Electrocardiographic and Plasma Potassium Responses Elicited on Cooling the Chest Wall of Man

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The application of ice to the anterior chest wall in human subjects resulted in retardation of repolarization of the anterior myocardium and was accompanied by a decrease in the plasma potassium. These phenomena were tentatively related to the effects of local cooling of the myocardium.

It has been demonstrated\(^1\)\(^-\)\(^6\) that indirect local cooling of the heart in man produces characteristic electrocardiographic changes analogous to those obtained by direct cooling of the myocardium in experimental animals.\(^7\)\(^-\)\(^10\) In particular, precordial cooling in man causes depression and inversion of the T wave over the site of the cooled myocardium.

In this study the precordium was cooled in 2 ethnic groups, African (Bantu) and European (white South African), in order to gain further information on the factors involved in the production of the altered pattern in the electrocardiogram. An attempt was made to correlate the T-wave changes with the decrease in the serum potassium levels that resulted from precordial cooling. In addition, further observations are presented on the different electrocardiographic response in the African as compared with the European.\(^5\)

METHODS

Ten African and 10 European healthy male students presented themselves for investigation either in the afternoon or morning after 6 to 12 hours of food deprivation; water was permitted ad lib. The subject rested in the reclining position for an initial period of 30 to 60 minutes (basal period). An icebag 10 1/2 inches in diameter was then placed on the anterior chest wall for 1 hour (experimental period). After removal of the icebag the subject remained in the same position for a further 60 minutes (recovery period).

During the basal period, recordings were taken of the arterial blood pressure and skin temperatures over the precordium and ankle, and venous blood was drawn for the chemical and other analyses listed below. At the end of the basal period these procedures were repeated and in addition an electrocardiogram was recorded immediately after the drawing of the second sample of blood. A baseline having thus been established, the icebag was applied and during the subsequent experimental period all the above procedures were repeated at 15-minute intervals. A final series of observations was made at the end of the recovery period.

The conventional 12-lead electrocardiogram was recorded for 2 respiratory cycles. During the experimental period at the 15-, 30-, and 45-minute intervals, lead V\(_2\) only was used, the electrode being placed under the icebag.

The blood samples drawn at all the intervals mentioned were analyzed for sodium and potassium\(^11\) in all the subjects, calcium\(^12\) in 9 subjects, hemoglobin and hematocrit values (the tubes were spun at 3,500 r.p.m., 2,050 G for 45 minutes) in 9 subjects, and glucose according to the Somogyi method in 6 subjects. In 10 subjects the number of eosinophils was determined\(^12\) in the blood sample drawn after cooling for 60 minutes and was compared with the number in the basal and recovery samples.

Sodium and potassium were also estimated in the urine\(^13\) in 5 subjects during the basal, experimental, and recovery periods. Six subjects either could not void urine or the volumes were insufficient to draw reliable conclusions.

To assess whether the local cooling of the precordium was responsible for the findings to be presented, each subject was reinvestigated on a subsequent occasion. Identical procedures were followed in each instance, except that the icebag was placed either on the abdomen or on the lateral aspect of the thigh. This experiment will be referred to as the control. In this control series the temperature readings of the cooled area of skin showed a decrease similar to that obtained over the precordium. The areas of skin cooled were similar in the case of the chest and abdomen, and somewhat less in the case of the thigh.

RESULTS

T Waves

Chest Leads. Depression or inversion of the T wave in lead V\(_2\) was observed 15 minutes after placing the icebag on the chest. The voltage decreased progressively and at the end of the experimental period depression or inversion

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Fig. 1. Serial electrocardiogram tracings and plasma potassium concentrations in an African subject (a) and European subject (b).

of the T wave was found in leads V1 to V4, while leads V5 and V6 showed minor or no change. At the end of the recovery period, the average amplitude of the affected T waves returned to a level only slightly below that of the basal height. These serial responses (figs. 1 and 2) were observed in all cases except 1 African. T-wave inversion occurred in leads V1, V2, and V3 in 3 Africans (fig. 1a) and in V1 or V3 in 2 more Africans. On the other hand, in 5 Europeans the T wave became inverted only in lead V1 (fig. 1b). In addition, the per-
FIG. 2(a)

