Electrocardiograms and Electrolytes

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The author studied various patterns of the electrocardiogram associated with changes in the plasma electrolytes composition observed wave forms according to the principles deduced from a parallel study of the intracellular potential. The role of electrolyte in the pathogenesis of certain arrhythmias were also clarified.

It is generally believed that the electrocardiogram is a composite sum of the electrical phenomena of individual cardiac muscle fibers and that the electrical phenomena of a single cardiac muscle fiber derive their origin essentially in the concentration gradient of the electrolytes across the cell membrane, i.e., concentration cell.

As an approach to the understanding of the electrocardiogram the author studied the effect of changing the extracellular electrolyte concentration on the electrocardiogram and the resting or action potential of a single cardiac muscle cell (Fig. 1).

I. ABNORMAL CONCENTRATIONS OF ELECTROLYTES AND THE ELECTROCARDIGRAM

(a) Abnormal concentrations of potassium

Upon a rapid increase in the plasma K concentration caused by the drip infusion of 1% KCl solution, the T wave became sharp and high with increase in T/R ratio; R wave became low; P became low and wide and then it disappeared. The duration of P, QRS and PQ was all prolonged and the impulse conduction was slowed down; R–R was shortened and QT time was prolonged.

With further increase in K concentration, the wave became that of giant triphasic form with a markedly widened QRS and the disappearance of the ST segment; this then led to bursts of heart block, extrasystole and finally to the cardiac standstill.

With a gradually produced hyperpotassemia effected by the ligation of the ureters and where the blood level of K was as high as 9–10 mEq/L, however, the P wave became wide but it did not disappear. While the absence of P waves is considered to be one

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Fig. 1. Action potential and ionic movement.

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characteristic feature of the hyperpotassemia, there remains much to be decided as to the reactivity, to K, of the auricular and ventricular muscle.

With hypopotassemia produced by insulin there was ST depression, flat T and decrease in T/R ratio; U waves were most frequently found over the transitional zone; T wave and U wave were difficult to discriminate in some leads; initially at least, there was shortening of QT time. Similar electrocardiograms resulted from the hypopotassemia produced by DOCA.

Thus the width of P wave, PQ interval were increased with increased K concentration, and the duration of QRS increased with increased K concentration; there was a significant correlation between the height of T wave and K concentration. The QT time was occasionally prolonged by the hyperpotassemia, but it was not necessarily prolonged by the hypopotassemia. As to the Q–II/QT ratio, abnormal concentrations of K produced Hegglin syndrome (Fig. 7).

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Fig. 7. Potassium concentration in plasma and QTrs/QT in ECG.

While the hypopotassemia was associated with no marked arrhythmia except for the rare incidence of extrasystole, hyperpotassemia was associated with various types of conduction slow-down, ectopic impulse formation or sinus standstill, in a certain relationship with the rate of the concentration change (Fig. 8).

(b) Abnormal concentrations of Ca

With hypercalcemia produced by the infusion of 5% CaCl₂ solution the duration of R–R, P, PQ and QRS became increased, QT shortened and ST–T elevated; the wave form change was such that the descending limb of QRS showed a prominent notching and the ST segment plunged from this point down into an inverted T wave. The presence or absence of inverted U wave was not clear. With Ca concentration increased further, ST and T became depressed in the “basin” type with the shortening of QT ratio, followed abruptly by a ventricular fibrillation. With hypocalcemia produced by EDTA 2Na or EDTA 4Na, QT ratio was prolonged and QaT/QT ratio was increased, ST segment was prolonged.

With increased plasma Ca concentration PQ interval tended to be prolonged (Fig. 9) and there was a significant inverse correlation with QT time (Fig. 10). With plasma Ca concentrations above 8 mEq/L there occurred various stages of heart block, escaped beats (Fig. 11) and suddenly a ventricular fibrillation without any definite relationship with the actual value of the concentration.
(c) Abnormal concentrations of Na

The infusion of 10% salt solution caused the duration of R–R, P, PQ to increase, QT ratio to be increased and Q–II s/QT ratio to be diminished, i.e., Hegglin syndrome; T/R ratio was decreased and T wave became inverted starting from its terminal portion.

With hyponatremia produced by the intraperitoneal injection of 1,000 cc of 5% glucose solution, T/R ratio was increased and the T wave became high. The concentration of Na was nearly inversely correlated to the increment of the T wave (Fig. 12); QT ratio was increased at high Na concentrations (Fig. 13).

Fig. 12. Sodium concentration in plasma and height of T wave in ECG.

