The Electrocardiographic Pattern of Hypopotassemia with and without Hypocalcemia

By Bohys Surawicz, M.D., and Eugene Lepeschkin, M.D.

Detailed analysis of the electrocardiogram in patients with hypopotassemia without hypocalcemia showed that the Q-U interval and its components (Q-aT, Q-aT, Q-T, and Q-aU) have essentially the same duration as in normal subjects for the same heart rate and sex. The typical hypopotassemia pattern is characterized by progressive depression of S-T, lowering and inversion of T and increase of U in left precordial leads. In hypopotassemia with hypocalcemia S-T and Q-T, but not Q-U, are prolonged, causing an increased degree of merging between T and U. Three methods of differentiation between completely merged T and U waves and true T waves of long Q-T duration are given.

It is commonly considered that a prolongation of the Q-T duration corrected for the heart rate (Q-Tc) is one of the most characteristic electrocardiographic features of an abnormally low serum potassium (hypopotassemia).2-10, 12, 14-13, 27-37 As early as 1939 the possibility was mentioned that in some cases of hypopotassemia the wide and notched T wave may include an abnormally high U wave.27 Other authors also emphasized that in most cases reported as showing a prolonged Q-T duration the U wave was mistakenly considered as the end of the T wave. This concerned diabetics treated with insulin13 as well as patients with other conditions associated with low serum potassium.19, 20, 24 Similar consideration caused McAllen26 recently to draw the conclusion that a prolongation of the Q-T interval is not commonly associated with a fall in the serum potassium.

The authors considered it important to clarify the divergence of opinion concerning the Q-T duration in hypopotassemia and to determine which are really the most important and characteristic electrocardiographic features associated with this condition. For this purpose the authors decided to apply the methods of accurate measurement of the Q-T duration proper, developed by them in a previous paper,21 to a larger number of cases of hypopotassemia. These methods included the synchronous registration of many standard and precordial leads together with the heart sounds, which has been carried out only in very few previously published cases. However, even these methods in many cases allowed only an approximate determination of the end of the T wave, and in some cases even an approximate location of this end proved impossible. The authors felt that in such cases measurement of the components of the Q-T duration which can be determined with greater
### Table 1.—The Intervals of the Ventricular Complex in Hypopotassemia without Hypocalcemia (Observations 1–26) and with Hypocalcemia (Observations 27–34)†

<table>
<thead>
<tr>
<th>Observation No.</th>
<th>Reference No.</th>
<th>Figure No.</th>
<th>Clinical Condition</th>
<th>Sex</th>
<th>Serum K (mEq./L.)</th>
<th>Serum Ca (mEq./L.)</th>
<th>R-R (in 0.01 sec.)</th>
<th>Q-oT (0.01 sec.)</th>
<th>Q-oT as % of normal Q-T</th>
<th>Q-aT (0.01 sec.)</th>
<th>Q-aT as % of normal Q-T</th>
<th>Q-T %</th>
<th>Q-aU (0.01 sec.) as % of normal Q-aU</th>
<th>Q-U (0.01 sec.) as % of normal Q-U</th>
<th>Q-U as % of normal Q-U</th>
<th>Q-2nd sound</th>
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<td>presum. normal</td>
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<td>F</td>
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<td>presum. normal</td>
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<td>9</td>
<td>2 10/12</td>
<td>Treatment of diabetic acidosis.</td>
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<td>4.5</td>
<td>72</td>
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<td>6 11/12</td>
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<td>5.25</td>
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<td>Intestinal obstruct.</td>
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<td>2.5</td>
<td>presum. normal</td>
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<td>100</td>
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<tr>
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<td>4</td>
<td>Vomiting and K-free infusions.</td>
<td>M</td>
<td>1.3</td>
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<td>68</td>
<td>22</td>
<td>72</td>
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<td>91</td>
<td>38</td>
<td>118</td>
<td>43</td>
<td>100</td>
<td>53</td>
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</table>

* What appeared to be the origin of T may have been the nadir of an initial negative phase of a diphasic T.
† Observation 12–26, see table 3A, observations 1, 2, 3, 4, 6, 7, 12, 13 and table 3B, observations 1, 2, 3, 5, 7. Observation 29–34, see table 3A, observations 5, 8, 10, 11 and B, Observations 6 and 8.
‡ The figure numbers refer to figures of this paper.
accuracy could lead to conclusions regarding the duration of the entire Q-T interval. To facilitate recognition of these components, it was planned to follow the appearance and/or disappearance of the hypopotassemia pattern at very close intervals.