FIG. 2(b)

Fig. 2. a. Mean decrements of plasma potassium (ΔKₚ) in both the control and experimental groups. Crosshatched blocks, experimental; clear blocks, control; continuous line, experimental mean values; broken line, control mean values. Number above the histogram represents number of control observations. Number below represents number of experimental observations. Inset: t test. b. Mean decrements in T wave in lead V₂ (ΔTV₂) in millivolts (MV) for both control (broken line) and experimental subjects (continuous line).
centage reduction in the amplitude of the T waves (leads V₁ to V₄) in the African and European students (table 1), also illustrates that the area of the myocardium subtended by the electrodes Vₛ, V₃, and V₄ was affected more in the African than in the European group.

Notching of the descending limb of the T wave in leads V₅, V₃, and V₄ was a striking feature in 5 Africans and 5 Europeans (fig. 1). In one of these subjects the notching preceded inversion of the T wave and in another notching was detected only at the end of the recovery period, having been preceded by inversion of the T wave during cooling. In these 2 subjects the notch and nadir of the inverted T wave were equidistant from the Q wave (fig. 1a; lead V₅, 60-minute cooling and recovery tracings). This observation suggested that the notch is an early stage in the genesis of the inversion.

Limb Leads. Slight depression of the T wave was observed in lead I (7 subjects), lead II (2 subjects), and lead aV₆ (10 subjects), with a small increase in positivity in leads III (12 subjects), aV₆ (16 subjects), or decrease in negativity in lead aV₆ (4 subjects).

Other Modifications in the Electrocardiogram

The P wave became flattened in V₂ in one subject and in leads V₁ and V₂ in another. In a third subject notching in lead V₂ disappeared after cooling the chest. Inspection of the QRS complexes and measurement of the Q-Tc (V₂) showed only minor variations from the basal Q-Tc. The ST segments in leads V₂, V₃, and V₄ were raised in 11 subjects and, with the exception of 2 subjects, showed bowing with an upward concavity. In every instance the U wave remained unaltered.

When the abdomen or thigh was cooled (control), no electrocardiographic changes were observed.

Plasma Potassium

The average basal plasma potassium was 4.74 (S.D. 0.28) mEq./L. prior to precordial cooling (experimental group) and 4.72 (S.D. 0.21) mEq./L. prior to abdominal or thigh cooling (control group). In figure 2a the serial decrements of the plasma potassium are shown for both groups. There was a relatively marked progressive decrease of plasma potassium in the experimental group (−0.39 mEq./L. at 60 minutes) as compared with the small decrease in the case of the control group (−0.10 mEq./L. at 60 minutes). Application of the t test showed that the difference was highly significant (fig. 2a). An hour after pre-
cordial cooling, the plasma potassium approximated the basal value.

The 2 ethnic groups showed similar responses but not all individuals reacted according to the pattern outlined above. A significant decrease of plasma potassium was taken as 3 × S.D. of the error of the estimation (3 × 0.086 mEq./L.). According to this criterion, 1 African subject showed an insignificant deviation on precordial cooling. A relatively marked drop in plasma potassium concentration occurred in 2 subjects with abdominal or thigh cooling. In one of these a maximum drop of 0.31 mEq./L. occurred at 45 minutes and persisted to the end of the recovery period; this drop however was not as great as that reached with precordial cooling, viz., 0.51 mEq./L. In the other subject a maximum decrease of 0.36 mEq./L. was found at the 30- and 60-minute intervals with recovery above the basal value an hour later; here again the decrease after cooling the chest was greater, i.e., 0.49 mEq./L. In general, however, the results clearly demonstrated that a decrease of plasma potassium was induced specifically by precordial cooling.

