Influence of Prolonged Hypothermia and Hyperthermia On Myocardial Sodium, Potassium and Chloride

By G. B. Spurr, Ph.D., and George Barlow, Ph.D.

In dogs cooled to 25 C. and in animals maintained at this rectal temperature for 2 and 4 hours there was a progressive increase in K and decrease in Na content of the left ventricular muscle, with no change in total Cl and H2O. Animals heated to a rectal temperature of 41.5 C. for 1 hour exhibited an elevated total K and no change in total Na, Cl and H2O contents of the myocardium.

The observation, that experimental hypothermia is associated with increased myocardial excitability as evidenced by cardiac arrhythmias and an increased incidence of ventricular fibrillation, is well documented.1, 2 Gollan, Rudolph, and Olsen3 found that in dogs induction of hypothermia to a rectal temperature of approximately 23 C. resulted in a significant decrease in potassium, increase in bromide and no change in sodium content of the atrium. These authors suggested that the increased myocardial excitability during hypothermia is caused or accompanied by a loss of potassium and an inability to extrude sodium. Covino and Hegnauer,4 on the basis of coronary arteriovenous differences, reported that hypothermic-hypercapnic dogs, that subsequently developed ventricular fibrillation, exhibited a loss of myocardial K and H ions and an apparent gain of Ca ion. Normocapnic and hypercapnic dogs that did not develop fibrillation failed to exhibit these changes. On the other hand, Swan5 found that at a rectal temperature of 30 C. the mildly acidotic dog shows a positive balance of potassium in the myocardium, as determined by coronary arteriovenous differ-

ences. In contrast to the in vivo situation, results on the perfused, excised rat heart have shown that during cooling to about 8 C. there is no significant loss of potassium from the myocardium.6

The present study was designed to determine myocardial electrolyte and water contents in hypothermia by direct analysis of left ventricular muscle. To supplement the observations made during hypothermia, experiments were performed on hyperthermic animals in an attempt to delineate the influence of wide spectrum temperature alterations on the parameters studied.

Methods

The results to be presented were obtained from two series of experiments on a total of 78 healthy, adult mongrel dogs varying in weight from 7 to 25 Kg. All animals were anesthetized with 30 mg./Kg. pentobarbital sodium administered intraperitoneally, and were prepared for the experiment by cannulation of the left common carotid artery for blood sampling and exposure of the right external jugular vein for intravenous injection. In the first series of experiments, the samples of left ventricular muscle were taken from the arrested heart 0.5 to 2 minutes following the rapid intravenous injection of 10 ml. of 7 per cent pentobarbital sodium. These experiments were divided into three groups of animals: Normothermia. Thirty normothermic animals served as controls. The cardiac tissue from 22 of these was taken within 30 minutes following anesthesia. After obtaining an arterial blood sample, the animals were injected with the 7 per cent pentobarbital solution, the thorax was opened, and a piece of left ventricular muscle taken from the arrested heart. Since the experimental animals were under anesthesia from 3 to 5 hours before the heart muscle samples were taken, S
additional dogs were maintained under anesthesia for 4 hours before the terminal experiment was performed. Arterial blood samples were obtained at the beginning of the 4-hour period and immediately before the 10 ml of pentobarbital was injected. There was no change in the plasma electrolytes during this time. As cardiac tissue analyses of these experiments were not significantly different from the larger group, the results were pooled to give 30 normothermic controls.

Hypothermia. The hypothermic group of this series consisted of 10 animals cooled to a rectal temperature of 25 ± 0.5 C, between the blankets of a Thermo-Rite Hypothermia Unit, and maintained at this level for a period of 2 hours. Artificial respiration with 100 per cent oxygen was instituted at a rectal temperature of 30 to 31 C. and continued at a rate of 10 to 12 cycles/min. until the termination of the experiment. Additional pentobarbital was administered as required, to keep shivering at a minimum during the period of cooling. When the rectal temperature had been reduced to 28 C, the temperature of the solution circulating through the coils of the blankets was increased to approximately 24 C. During this warming process the animals' rectal temperatures fell to approximately 25 C, where they were maintained. At the end of 2 hours samples of left ventricular muscle were obtained, as in the normothermic animals.