Another aspect which had not been taken into consideration in many of the previous reports was the possibility that other factors concomitant with a low serum potassium were influencing the Q-T duration. The concentration of ionized calcium is among the factors having greatest influence on the Q-T duration. Since disturbances in the concentration of the calcium ion frequently accompany those of potassium metabolism, it seemed imperative to include studies of the blood calcium in the plan of this investigation.

**Method of Study**

For the purpose of detailed study, the ventricular complex of the electrocardiogram was subdivided into a number of components. In order to measure these components accurately, it was necessary to define certain points of the ventricular complex. The beginning of QRS was defined as the earliest point of QRS in synchronous or synchronized leads. The origin of the T wave or the end of the S-T segment was defined as the point most distant from a straight line connecting the S-T junction with the apex of the T wave; it was designated by the symbol “eT.” The points “aT” and “aU” represented the apices of the T or U waves respectively. The point “eT” or the end of the T wave was defined as the point where this wave reached the base line; in cases where T did not return to the base line because of partial fusion with the U wave, the notch or kink between the T and U waves was used to determine the approximate end of T. If this point was situated more than 1 mm. from the base line, the accuracy of determination of the end of T was poor; the values obtained in such cases were provided with a question mark. The point “eU” or the end of the U wave could be determined more or less accurately only at low heart rates and with a stable base line. When there was superposition of P on U at high heart rates the measurement was unreliable and the results therefore provided with a question mark.

The beginning of the second heart sound (2S) of the phonocardiogram was taken at the first rapid vibrations of this sound.

The points aT, aT, and eT were used for calculation of the intervals in limb leads showing the highest T waves and in chest leads most distant from the transition zone, usually V4, V3, and V2. The points aU and eU were measured in the lead showing the highest voltage of U (usually V3). In all cases used for this study except one the duration of QRS was normal. In the one case which showed right bundle branch block the difference between the actual duration of QRS and the accepted upper normal limit of 0.10 second was subtracted from all measurements which included the QRS complex, such as Q-aT, Q-aT.

In order to obtain information concerning the normal range of the components described above and their relation to the heart rate, these components were measured in 100 normal persons. The results are presented in detail in a separate paper and summarized in table 4.

In the first part of the present study the electrocardiographic intervals were measured as outlined above in a group of 25 cases of pure hypopotassemia without hypocalcemia. Eighteen of these cases were selected from the literature; only those observations were used which were made when the serum potassium was lower than 3.0 mEq. per liter and when the serum calcium was either found normal by chemical determination or was presumed to be normal because the clinical condition in question is known not to be accompanied by a decrease in the ionized serum calcium. In all cases the serum electrolyte studies were done on the same day as the electrocardiogram. Only cases were included in which a sufficient number of leads was reproduced to enable adequate differentiation between the T and U waves. Among the published cases, only those could be used in which the size of the illustration and the quality of reproduction permitted exact measurements.

In our personal material, all patients admitted to the Bishop DeGoesbrand Hospital in whom hypopotassemia was suspected clinically and all patients in whom the electrocardiogram showed or resembled the hypopotassemia pattern were subjected to detailed studies. The serum potassium and sodium were determined by means of the flame photometer. The serum calcium was determined by the Clark-Collip modification of the Kramer-Tidsall method. The electrocardiogram was registered with the Sanborn direct-writing four-channel electrocardiograph synchronously with the heart sounds; the latter were taken with a magnetic microphone without filter from the aortic region. In some cases it was necessary to change the location of the microphone many times before a satisfactory definition of the second heart sound could be obtained. Our personal material included eight cases. The measurements of this group are presented in table 1 and the results summarized in table 4.