II. ABNORMAL CONCENTRATIONS OF ELECTROLYTES AND THE INTRACELLULAR POTENTIAL

(a) Changes in the intracellular potential with altered extracellular K concentrations

When placed from a medium to another medium with a different concentration of K, a cardiac muscle preparation gave bursts of the spontaneous activity. According to the view that the resting membrane potential derives its origin from the concentration gradient of K across the cell membrane, the resting potential is expected to fall as the extracellular K concentration rises and to rise as the extracellular K concentration falls. However, this is not always the case. In a very low concentration of extracellular K one can not neglect the influence of Na (Fig. 14). Calculated from the intracellular K contents in the bull-frog’s cardiac muscle cell and the observed resting membrane potential, the cardiac muscle cell membrane must be about 2~3% as permeable to Na⁺ as it is to K⁺ within the normal range of the extracellular K⁺ concentration.

When treated with insulin and glucose, the cardiac muscle preparation gave extraordinary high resting membrane potential in a better agreement with the theory; this suggests that insulin increases the permeability of the cell membrane to K⁺ relatively than that to Na⁺ (Fig. 15).

With the extracellular K concentration as high as 8 mEq/L the overshoot became markedly small, possibly because the rate of the upstroke was abruptly reduced. When
Fig. 14. Cellular potential of toad auricle and K concentration in the medium.

Fig. 15. Cellular potential of toad auricle and K concentration in the medium.

It was shown by Weidmann that the rate of the upstroke was not directly affected by the extracellular K concentration but it depended on the pre-existing resting membrane potential; in accordance with this finding even under the influence of insulin there was no obvious deviation from this rule (Fig. 17).

Some of these findings obtained from the intracellular potential recording can be applied to the interpretation of the electrocardiogram. A low extracellular K concentration is expected, on this ground, to accelerate or to cause no

Fig. 16. Action potential duration and K concentration in the medium.

Fig. 17. Insulin and maximal rate of rise.

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change in the conduction velocity and the treatment with insulin is expected to speed up the conduction velocity. Since the duration of the action potential was prolonged under this circumstance, one would expect the QT time to be prolonged. However, the fact is that it is shortened only when the hypopotassemia is produced by insulin it may be shortened (Fig. 18).

![Cellular Potential Diagram]

Fig. 18. Hypopotassemia.

In the presence of high extracellular K concentration there was a fair agreement, i.e., the conduction velocity was slowed, and the heart block was apt to occur. The observed shortening of the action potential corresponded well with the shortening of the ST segment. If the spatial distribution of the ionic flux density during an action potential should determine the vector of the electromotive force of a exciting membrane, be it for a single cardiac muscle cell or for the whole heart, it should follow that, since the resting potential is high and the rate of the upstroke is high in the presence of low K concentration extracellularly, P and QRS must be high in voltage and all spikes must be narrow and high under this circumstance, provided that the route of the impulse propagation stays constant. With a high K concentration extracellularly, the reverse must be the case, i.e., low voltage of P, QRS and wide and flat spikes. These theoretical extrapolations were not sustained actually, and this may be because the route of the impulse propagation does not stay constant. As for the T wave, since the permeability to K becomes low with a low extracellular K concentration and become high with a high extracellular K concentration, the T wave changes (i.e., becomes wide or narrow) in the opposite direction to the P and QRS changes. With K concentrations above a certain limit, it does not necessarily become high and peaked (Fig. 19).

![Hyperpotassemia Diagram]

Fig. 19. Hyperpotassemia.

Concerning the U wave there was fact that RS₃ was occasionally markedly prolonged in the case of a low extracellular K concentration. And this can be also interpreted as a change leading to a negative afterpotential.

When the concentration of K and that of Ca in the extracellular fluids were changed simultaneously the resting and action potential was always modified by the concentration of K to a greater extent than by that of Ca.

The heart muscle preparations from different parts of the heart were compared in terms of the stability of the wave form while being bathed in a high-K solution, the degree to which it may be changed under this circumstance, and the degree to which the wave form may be reversed when put back in the original fluid media. It was found that the cardiac muscle from the auricle was more vulnerable to a high-K solution than that from the ventricle; this fact may expect the relatively early disappearance of the P wave in hyperpotassemia (Fig. 20).

(b) Changes in the intracellular potential with the extracellular Na concentration

Replacing a part of the extracellular Na with choline did not affect the resting potential; as the extracellular Na concentration was decreased the overshoot became small, the plateau
shortened and the duration of the action potential became markedly shortened.

While increasing the extracellular Na concentration again caused no change in the resting potential, it caused the overshoot to become large and the duration of the action potential to be prolonged. This finding corresponds with the observed prolongation of QT time in the electrocardiogram in hypernatremia.

(c) Changes in the intracellular potential with the extracellular Ca concentration

In Ca-free fluids the resting potential showed a slight decrease or no decrease. The overshoot of the action potential became high, the plateau markedly prolonged, and the duration of the action potential markedly prolonged; the junction between RS₁ and RS₂ mostly formed a sharp angle, and RS₃ presented itself as an abrupt and steep descent from the plateau. When treated with citrate or EDTA, the resting potential was gradually diminished, and the duration of the action potential was made to be prolonged over 20 times as long as the normal value; this process was entirely reversible (Fig. 21).