Relation Between T Wave and Potassium Changes

A parallel drop in the T wave and plasma potassium is illustrated by the mean decre-

TABLE 1.—Average Percentage Reductions in Amplitude of T Waves after Sixty Minutes of Precordial Cooling

<table>
<thead>
<tr>
<th>Precordial leads</th>
<th>V₁</th>
<th>V₂</th>
<th>V₃</th>
<th>V₄</th>
</tr>
</thead>
<tbody>
<tr>
<td>African</td>
<td>68</td>
<td>72</td>
<td>65</td>
<td>57</td>
</tr>
<tr>
<td>European</td>
<td>99</td>
<td>59</td>
<td>38</td>
<td>31</td>
</tr>
</tbody>
</table>

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ments were however uncorrelated. The correlation coefficient between the decrements of the T-wave amplitude and the decrease of plasma potassium was calculated for the data at the 60-minute time interval. The variables taken were the percentage deviations from the basal values. For these data \( r = +0.381 \) (t = 1.75, D.F. = 18, \( p > 0.10 \)), which represent an insignificant correlation. In addition, there were exceptional cases. Firstly, with precordial cooling the one African student whose electrocardiogram did not change showed a drop in the potassium \((-0.46 \text{ mEq.} / \text{L.})\); secondly, the reverse occurred in another African; and thirdly, in the control studies 2 subjects showed a drop in the plasma potassium on abdominal or thigh cooling without any alterations in the electrocardiogram.

Other Investigations

The decrease in the plasma potassium concentration could not be accounted for by any change in the plasma volume (calculated according to the formula \( PV \) = plasma volume, \( Hb = \) hemoglobin in Gm./100 ml., \( Ht = \) hematocrit) nor by an excess excretion of potassium in the urine. No significant modifications in the plasma sodium and calcium were obtained.

The precordial cooling was accompanied by a reduction in the pulse rate. The blood pressure rose, the diastolic more than the systolic, and the skin temperature over the ankle dropped with cooling of the chest and of the abdomen or thigh. All these alterations (table 2) were more marked in the African group.

The eosinophil counts and the levels of blood glucose did not indicate that cooling elicited an adrenal response. These findings do not necessarily rule out an adrenocortical response selectively affecting the plasma potassium level.

**DISCUSSION**

The progressive depression and inversion of the T waves in leads V₁ to V₄ are theoretically due to delayed repolarization of the anterior surface of the ventricles, lying adjacent to the recording electrodes. Similarly, the notching of an otherwise smooth descending limb of the T wave would be compatible with a disparity in the rate of the repolarization between portions of the myocardium. The findings in the limb leads are also consistent with involvement of the anterior surface of the heart. The assumption is made, therefore, that these manifestations were due to cooling of the anterior surface of the myocardium as a result of penetration of cold through the chest wall. The analogous responses of the electrocardiogram obtained in experimental animals, in which the hearts were cooled directly, support this hypothesis. The direct correlation between experimentally produced temperature changes of the heart in dogs and the concomitant alterations in the voltage of the T wave¹⁴ also favors this supposition.

The exaggerated response of the electrocardiogram in the African could therefore be attributed to a greater degree of cooling of portions of the epicardial surface. Certain factors would appear to facilitate the conduction of the cold through the chest wall to the heart in the African. Firstly, the African students had a relatively thin skin fold over the precordium. Taken in conjunction with

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**Table 2.—Average Alterations (Compared with the Basal Values) of the Pulse Rate, Blood Pressure, and Skin Temperature**

<table>
<thead>
<tr>
<th></th>
<th>Pulse per min.</th>
<th>B.P. mm. Hg</th>
<th>Skin temperature (ankle) °C.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>60-min. cooling</td>
<td>Recovery</td>
<td>Maximal change 15-60 min. cooling</td>
</tr>
<tr>
<td>European</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest</td>
<td>-3.9</td>
<td>-3.1</td>
<td>+4.6</td>
</tr>
<tr>
<td>Control</td>
<td>+0.2</td>
<td>-0.5</td>
<td>+6.2</td>
</tr>
<tr>
<td>African</td>
<td>-7.6</td>
<td>-6.1</td>
<td>+6.2</td>
</tr>
<tr>
<td>Control</td>
<td>-2.1</td>
<td>-2.8</td>
<td>+11.0</td>
</tr>
</tbody>
</table>
the lower average weight of the African compared with the European group, the possibility exists that the heart in the African is not as well insulated by subcutaneous and possibly also by deep fat. Indeed, Rahman and co-workers noted that in poorly nourished subjects the electrocardiographic response to precordial cooling was greater than in well nourished individuals. The observations of Piaggio Blanco and associates are also relevant; they obtained the most marked modifications in the T wave in a subject with a rib resection whose heart was close to the skin; conversely, the least alterations in the T wave were seen in subjects with pneumothorax or emphysematous bullae, where the air acted as a poor conductor between the icebag and the heart.