Hyperthermia. Ten animals were heated in a hyperthermia cabinet to a rectal temperature of 41.5 ± 0.5 C, by exposure to an ambient temperature of 50 C. generated by shielded infrared heat lamps. This elevated body temperature was maintained for 1 hour prior to taking the cardiac tissue samples, which were obtained in the same manner as in the normothermic and hypothermic animals.

Because of the surprising nature of the results obtained on the animals cooled to 25 C, for 2 hours, a second series of experiments was performed consisting of two additional hypothermic groups. In one of these groups, cardiac tissue was obtained from 10 animals immediately upon their reaching a rectal temperature of 25 C. In another group of 8 dogs, the rectal temperature was maintained at 25 C, for a period of 4 hours before samples were taken of left ventricular muscle. The injection of the 10 ml of 7 per cent pentobarbital sodium was omitted in this series of experiments, to rule out its possible direct or indirect influence. Thus the samples of cardiac tissue were taken directly from the beating heart. Ten additional experiments were made in the same manner on normothermic dogs, a blood sample and the cardiac tissue being obtained within 30 minutes of anesthetization. In these dogs artificial respiration was commenced with room air shortly before opening the thorax and continued until the tissue sample was taken.

Control blood samples were obtained in all experimental animals before cooling or heating and again immediately before the pentobarbital injection and/or thoracotomy. All blood samples (15 ml.) were taken directly from the carotid arterial cannula into centrifuge tubes containing 3 drops of 1 per cent heparin solution delivered from a size 24 hypodermic needle. Immediately after collection, a hematocrit was determined by the microcapillary technic and the remainder of the blood was centrifuged at approximately 20,000 G in a Servall Supercentrifuge. Plasma concentrations of Na and K were determined with the use of a Perkin-Elmer Flame Photometer. Chlorides were analyzed chemically by an electrometric modification of the Volhard method.

The left ventricular tissue was carefully dissected free of any visible fat and blotted with absorbent paper to remove surface blood. Tissue water content was determined by weighing a 0.5 to 1.0 Gm. sample and drying to a constant weight in an oven at 105 to 110 C. The remainder of the tissue was prepared for analysis in the manner described by Flanagan, Davis, and Overman.

Plasma water was also determined, in the second series of experiments, by the same means as tissue water. Rectal temperatures were taken by means of a thermistor probe inserted approximately 12 cm. Lead II of the electrocardiogram was monitored continuously in all experimental groups by means of a Sanborn Viso-Scope.

Statistical Analysis. The statistical analysis within experimental groups was made on the basis of paired sample data. The comparisons between groups were made on the basis of unrelated data and, in either case, the "null" hypothesis was rejected at the 5 per cent level.

Results

The hypothermic dogs were cooled to 25 C. in 2.5 to 3 hours. These animals exhibited the usual changes in the electrocardiographic pattern with slowing of the rate, widening of the complexes, frequent occurrence of an elevated S-T segment, and ventricular ectopic beats. Heating to a rectal temperature of 41.5 C. was accomplished in approximately 1 hour. The only observable change in the ECG was an increase in cardiac rate to about 200 beats/min.

Left Ventricular Muscle. Series 1. The results of the analysis of cardiac tissue for Na, K, and Xa and K were determined with the use of a Perkin-Elmer Flame Photometer. Chlorides were analyzed chemically by an electrometric modification of the Volhard method.

Heparin generously supplied by Abbott Laboratories.
TABLE 1—Means and Standard Deviations of the Na, K, Cl and H2O Contents of Left Ventricular Muscle in Normothermic, Hypothermic and Hyperthermic Dogs