In high-Ca fluids the resting potential was large and RS was very steep and it plunged into a short and steep plateau, followed by a gentle and long RS₃. In abnormally high-Ca fluids a positive after-potential made its appearance frequently, and the duration of the action potential was markedly shortened and conduction blocks were inescapable (Fig. 22).

The correlation between the intracellular potential and electrocardiogram under the influence of abnormal Ca concentrations is such, that the duration of the action potential was prolonged with low-Ca concentration and shortened with high-Ca concentration finds its ready counterpart in the fact that QT time was prolonged in hypocalcemia and shortened in hypercalcemia.

Since the change in RS₃ was manifold in pattern, one reasonably anticipates various changes in the corresponding segment, e.g., inverted T wave.

Although EDTA is said to be effective in the treatment of the arrhythmias caused by digitalis, the author’s experience indicates that, while this was effective in normalizing arrhythmias of ventricular tachycardia type, it rather aggravated the heart block, causing more diverse blocks or leading to the ventricular fibrillation (Fig. 23).

A toxic dose of digitalis caused the repolarization phase of the intracellular action potential to become steep and the duration of the action potential to be markedly shortened, and this change was a function of the extracellular Ca concentration; thus the onset of the
Fig. 21. Effects of the extracellular Ca concentrations upon the cardiac cellular potentials
Part (3) chelating agents effect of EDTA.

Fig. 22. Effects of extracellular Ca concentrations upon the cardiac cellular potentials
Part (4) high Ca.

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The course of arrhythmias after the infusion of EDTA

<table>
<thead>
<tr>
<th>Exp. No.</th>
<th>Course of arrhythmias after the infusion of EDTA</th>
<th>Doses of EDTA (g)</th>
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<tbody>
<tr>
<td>0</td>
<td>V. T. (+ I.D.) → S. R. → V. T. (variable QRS types) → V Fibrill.</td>
<td>0.88</td>
</tr>
<tr>
<td>18</td>
<td>V. T. → same rhythm → PP unchange RR elongated → S. R. (Wenckebach type → PQ prolongation)</td>
<td>1.10</td>
</tr>
<tr>
<td>39</td>
<td>V. T. → PP RR elongated → variable PQ &amp; aber. Cond. → S. R. (PQ prolongation)</td>
<td>1.48</td>
</tr>
<tr>
<td>50</td>
<td>Incompl. A-V Bl. + multifocal ex. → same rhythm → PQ prolongation → Wenckebach type &amp; escaped beats</td>
<td>1.50</td>
</tr>
<tr>
<td>63</td>
<td>Wenckebach block → same → PQ prolongation</td>
<td>0.40</td>
</tr>
<tr>
<td>7</td>
<td>PQ prolongation → Wenckebach type and Incompl. A-V Block → Vent. Fibrill.</td>
<td>0.80</td>
</tr>
<tr>
<td>29</td>
<td>V. T. (+ I.) → V. T. (Complete)</td>
<td>0.20</td>
</tr>
<tr>
<td>25</td>
<td>Wenckebach (partly ↑ V. T.) → partly auric fibrill. → Wenckebach type → Vent Fibrill.</td>
<td>0.46</td>
</tr>
<tr>
<td>49</td>
<td>Comp. A-V Bl. widened QRS → A-V Block, QRS (2 types) → Compl. A-V Block, Vent. automatism.</td>
<td>1.70</td>
</tr>
</tbody>
</table>

Fig. 23

The toxic effect was retarded in a low-Ca medium and accelerated in a high-Ca medium. When EDTA was made to act on a piece of cardiac muscle intoxicated by digitalis, there was an improvement in the wave form; when fluids containing Ca were dropped on this the wave form became that of the intoxicated cardiac muscle again; the addition, then, of a few drops of EDTA improved the wave form (Fig. 24). As to the mechanism of the action of EDTA on the digitalis-intoxicated cardiac muscle, there are reasons to believe that the two substances act antagonistically on the membrane potential, neutralizing the effect each other, and that Ca-ion is involved in one way or another in this antagonistic action.

III. The Electrolyte Composition of the Interstitial Fluids and Its Relation to the Histology and Electron-Microscopic Findings of Myocardial Cells

As to the concentration of the electrolytes in the cell, there was no marked change under the studied circumstance except that the intracellular Na concentration was increased in the case of high extracellular Na concentration. Therefore it appears that the studied electrocardiographic changes depends on the change in the extracellular electrolyte concentrations.

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Fig. 24. Effect of EDTA and calcium on the digitalis intoxicated cardiac potential.