Secondly, measurements of the circumference and anteroposterior diameters between bony points at various levels revealed that the chest was smaller in the African than in the European. Thus, in the smaller thoracic cage of the African the heart may be close to the anterior chest wall; consequently the heart would be more readily cooled by an icebag on the precordium. While the precordial thickness of fat and size of the chest may contribute to the differences in the response of the electrocardiogram in the 2 ethnic groups, there were a number of exceptions. A comparative study on a larger scale of the orientation and insulation of the heart in the 2 ethnic groups may provide evidence to confirm the postulates made. Whether there is a relationship between this readily producible inversion of the precordial T waves in the African and the so-called spontaneous inversion in Africans and American Negroes requires consideration.

The cooling of the myocardium was also probably responsible for the slowing of the heart rate (table 2). However, it is unlikely that the heart was cooled sufficiently (the precordial skin temperature having been decreased by 18 C.) to produce an "injury potential" of the myocardium. The possibility may be entertained that the raised ST segment, found in 11 subjects, could be due to the slowing of the recovery process resulting in a continuum of the potential imbalance from one cycle to another.

The mechanisms whereby cold retards the rate of repolarization remains to be explained. Coronary vasoconstriction with consequent diminution in blood supply is a suggested mechanism. A vagotonic response to cold, which is alleged to be exaggerated in the African (Bantu), has been implicated. The present investigation does not permit an assessment of these possibilities.

Current theory holds that the ionic transfer, particularly of sodium and potassium, across the membrane is related to the potential changes in nerve and muscle. The relationship of the plasma potassium concentration to the T wave has been comprehensively reviewed. In the present experiment it was demonstrated that the plasma potassium concentration and the height of the T wave decreased progressively in a parallel fashion (fig. 2). Whether these 2 variables are mutually dependent or are independent manifestations of precordial cooling cannot easily be assessed. Presumably, the drop in the plasma potassium level was a parameter of an altered intracellular and extracellular potassium balance in the cardiac muscle, modifying the T wave. Admittedly, there was a lack of correlation between the decrements of the concentration of plasma potassium and the amplitude of the T wave. But the plasma potassium level per se is no indication of the intracellular and extracellular equilibrium of potassium in the heart. Furthermore, the individual sensitivity of the heart to a decrease in the plasma potassium must also be taken into account.

The mechanism whereby precordial cooling lowers the plasma potassium remains to be established. The decrease in the concentration cannot be accounted for by hemodilution or increased urinary excretion. While further blood volume studies and more urinary estimations are necessary to confirm these results, it is to be inferred at present that a change in the intracellular-extracellular potassium balance has occurred. It is unlikely that the heart alone retained the amount of potassium lost from the extracellular compartment. The average maximum decrease in the plasma
potassium of the subjects investigated was 0.39 mEq./L.; if an extracellular fluid volume of 20 per cent of the body weight is assumed, the loss from the extracellular compartment for these subjects can be calculated as 5 to 6 mEq. Since the heart contains approximately 25 mEq. of potassium,\textsuperscript{22} it would have meant an extremely high proportion of potassium uptake by the cardiac muscle alone. An increased uptake of potassium by the heart would indeed be contrary to the findings reported on generalized hypothermia of an increased output of potassium by the heart.\textsuperscript{23} Furthermore, it has been shown that cooling of isolated striated muscle (rat diaphragm) produces a decrease in the rate of inflow of potassium into the muscle.\textsuperscript{24} In our control experiments cooling of striated muscle (abdominal and thigh) did not generally alter the plasma potassium concentration.