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of animals</th>
<th>Na (mEq./Kg.*)</th>
<th>K (mEq./Kg.*)</th>
<th>Cl (mEq./Kg.*)</th>
<th>H2O content (ml./Kg.*)</th>
<th>K/Na</th>
</tr>
</thead>
<tbody>
<tr>
<td>Series 1, cardiac tissue after pentobarbital</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normothermia</td>
<td>30</td>
<td>39.8±3.8</td>
<td>80.7±6.5</td>
<td>28.1±2.7</td>
<td>776±11</td>
<td>2.04±0.24</td>
</tr>
<tr>
<td>Hypothermia (rectal temp.=25 C. for 2 hrs.)</td>
<td>10</td>
<td>35.4±2.5</td>
<td>91.9±3.9</td>
<td>28.5±4.3</td>
<td>777±8</td>
<td>2.61±0.29</td>
</tr>
<tr>
<td>Hyperthermia (rectal temp.=41.5 C. for 1 hr.)</td>
<td>10</td>
<td>39.6±2.6</td>
<td>86.8±4.9</td>
<td>28.0±1.6†</td>
<td>772±6</td>
<td>2.21±0.18</td>
</tr>
<tr>
<td>Series 2, cardiac tissue from beating heart</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normothermia</td>
<td>10</td>
<td>39.7±2.8</td>
<td>82.4±2.8</td>
<td>29.6±2.5</td>
<td>775±7</td>
<td>2.09±0.23</td>
</tr>
<tr>
<td>Hypothermia (rectal temp.=25 C.)</td>
<td>10</td>
<td>35.0±2.5</td>
<td>88.1±2.9</td>
<td>29.0±3.5</td>
<td>778±6</td>
<td>2.53±0.21</td>
</tr>
<tr>
<td>Hyperthermia (rectal temp.=25 C. for 4 hrs.)</td>
<td>8</td>
<td>32.4±1.7</td>
<td>96.4±3.3</td>
<td>27.4±4.2</td>
<td>775±6</td>
<td>2.99±0.23</td>
</tr>
<tr>
<td>Series 1 and 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normothermia</td>
<td>40</td>
<td>39.8±3.4</td>
<td>81.1±5.9</td>
<td>28.4±2.7</td>
<td>776±10</td>
<td>2.06±0.24</td>
</tr>
</tbody>
</table>

*Wet weight of tissue.
†4 animals.

K, Cl and H2O contents, and the calculated K/Na ratio of 30 normothermic, 10 hypothermic, and 10 hyperthermic dog hearts are summarized in table 1. Following 2 hours at a rectal temperature of 25 C, the Na content of left ventricular muscle was reduced from an average of 39.8 to 35.4 mEq./Kg. (p < 0.001). At the same time the K content was significantly elevated from a mean normothermic value of 80.7 to 91.9 mEq./Kg. (p < 0.001). There were no changes from the normothermic levels in the Cl or H2O contents, and the K/Na ratio was elevated from a mean of 2.04 to 2.61 (p < 0.001), as would be expected from the observed changes in Na and K.

In the animals heated to a rectal temperature of 41.5 C. for 1 hour there was no alteration in Na content of left ventricular muscle. However, the K content was also significantly elevated in these animals to a mean of 86.8 mEq./Kg. (p < 0.01). The K content of cardiac tissue in hyperthermia was not as greatly elevated as in the animals maintained at a rectal temperature of 25 C for 2 hours (p < 0.02). As in the hypothermic dogs, Cl and H2O contents of the hyperthermic hearts remained unchanged, while the K/Na ratio was significantly elevated to a value of 2.21 (p < 0.05).

Series 2. The results of the analysis of cardiac tissue, taken directly from the beating hearts of 10 normothermic dogs, 10 animals immediately upon reaching a rectal temperature of 25 C, and 8 dogs 4 hours following the reduction of temperature to 25 C, are also summarized in table 1. There were no statistically significant differences between the 10 normothermic control animals of this series and the 30 normothermic controls of series 1. Furthermore, the results of the statistical analysis were the same, whether the experi-
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TABLE 2.—Mean Values and Standard Deviations of Na, K, Cl and H2O in the Plasma of Hypothermic and Hyperthermic Dogs Before and After Cooling or Heating