The second group of measurements was performed in 25 cases of pronounced hypocalcemia compiled from the literature. All these cases had a serum calcium below 4 mEq. per liter and complied with the requirements outlined in the preceding paragraphs. They are presented in table 2 and the pertinent results summarized in table 4.
Table 2.—The Intervals of the Ventricular Complex in Twenty-Five Cases of Hypocalcemia

<table>
<thead>
<tr>
<th>Observation No.</th>
<th>Reference No.</th>
<th>Figure No.</th>
<th>Clinical Condition</th>
<th>Sex</th>
<th>Serum Ca (mEq/L)</th>
<th>R-R (0.01 sec.)</th>
<th>Q o-T (0.01 sec.)</th>
<th>Q o-T as % of normal Q-T</th>
<th>Q o-T as % of normal Q-T</th>
<th>Duration of T-wave (in 0.01 sec.)</th>
<th>Q-T (0.01 sec.)</th>
<th>Q-T as % of normal Q-T</th>
<th>Q o-U as % of normal Q aU</th>
<th>Q-U as % of normal Q-U</th>
<th>Q-U as % of normal Q-U</th>
<th>Q-2nd sound (0.01 sec.)</th>
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<td>15</td>
<td>88a</td>
<td>Tetany</td>
<td>F</td>
<td>2.25</td>
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<td>91a</td>
<td>Tetany</td>
<td>F</td>
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<td>42</td>
<td>132</td>
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</tr>
</tbody>
</table>

* What appeared to be the origin of T may have been the nadir of an initial negative phase of a diphasic T.
The third series of measurements was carried out in eight cases of hypopotassemia with concomitant hypocalcemia. These cases had a serum potassium lower than 3.7 mEq per liter and a serum calcium lower than 4.2 mEq per liter. Only six published cases and two personal cases met the requirements of this study. The measurements in these cases are included in tables 1 (cases 26-27), 3A (cases 5, 8, 10 and 11) and 3B (cases 6 and 8). The results are summarized in table 4. In one additional case, which was included for the purpose of comparison, hypocalcemia was present in addition to hypopotassemia (table 3B, case 4).

The fourth series of measurements concerned cases of hypopotassemia in which only one of the serum electrolytes (potassium or calcium) was altered while the other remained unchanged. In 13 of these the measurements were made in illustrations published by other authors. These include 10 observations in which potassium was given until the serum potassium level became normal, and three observations in which calcium was given. Our personal material consists of five cases in which potassium was given, one case in which the serum potassium changed spontaneously, and two patients in whom calcium was injected intravenously.

**The RS-T Segment and the Q-oT Interval**

In our studies in normal subjects we found that the duration of the interval from the beginning of QRS to origin of the T wave (Q-oT interval) showed the same dependence on the heart rate and sex as the Q-T interval. Expressed as a percentage of the Q-T interval expected for the heart rate, it ranged between 49 per cent and 63 per cent, averaging 56 per cent (table 4) independently of heart rate and sex. The normal limits, therefore, could be considerably reduced if the Q-oT interval in all cases was expressed as a percentage of Q-T rather than as an absolute value. As in many cases the Q-T interval could not be determined accurately, the Q-oT interval was expressed as a percentage of the normal Q-T interval expected for the heart rate. We designated this value the “corrected Q-oT interval” or “Q-oTc.” In our group of hypocalcemia cases Q-oTc exceeded the normal upper limit of 63 per cent in all cases, reaching values as high as 113 per cent; the average was 88 per cent, which was 58 per cent higher than the normal average (tables 2 and 4).

Of the 25 cases of hypopotassemia included in table 1, eight showed a horizontal or ascending course of the S-T segment in leads with upright T waves (figs. 1, 4A, 7A). In these cases the origin of the T wave and the Q-oT duration could be identified and measured without difficulty. In cases showing a more fully developed hypopotassemia pattern the S-T segment begins to slope downward, terminating in a diphasic (negative-positive) T wave in the left precordial leads. If the Q-oT interval is measured in these leads, pseudo-short values would be obtained. In such cases the Q-oT interval was measured in those leads which showed a fully monophasic upright or inverted T wave. In figures 2 and 6a-j, for instance, leads II, aVf, aVr, and V4, V5 and V6 have diphasic T waves, but lead aV1 has a monophasic upright wave; the Q-oT duration was accordingly measured in these leads. In figure 3A leads I, II, III and V4 have diphasic T waves, while leads V1 and V2 have monophasic upright waves and lead V6 has a monophasic inverted T wave; the Q-oT interval was accordingly measured in the latter lead.