From the available literature, no information was obtained about the movements of electrolytes during local cooling of the heart in the intact animal or in man. During generalized hypothermia, however, a rise in the potassium has been reported in rats,\textsuperscript{25} dogs,\textsuperscript{26, 27} and unanesthetized human subjects.\textsuperscript{28} On the other hand, a fall in the potassium has also been obtained in dogs.\textsuperscript{27, 29, 30} The rise in the plasma potassium in the case of the cooled rats was attributed to shivering and an associated, increased liver glycolysis. Shivering could also have accounted for the rise in plasma potassium in the human subjects. The cause for the fall in the plasma potassium in dogs was considered in terms of a rise in pH produced by hyperventilation, but a decrease in the plasma potassium was also obtained.\textsuperscript{30} The carbon dioxide content of the blood could not be correlated with the changes in the plasma potassium.\textsuperscript{27} In our experiments, shivering did not occur nor were there any obvious changes in the rate and depth of respiration. Hence these complications did not disturb the plasma potassium level.

As the modifications, both in the electrocardiogram and in the level of the plasma, were detected only with cooling of the chest, it is tempting to ascribe the cause of these modifications to a common factor. In general terms it may be postulated that the cold inhibited a chemical system in the myocardium concerned with the ionic exchange related to the repolarization process. Disturbance of this system may have triggered a reaction affecting the potassium transfer from the extracellular to the intracellular compartment. Perhaps the affected system involved the acetylcholine-cholinesterase relationship to the potassium and the repolarization process.\textsuperscript{31} While it is well known that potassium profoundly affects cardiac activity, the results of our experiments suggest that a decrease in temperature of the heart may in turn affect potassium metabolism in general.

**Summary**

Cooling of the anterior chest wall in 20 students (10 African and 10 European) resulted in depression and inversion of the T wave in leads V\textsubscript{1} to V\textsubscript{4} and a concomitant decrease in the plasma potassium concentration. The most marked T-wave modifications occurred in African students and this has been attributed to a greater penetration of cold to the myocardium.

From investigations of the urinary potassium excretion and from calculations of the plasma volume it has been inferred that the decrease of the plasma potassium concentration was due to a passage of potassium into the intracellular compartment.

As the T-wave modifications and the decrease of the plasma potassium concentration occurred specifically with cooling of the chest wall and not when other localized areas of the body were cooled, it is postulated that cooling of the heart affected a mechanism that influenced both the repolarization process and the regulation of potassium metabolism.

**Acknowledgment**

We wish to thank Professor Joseph Gillman, Dr. S. Brenner, and Dr. B. van Lingen for helpful criticism and advice during the preparation of this paper. We are grateful to those students of the 1953 physiology class for volunteering as experimental subjects. Thanks are due to the University Research Committee for a grant to one of us (B. K.) to purchase a Sanborn electrocardiograph.

**Summario in Interlingua**

Frigidation del pariete antero-thoracice in 20 studentes (10 african, 10 europee) resultava
in le depression e inversion del unda T in le derivationes V1 a V6 e un reduction concomitante in le concentration del kalium plasmatic. Le plus marcate modificationes del unda T occurreva in studentes african, un facto al presente penetration del frigido usque al myocardio.

Super le base de investigationes del excretion urinari del kalium e de calculationes del volumine plasmatic il ha esse possibile concluer le reduction del concentration del kalium in le plasma esseva le resultato de un passage del kalium a in le compartimentos intracellular.

Proque le modificationes del unda T e le reduction del concentration del kalium in le plasma occurreva specificemente post frigidation del pariete thoracic e non quando altare areas localisate del corpore esseva frigidate, il es possibile postular que le frigidation del corde afficeva un mechanismo que influenziava tanto le processo de repolarisation e le regulation del metabolismo del kalium.

REFERENCES


Hypotensive agents were administered to a series of patients, some hospitalized, some ambulatory, with hypertensive disease of all degrees of severity. Dosages were such as to produce either apparent lowering of blood pressure or undesirable side effects. Hydralazine, hexamethonium, rauwolfia, veratrum alkaloids, and the low-sodium diet were used. It is pointed out that the usual method of evaluation fails to give an accurate picture of the specific role of these drugs in a treatment regimen. Data indicated that (1) inclusion of a patient in a special study may exert a hypotensive effect; (2) medicaments exert an additional effect (controlled by placebo-drug alternation); (3) nonpharmacologic stimuli in the experimental situation may have equal effect to the drug. The appraisal method outlined is of critical importance in the study of specific effects of hypotensive drugs. Of the drugs that were tried, none was found to have a specific role in treatment of hypertensive disease.

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