<table>
<thead>
<tr>
<th>Group</th>
<th>Electrolytes (mEq./L.)</th>
<th>Cl (Gm./Kg.)</th>
<th>Hematocrit (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Na</td>
<td>K</td>
<td></td>
</tr>
<tr>
<td>Series 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothermia (rectal temp.=25 C. for 2 hrs.)</td>
<td>148.0±3.4</td>
<td>3.9±0.4</td>
<td>108.7±0.5</td>
</tr>
<tr>
<td>Hyperthermia (rectal temp.=41.5 C. for 1 hr.)</td>
<td>144.0±3.5*</td>
<td>3.6±0.6*</td>
<td>104.9±0.6</td>
</tr>
<tr>
<td>Series 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothermia (rectal temp.=25 C.)</td>
<td>145.4±5.9</td>
<td>3.9±0.4</td>
<td>107.8±7.8</td>
</tr>
<tr>
<td>Hyperthermia (rectal temp.=25 C. for 4 hrs.)</td>
<td>148.2±5.9</td>
<td>4.5±0.6*</td>
<td>112.4±8.8</td>
</tr>
</tbody>
</table>

*Significantly different from the control value, p < 0.05.
†Before cooling.
‡Before heating.

mental groups of dogs were compared to the two normothermic groups individually, or in combination. Consequently, the normothermic data were pooled to give 40 control animals (table 1). Because of this lack of difference in the two normothermic groups of dogs, direct comparisons, of the 10 animals of series 1, maintained for 2 hours at a rectal temperature of 25 C., with the other hypothermic groups and the 40 control animals, were considered justified.

Cooling to a rectal temperature of 25 C. resulted in a significant reduction in left ventricular Xa from 39.8 to 35.0 mEq./Kg. (p < 0.001). After 2 hours of stable hypothermia the Na content had not changed, although it was still lower than in the normothermic dogs (p < 0.001). Four hours after cooling to 25 C. the Na content was reduced further to an average of 32.4 mEq./Kg. This value was significantly less than the normothermic (p < 0.001) and the other two hypothermic groups of animals.

The K content of left ventricular muscle exhibited a progressive and statistically significant increase upon cooling of intact animals to a rectal temperature of 25 C., and at 2 and 4 hours following the attainment of this degree of hypothermia. Upon reaching 25 C., myocardial K had increased from 81.1 to 88.1 mEq./Kg. (p < 0.001). Two hours later it was significantly elevated above this value to a mean of 91.9 mEq./Kg. (p < 0.05), and at 4 hours was further increased to 96.4 mEq./Kg. (p < 0.02). Chloride and water contents did not differ significantly in the normothermic and three hypothermic groups of dogs. The K/Na ratio followed the same pattern as the K content, with the exception that there was no statistically significant difference between these values in animals that were cooled only to 25 C. and in those maintained at this level for a period of 2 hours.

Plasma. The plasma Na, K, and Cl concentrations, plasma H2O contents, and hematocrits for the hypothermic and hyperthermic groups of dogs are summarized in table 2.

Plasma Na and K concentrations decreased significantly in all three groups of hypothermic dogs. Chloride concentrations were unchanged except in the animals cooled only to 25 C., where the mean value increased significantly from 109.0 to 112.2 mEq./L. (p < 0.001). Hematocrits were significantly ele-
TABLE 3.—Derived Left Ventricular Tissue Data for Hypothermic and Hyperthermic Animals
Before and After the Induced Change in Body Temperature