In four of the 25 cases a monophasic upright or inverted T wave could not be found in any of the recorded leads; as the RS-T segment in these cases had a straight downward course, the origin of the T wave, strictly speaking, could not be determined. In such cases it was felt that the nadir of the initial negative phase of T represented the nearest approach to the origin of T, and this nadir was therefore measured instead of the point of T (figs. 6b and 8A). The value of the Q-oT duration measured in this way was slightly greater than the true Q-oT value, and therefore was designated with an asterisk in the table.

In a few cases of hypopotassemia the sudden increase in the slope of the S-T segment corresponding to the origin of the T wave was preceded by an additional kink or change in slope, which could be mistaken for a very early origin of the T wave. This pattern could be seen in figure 1 of reference 36a, figure 4c-d of reference 26 and is well illustrated by leads I and V4, V5 and V6 of figure 6c. These leads may convey the impression that there is a very short descending S-T segment followed by an early upright T wave. Comparison with the same leads taken previously or following the tracings displaying this pattern (figs. 6a, b and d) shows, however, that this segment corresponds in time to a slurred terminal portion of the QRS group. Accordingly the tracing should be interpreted as showing an ascending S-T segment followed by an inverted first phase of a diphasic T wave. It is of interest that all cases showing this pattern had serum potassium levels lower than 2 mEq per liter. In figure 6 the purest pattern of a monophasic positive T was found in lead aV1, and the Q-oT interval was accordingly measured in this lead.

As can be seen in table 4, the corrected Q-oT interval is normal in hypopotassemia,
Table 3.—The Effect of Changes in the Concentration of Serum K or Ca on the Intervals of the Ventricular Complex in Hypokalaemia

A. Observations from Literature

<table>
<thead>
<tr>
<th>Observation No.</th>
<th>Reference No.</th>
<th>Figure No.</th>
<th>Short Description of the Case</th>
<th>Serum K (mEq/L.)</th>
<th>Serum Ca (mEq/L.)</th>
<th>R-R (0.01 sec.)</th>
<th>Q-T (0.01 sec.)</th>
<th>Q-T as % of normal Q-T</th>
<th>Q-T as % of normal Q-T</th>
<th>Q-T (0.01 sec.)</th>
<th>Q-Tc in %</th>
<th>Q-U (0.01 sec.)</th>
<th>Q-U as % of normal Q-U</th>
<th>Q-U as % of normal Q-U</th>
<th>Q-U expressed as Q-Uc in %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>1A</td>
<td>Cholecytisitis, vomiting.</td>
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<td>115</td>
<td>108</td>
<td>115</td>
<td>57</td>
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</table>
### B. Personal Cases

