracellular sodium, while the plasma bicarbonate concentration tended to be increased and the plasma chloride to be reduced. However, the concentrations of plasma chloride and bicarbonate can apparently be restored to normal in such dogs by dietary supplementation with sodium chloride, even though the muscle composition with respect to potassium and intracellular sodium remains distorted.

**DISCUSSION**

From the work carried out in a number of laboratories it is well established that potassium deficiency in rats induced by the dietary restriction of this element or by the repeated injection of DCA leads to a deficit of muscle potassium and a gain of intracellular sodium. The recent observation by Darrow and his coworkers (2) that these changes in muscle composition are associated with an increased plasma bicarbonate concentration is confirmed in the present study. In this connection, the observations of Hegnauer (13), who studied the effect of a low potassium diet and of DCA on the electrolyte content of rat blood and muscle, are of interest. This author noted a diminished plasma chloride concentration, particularly in the animals receiving DCA. Although CO₂ determinations were not carried out, Hegnauer predicted on the basis of a fall of the plasma chloride concentration unaccompanied by a decrease of plasma cation that the alkali reserve would be found to be increased. It is true that the plasma cation concentration undergoes a relatively small change. Consequently, it would appear that the simultaneous fall of the plasma chloride represents an important factor determining the rise of the plasma bicarbonate concentration encountered in potassium-deficient animals. In the present study, a pronounced fall of the plasma chloride concentration, accompanied by an approximately equivalent increase of the plasma bicarbonate concentration, was observed in rats maintained on a diet low in potassium and normal with respect to sodium and chloride. However, when the low potassium diet was altered to contain chloride in excess of sodium, the fall of the plasma chloride concentration and the accompanying increase of the plasma bicarbonate concentration were found to be of a smaller magnitude, even though there was an equal deficit of muscle potassium.

A comparison of the results of the analysis of plasma and muscle of dogs with those obtained with rats under comparable experimental conditions leads to the impression that the plasma chloride concentration can be better maintained in dogs. For example, when DCA was administered to dogs receiving a low potassium but normal or high sodium chloride diet, the changes of muscle potassium and intracellular sodium were found to be of a degree comparable to those observed in potassium-deficient rats. However, the plasma chloride deficit was less in dogs than in rats, and the ac-
companying increase of the plasma bicarbonate concentration was also less. Thus, with administration of DCA to dogs on a diet deficient in potassium, but adequate with respect to chloride, a tendency toward stabilization of the plasma chloride concentration was observed. In contrast, when the diet was made deficient in chloride as well as potassium, the administration of DCA was found to lead to a striking fall of the plasma chloride concentration and an approximately equivalent increase of the plasma bicarbonate concentration, in addition to the marked alteration of the muscle composition with respect to potassium and sodium.

The results of the present experiments, dealing primarily with the effects of a deficiency of potassium, appear inadequate for a discussion of the following question: Do the changes of the plasma bicarbonate and chloride levels constitute an adjustment in response to an altered muscle composition with respect to potassium and sodium, or, do the changes in the composition of the plasma and muscle represent simultaneous processes related to the renal excretion of specific anions and cations? Further work is now in progress on this problem.

SUMMARY

A study was made of the electrolyte composition of plasma and skeletal muscle of rats and dogs with potassium deficiency induced by the administration of DCA and by maintenance on a low potassium diet. The effect of altering the dietary intake of sodium and chloride was also studied. The various findings may be briefly summarized as follows:

1. Potassium deficiency in rats led to a loss of muscle potassium and a gain of intracellular sodium, and, in agreement with the observations of Darrow et al., these changes in muscle composition were found to be accompanied by an increased concentration of plasma bicarbonate. Evidence was obtained that a simultaneous fall of the plasma chloride concentration represented an important factor determining the extent of the plasma bicarbonate increase, since the total cation concentration of the plasma was found to undergo only a relatively small change.

2. Deficits of muscle potassium and increases of intracellular sodium of magnitudes similar to those observed in rats were encountered in dogs when potassium deficiency was induced by the administration of DCA to animals maintained on a diet low in potassium but normal or high with respect to sodium and chloride. In these dogs, however, the fall of the plasma chloride concentration and the rise of the plasma bicarbonate concentration were found to be much less than were observed in the rats.

3. The latter observation lends support to the belief that the plasma chloride concentration was better maintained in dogs than in rats when potassium depletion was induced in the presence of adequate dietary cho-
ride. When DCA was administered to dogs receiving a diet low in chloride as well as potassium, the changes in muscle composition were accompanied by a striking deficit of the plasma chloride concentration and by a marked increase of the plasma bicarbonate concentration.

4. Dogs receiving a low potassium, low chloride but normal sodium diet for a period of 12 weeks exhibited some deficit of muscle potassium and gain of intracellular sodium, while there was a tendency toward a decrease of the plasma chloride and an increase of the plasma bicarbonate concentration. The supplementation of the diet with sodium chloride led to a prompt increase of the plasma chloride concentration and a fall of the plasma bicarbonate, without any further change in muscle potassium or intracellular sodium.

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