<table>
<thead>
<tr>
<th>Group</th>
<th>(H₂O)K₂ (Gm./Kg.)</th>
<th>(H₂O)K₃ (Gm./Kg.)</th>
<th>[Na⁺] (mEq./Kg.)</th>
<th>[K⁺] (mEq./Kg.)</th>
<th>[Cl⁻] (mEq./Kg.)</th>
<th>[Ca²⁺] (mEq./Kg.)</th>
<th>[Mg²⁺] (mEq./Kg.)</th>
<th>[Na⁺]/[K⁺]</th>
<th>[K⁺]/[Cl⁻]</th>
<th>Nernst membrane potential (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothermia (rectal temp.=25 C.)</td>
<td>Control*</td>
<td>216</td>
<td>650</td>
<td>11.6</td>
<td>143.3</td>
<td>4.1</td>
<td>13.3</td>
<td>34.6</td>
<td>94.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>218</td>
<td>560</td>
<td>3.9</td>
<td>156.0</td>
<td>3.4</td>
<td>38.7</td>
<td>45.7</td>
<td>98.3</td>
<td></td>
</tr>
<tr>
<td>Hypothermia (rectal temp.=25 C. for 2 hrs.)</td>
<td>Control*</td>
<td>216</td>
<td>650</td>
<td>10.2</td>
<td>143.3</td>
<td>4.1</td>
<td>15.4</td>
<td>34.5</td>
<td>94.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>227</td>
<td>550</td>
<td>1.1</td>
<td>165.4</td>
<td>3.8</td>
<td>139.4</td>
<td>43.2</td>
<td>96.8</td>
<td></td>
</tr>
<tr>
<td>Hypothermia (rectal temp.=25 C. for 4 hrs.)</td>
<td>Control*</td>
<td>209</td>
<td>567</td>
<td>12.7</td>
<td>141.4</td>
<td>4.0</td>
<td>12.3</td>
<td>34.8</td>
<td>95.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>204</td>
<td>571</td>
<td>2.1</td>
<td>167.6</td>
<td>3.5</td>
<td>72.7</td>
<td>48.9</td>
<td>100.0</td>
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</tr>
<tr>
<td>Hyperthermia (rectal temp.=41.5 C. for 1 hr.)</td>
<td>Control*</td>
<td>218</td>
<td>558</td>
<td>10.8</td>
<td>143.8</td>
<td>4.1</td>
<td>14.3</td>
<td>34.6</td>
<td>94.8</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>203</td>
<td>569</td>
<td>14.0</td>
<td>150.7</td>
<td>4.7</td>
<td>11.1</td>
<td>31.5</td>
<td>93.5</td>
<td></td>
</tr>
</tbody>
</table>

*Calculated by using the mean values obtained by the analysis of left ventricular muscle of 40 normothermic animals together with the control plasma values of each of the individual groups.

( ) = Per Kg. of left ventricular tissue.
[ ] = Per Kg. of water.
E = Extracellular.
I = Intracellular.

vated in all hypothermic animals. The plasma H₂O contents were slightly reduced upon cooling to 25 C. and after 4 hours of a rectal temperature of 25 C. (table 2).

The hyperthermic animals exhibited a statistically significant elevation in plasma K from a preheating mean of 3.9 to 4.5 mEq./L. (p < 0.05) 1 hour after reaching a rectal temperature of 41.5 C. The hematocrit was also significantly elevated at this time. There was no alteration in plasma Na or Cl in these animals.

Derived Data. The derivations of extracellular and intracellular concentrations of electrolytes and water were made by assuming that electrolytes are distributed between plasma and interstitial fluid in a Gibbs-Donnan equilibrium. A Donnan factor of 0.98 was used on the basis of the observation by Drinker et al. of a 4 per cent protein concentration in dog cardiac lymph. In order to convert electrolyte concentrations from mEq./L. to mEq./Kg. of water, plasma was assumed to be 92 per cent water in the dogs of series 1, and that it remained constant. The small reduction in plasma water observed in the hypothermic animals of series 2 (table 2) introduces a negligible error into the calculation. In the animals of series 2, the measured values of plasma water were used. Extracellular water was derived by assuming that, because of the predominant extracellular distribution of Na, K and Cl are distributed across the cell membrane in such a way that extracellular K closely approximates intracellular Cl. The equations utilized have been presented by Robertson and Peyser, and by Benson et al.

The results of the derivations are presented in table 3. In making the calculations, only the mean values were used. Furthermore, the average figures for cardiac electrolytes of the 40 normothermic dogs (table 1) were used together with the mean control plasma values (table 2) of each of the four experimental groups of animals, to determine precooling or preheating levels. Consequently, the values
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in Table 3 are presented only as a qualitative indication of the direction of change. However, the estimated levels for extracellular and intracellular water and intracellular electrolytes show good agreement with those obtained by others. The estimated resting membrane potentials, calculated from the $[K]_e/[K]_i$ gradients, are near the high end of the normal range. Cranefield and Hoffman have pointed out that the calculated resting membrane potentials exceed measured resting potentials, probably partly because of the contribution of other ions to the transmembrane potential.