<table>
<thead>
<tr>
<th>Observation No.</th>
<th>Patient</th>
<th>Date</th>
<th>Short Description of the Case</th>
<th>Serum K (mEq./L.)</th>
<th>Serum Ca (mEq./L.)</th>
<th>R-R (0.01 sec.)</th>
<th>Q-T (0.01 sec.)</th>
<th>Q as % of normal Q</th>
<th>Q vs T as % of normal Q-T</th>
<th>Q-T as % of normal Q-T</th>
<th>Q-Tc in %</th>
<th>Q as % of normal Q-U</th>
<th>Q-U (0.01 sec.)</th>
<th>Q-U as % of normal Q-U</th>
<th>Q-U (0.01 sec.)</th>
<th>Q-U as % of normal Q-U</th>
<th>Q-2nd sound</th>
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<tbody>
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<td>1</td>
<td>Bus. 23</td>
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<td>Vomiting in pregnancy After infusion 30 mEq. K</td>
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<td>3.13</td>
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<td>58</td>
<td>28</td>
<td>82</td>
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<td>108</td>
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<td>98</td>
<td>53</td>
<td>96</td>
<td>37</td>
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<tr>
<td></td>
<td></td>
<td>3/7 9 p.m.</td>
<td>After infusion 60 mEq. K.</td>
<td></td>
<td></td>
<td>69</td>
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<td>58</td>
<td>28</td>
<td>82</td>
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<td>53</td>
<td>96</td>
<td>37</td>
</tr>
<tr>
<td>2</td>
<td>Wal. 80</td>
<td>5/7</td>
<td>Sigmoid car.; diarrhea. After infusion 60 mEq. K</td>
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<td>63</td>
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<td>74</td>
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<td>28</td>
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<tr>
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<td></td>
<td>5/8</td>
<td>After infus. 60 mEq. K. &amp; whole blood.</td>
<td></td>
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<td>62</td>
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<td>74</td>
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<td>102</td>
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<td>3</td>
<td>War. 63</td>
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<td>Intestinal obstruction; vomiting. After infusion 145 mEq. K</td>
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<tr>
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<td></td>
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<td>After infusions of K.</td>
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<tr>
<td>4</td>
<td>DeC. 56</td>
<td>2/11 9:00</td>
<td>Ret rail cell sarcoma; cachexia, vomiting. After infusion 45 mEq. K</td>
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<td>17</td>
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<td>24</td>
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<td>49</td>
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<td>27</td>
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<td>7:30</td>
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<tr>
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<td>3/10 10a.m.</td>
<td>After infusion 145 mEq. K</td>
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<td>63</td>
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<td>—</td>
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<td>3/16</td>
<td>After recovery.</td>
<td>4.0</td>
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<td>26</td>
<td>87</td>
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<td>—</td>
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<tr>
<td>6</td>
<td>Hal. 47</td>
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<td>Uremia in bladder car.</td>
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<td>70</td>
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<td>74</td>
<td>31</td>
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<td></td>
<td>12/4</td>
<td>5 min. p. 10 cc. 10% CaCl₂ I.V.</td>
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<td>70</td>
<td>19</td>
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<td>25</td>
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<tr>
<td>7</td>
<td>Cl. 56</td>
<td>11/7</td>
<td>Colon car., colostomy, diarrhea. 4 min. after 20 cc. 10% Ca glucose I.V.</td>
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<td>4.9</td>
<td>56</td>
<td>20</td>
<td>69</td>
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<td>100</td>
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<td>11/7</td>
<td>After infusion 60 mEq. K.</td>
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<td></td>
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<td>58</td>
<td>28</td>
<td>96</td>
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<td>8</td>
<td>Aus. 37</td>
<td>3/25</td>
<td>Uremia in bladder car.</td>
<td>5.8</td>
<td>4.4</td>
<td>61</td>
<td>20</td>
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<td>27</td>
<td>82</td>
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<td>After infusion 45 mEq. K.</td>
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<td>98</td>
<td>50</td>
<td>98</td>
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</tbody>
</table>

*What appeared to be the origin of T may have been the nadir of an initial negative phase of T.*
### Table 4.—Summary of the Most Important Values for the Duration of the Components of Ventricular Activity in Relation to the Serum Potassium and Calcium

<table>
<thead>
<tr>
<th>Condition</th>
<th>No. of observations</th>
<th>Mean serum concentration (mEq./L.)</th>
<th>Q-oTc (as % of normal Q-T)</th>
<th>Q-aTc (as % of normal Q-T)</th>
<th>Q-Tc (as % of normal Q-T)</th>
<th>Q-aUc (as % of normal Q-aU)</th>
<th>Q-Uc (as % of normal Q-U)</th>
<th>aT-2nd sound (0.01 sec.)</th>
<th>T-2nd sound (0.01 sec.)</th>
<th>aU-2nd sound (0.01 sec.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>K</td>
<td>Ca</td>
<td>min.</td>
<td>aver.</td>
<td>max.</td>
<td>min.</td>
<td>aver.</td>
<td>max.</td>
<td>min.</td>
</tr>
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<td>Normals</td>
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<td>56</td>
<td>63</td>
<td>62</td>
<td>78</td>
<td>92</td>
<td>90</td>
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<td>2.7</td>
<td>63</td>
<td>88</td>
<td>113</td>
<td>88</td>
<td>110</td>
<td>135</td>
<td>115</td>
<td>135</td>
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<td>Deviation from normal in %</td>
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<td>+58</td>
<td>+41</td>
<td>+34</td>
<td>+3</td>
<td>+2</td>
<td>+3</td>
<td>+3</td>
<td>+3</td>
<td>-6</td>
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<tr>
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<td>44</td>
<td>57</td>
<td>74</td>
<td>64</td>
<td>80</td>
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<td>+3</td>
<td>-6</td>
<td>-4</td>
<td>-3</td>
<td>-3</td>
<td>-3</td>
<td>-3</td>
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<td>2.5</td>
<td>3.1</td>
<td>54</td>
<td>73</td>
<td>95</td>
<td>82</td>
<td>100</td>
<td>120</td>
<td>112</td>
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<tr>
<td>Deviation from normal in %</td>
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<td>+30</td>
<td>+29</td>
<td>+22</td>
<td>+3</td>
<td>0</td>
<td>-3</td>
<td>0</td>
<td>-3</td>
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<tr>
<td>Hypopotassemia with hypercalcemia</td>
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<td>3.2</td>
<td>6.7</td>
<td>50</td>
<td>64</td>
<td>100?</td>
<td>100?</td>
<td>16</td>
<td>6?</td>
<td>-5?</td>
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<tr>
<td>Deviation from normal in %</td>
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<td>+31</td>
<td>-11</td>
<td>-18</td>
<td>-18</td>
<td></td>
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</tr>
</tbody>
</table>

* Based on 11 cases only.
† Based on 8 cases only.
‡ Based on 2 cases only.
§ Based on 9 cases only.
|| Based on 19 cases in which Q-T could be measured accurately. See discussion.
but increased when hypopotassemia is accompanied by hypocalcemia and decreased when it is accompanied by hypercalcemia. In the 15 cases of hypopotassemia in which potassium was given (table 3), the Q-oTc duration showed an average increase of 1.6 per cent, the changes ranging from a decrease of 3 per cent to an increase of 9 per cent.

These are insignificant changes, so that the conclusion can be made that the Q-oTc duration is not influenced by potassium.

In case 5 of table 3B (fig. 6) infusion of potassium over a period of six hours caused an increase of Q-oTc from 48 per cent to 63 per cent (a total of 15 per cent). During this period of time the patient continued to have severe diarrhea, so that it is probable that the serum calcium became progressively lower toward the end of the infusion. This might explain the exceptionally large increase of the Q-oTc duration in this case. In all except two cases, administration of potassium caused the S-T segment in the left ventricular epicardial leads to change from a descending "sagging" course to a horizontal and finally to a normally ascending course (figs. 1, 3, 6, 8B and 9). In the exceptions (figs. 4 and 6) the S-T segment became more descending in spite of continuing potassium administration. In figure 6 this change was transient and could have been caused by increased depletion of potassium and/or calcium due to persistent diarrhea. In figure 4 the serum potassium continued to rise, but the serum calcium became lower. These two cases will be discussed in detail later.

In the five cases of hypopotassemia in which calcium was injected, the Q-oTc duration decreased from 11 to 35 per cent (on the average 22 per cent). The course of the S-T
segment was not significantly changed (figs. 7 and 8).

**Fig. 3.** Observation 2, table 3B. Hypopotassemia due to persistent diarrhea in sigmoid carcinoma and terminal intestinal obstruction with vomiting. Heart sounds (HS) synchronous with leads I, II and III.

(A) Serum potassium = 2.1, sodium = 129, calcium = 5.25, chloride = 81, and carbon dioxide = 31.2 mEq. per liter. Nonprotein nitrogen 59 mg. per 100 cc. Depression and downward course of S-T; diphasic (minus-plus) T waves partly fused with elevated upright U waves in leads I, II and III and V₄. Negative T in V₆. Upright T waves completely fused with elevated U waves in leads V₁ and V₂. The apex of the T plus U complex is formed by the apex of U. (B) After infusion of potassium. Upper nodal rhythm; amplitude of U diminished. (C) Serum potassium = 3.59, sodium = 141.8 mEq. per liter. After further administration of potassium. Nodal rhythm persists but T is more positive. (D) After further infusion of potassium. Restitution of sinus rhythm. The T waves are now upright in all leads except V₃; the apex of the T plus U complex is formed by the apex of T.