Table 3 indicates that hypothermia resulted in an intracellular loss of Na and gain of K, with little change in Cl or H$_2$O, except in the animals maintained at a rectal temperature of 25 C. for 2 hours, where there appeared to be a slight shift of water out of the cardiac cells. However, this change was too small to account for the elevated intracellular K concentration. The estimated membrane potentials of the three groups of hypothermic animals were increased only slightly. Hypothermia resulted in a proportionately greater increase in the Na differential ($[Na]_e/[Na]_i$) across the cardiac cell membrane than in the K differential ($[K]_e/[K]_i$).

Elevation of the body temperature, on the other hand, resulted in a slight increase in intracellular Na, K, and Cl. There was also a small inward movement of water from the extracellular to the intracellular space.

DISCUSSION

The most acceptable form of reporting the results of tissue analysis is in terms of blood-free, fat-free tissue. This is particularly true when comparisons of electrolyte contents are made between different tissues, or when a tissue of control animals is compared to the same tissue of animals subjected to a chronic experimental situation of several days or weeks' duration. However, in the acute experiments reported herein, alterations in fat content have not been considered to play any role in the observed changes in myocardial electrolytes. On the other hand, changes in blood content of left ventricular muscle might appear to contribute to the modifications of cardiac electrolytes in the present experiments, particularly to the observed decrease in tissue Na content in hypothermia. Two lines of reasoning tend to negate this possibility. First, if a decrease in the blood content of left ventricular muscle during hypothermia was the cause of the observed decrease in Na content, there should have been a concomitant reduction in tissue Cl. This did not occur (Table 1). Secondly, it is possible to estimate the approximate contribution of blood Na to the total tissue Na. Benson et al. have reported that the left ventricular muscle of 7 normal dogs contained an average of 10.6 ml. blood/100 Gm. of fat-free tissue solids, or approximately 23 ml./Kg. of wet tissue. If a blood Na concentration of 145 mEq./L. is assumed, 23 ml. of blood would contribute about 3.3 mEq./Kg. to the total tissue Na. This is a slight overestimation, since dog erythrocytes contain only 115 to 120 mEq./L. of Na. The smallest decrease in tissue Na amounted to a mean reduction of 4.4 mEq./Kg. 2 hours after cooling to a rectal temperature of 25 C. (Table 1). Consequently, even the complete removal of blood from the ventricular muscle could not account for the observed reduction in tissue Na in hypothermia, and, while small decreases in blood content of the myocardium may have contributed to the observed changes in Na content, this could not be a major factor. Therefore, under the conditions of the present experiments, cooling of the body temperature to 25 C. resulted in an intracellular loss of Na.

The progressive increase in K content of left ventricular muscle resulting from prolonged hypothermia of this degree could only be the result of an intracellular accumulation of the ion (Table 3). These results are not in accord with those of Gollan et al. and of Covino and Hegnauer. However, Swan has reported a positive myocardial K balance at rectal temperatures of 30 C., and Montgomery, Prevedel and Swan, on the basis of coronary arteriovenous differences in K, have shown that in hypothermic dogs hypoventilation resulted first in an accumulation of K in cardiac tissue,
then in a gradual development of a state of myocardial K balance when the dogs were artificially hyperventilated. Reversal of the procedure reversed the order of the results, i.e., myocardial K balance followed by accumulation of K during the subsequent period of hypoventilation. It has been suggested that these observations were the result of treatment with acetylcholine, vagal stimulation or prostigmine to prevent ventricular fibrillation during the coronary sinus catheterization procedure. Acetylcholine and vagal stimulation have been shown to increase loss of K from the normothermic and cold heart. Since the results of the experiments of Montgomery et al. were the same, whether hypoventilation followed hyperventilation or vice versa, it is difficult to ascribe their findings entirely to the drugs that were administered.

The hypothermic animals in this study exhibited an electrocardiographic pattern indicative of increased myocardial excitability. The question of how the increased cardiac K and decreased Na are related to the changes in ventricular excitability, known to occur in hypothermia, is uncertain. Elevated intracellular K appears to produce little effect on the resting membrane potential, and it may be that K does not determine the ventricular excitability changes during cooling of dogs to 25°C for periods of up to 4 hours. On the other hand, it has been shown that reduction of the Na gradient across the cell membrane reduces the excitability of skeletal muscle, whereas elevation of this gradient increases the excitability of nerve. The large increments in Na gradients in the hypothermic hearts of the present experiments may indicate a contributory role for Na, in addition to Ca and H ions, in the cardiac excitability alterations which occur in hypothermia of this degree.

The animals heated to a rectal temperature of 41.5°C exhibited an elevated K content of left ventricular muscle with no change in the total Na, Cl, or H₂O contents (table 1). The derived data indicate that the K elevation was an intracellular one, and, further, that there was a slight elevation in intracellular Na associated with a small movement of H₂O from the extracellular into the intracellular compartment (table 3). These changes may be due to the cell permeability alterations which have been shown to accompany the pyrexic state. The increased plasma K levels observed in these experiments (table 2) may also have contributed to the elevation in K concentration of cardiac tissue. The rise in plasma K in hyperthermia has been attributed to a possible release from the respiratory musculature, associated with the marked muscular effort of panting, and/or to a release of epinephrine.

The lack of appreciable change in the Na and K gradients across the cardiac tissue cell membrane and in the estimated resting membrane potential at a rectal temperature of 41.5°C (table 3) is in keeping with the absence of electrocardiographic evidence of cardiac excitability alterations in this degree of hyperthermia, both in the present experiments and in the experiments of others.

**Summary**

Direct analyses of left ventricular muscle for Na, K, Cl and H₂O contents have been made in dogs subjected to prolonged lowering and elevation of the body temperature.

Induction of hypothermia to a rectal temperature of 25°C for periods of time of up to 4 hours resulted in a progressive loss of Na and an accumulation of K in the myocardium. Indirect calculations demonstrate these alterations to be intracellular in nature. No changes were observed in the Cl or H₂O contents. The results indicate a possible contributory role for Na in the excitability changes known to occur in the hypothermic heart.

Induction of hyperthermia to a rectal temperature of 41.5°C for a period of 1 hour resulted in a rise in left ventricular K content with no significant alteration in total Na, Cl, or H₂O contents. Calculations of intracellular concentrations of these variables suggest that in the hyperthermic heart there is a slight movement of the electrolytes and water into cardiac tissue cells commensurate with the known effects of pyrexic states on cellular permeability.
The data presented do not provide an explanation of the possible mechanisms by which altered body temperature results in the observed changes in myocardial electrolytes.

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SUMMARIO IN INTERLINGUA

Analyses directe del contento de Na, K, Cl, e H2O in musculo sinistro-ventricular de canes esseva effectuate post subjection del animals a prolongate periodos de reduction e de augmentation del temperatura corporea.

Le induction de un hypothermia al nivello de un temperatura rectal de 25 C resultava post su mantenentia durante periodos de usque a 4 horas in un perdita progressive de Na e un accumulation progressive de K in le myocardio. Calculations indirecte demonstra que iste alterationes es de character intracellular. Nulle alterationes esseva observate in le contento de Cl o H2O. Le resultatos indica un possibile rolo contributori de Na in le alterationes del excitabilitate que occurre cognoscemente in le corde hypothermic.

Le induction de un hyperthermia al nivello de un temperatura rectal de 41,5 C resultava post su mantenentia durante un periodo de 1 hora in un augmento del contento de K in le ventriculo sinistre, non accompaniate de alterationes significative in le contento total de Na, Cl, o H2O. Calculations del concentration intracellular de iste variables suggere le existentia, in un corde hyperthermic, de leve movimentos del electrolytos e de aqua a in le celular del histo cardiac, commensurate con le cognoscite efectos de statos pyrexic super le permeabilitate cellular.

Le datos presentate non provide un explication del possibile mechanismos per le quales alterate temperaturas corporee resulta in le observate alterationes del electrolytos myocardial.

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