**The T Wave and the Q-T and Q-T Durations**

In our studies in 100 normal persons we found that the duration from the beginning of QRS to the end of T (Q-T duration) showed a dependence on the heart rate according to the empiric curve derived by one of us from 1000 personal and 3000 published normal cases. 

This curve is situated approximately midway between the logarithmic curve of Ashman and the square-root formula of Bazzett. The values for females were, however, about 7 per cent above this curve. In order to obtain the predicted normal Q-T duration for the heart rate, the values obtained from this curve were used without modification for males but 7 per cent was added in the case of females. The
actual Q-T duration was expressed as a percentage of the predicted normal Q-T duration for the heart rate and sex. The duration from the beginning of QRS to the apex of the T wave (Q-aT duration) was found to show the same dependence on the heart rate and sex as the entire Q-T duration; when it was expressed as a percentage of the predicted Q-T duration for the heart rate and sex, it became practically independent of these factors. It ranged from 62 per cent to 92 per cent with an average of 78 per cent.

As can be seen in table 4, the average corrected Q-T duration in hypocalcemia was 35 per cent longer while the corrected Q-aT duration was 41 per cent longer than in normal persons. The duration of the T wave, expressed as a percentage of this duration in normal persons for a given heart rate, ranged from 73 per cent to 136 per cent of normal, but the average was 100 per cent. This confirms the findings of other authors* that the duration of T is not increased in hypocalcemia and the prolongation of Q-Tc is due entirely to a lengthening of the S-T segment.

Because of the profound changes which the T wave undergoes in hypopotassemia, the method of measurement of the apex and end of this wave requires a special discussion. In those cases of hypopotassemia where the T wave still retains its normal direction, the identification of the apex of T presents no difficulties (fig. 1). The difficulties arise when the T wave becomes either isoelectric or diphasic. In the great majority of cases one or more leads can be found in which the T wave is monophasic (upright or inverted). In figures 2 and 6, lead aV1 shows a monophasic upright T, while in figure 3A lead V6 shows monophasic inverted T waves; these leads were accordingly used to measure the apex of T. In four cases from the literature and in one of our own cases (fig. 4B-C) all of the registered leads showed diphasic T waves. In these cases the apex of the first negative phase of T was used instead of the true apex of T; and in the tables the values of Q-aT obtained in this way were designated by a “prime” (') sign. In one case the T wave was nearly isoelectric in all registered leads, so that its apex could not be determined accurately; in this case the values were provided with a question mark.

As mentioned under “Methods,” accurate determination of the end of the T wave and therefore of the Q-T duration could be made only in cases where the T wave retained its normal configuration and showed no appreciable merging with the U wave (fig. 1a). This occurred only in cases of mild hypopotassemia (fig. 1). With further development of the hypopotassemia pattern, the T wave becomes lower and the U wave becomes higher. This causes the notch between the T and U to become displaced further from the base line and to become less accurate as an indication of the end of T. In these cases, as well as in those in which the notch was indistinct, the values of Q-T were provided with a question mark (fig. 4, leads V4, V5, and V6). When the T wave becomes diphasic (negative-positive), there is usually a definite notch between the terminal phase of T and the U wave (fig. 2, lead V4); if this notch is indistinct, the measurements are again provided with a question mark (figs. 4C, 6C, d). When the T wave becomes negative, its ascending branch usually makes a definite kink with the U wave, but sometimes this kink was indistinct; under these circumstances the Q-T duration was again provided with a question mark (fig. 3A).
ELECTROCARDIOGRAPHIC PATTERN OF HYPOPOTASSEMIA

It is apparent from table 4 that the average corrected Q-T and Q-aT duration in “pure” hypopotassemia does not deviate significantly from the values in normal persons. When hypopotassemia is accompanied by hypocalcemia, both these values are significantly prolonged, while when it is accompanied by hypercalcemia, they are significantly shorter than in normal persons. In the 15 cases of hypopotassemia in which potassium was given (table 3), Q-aTc showed an average increase of 4.0 per cent, the changes ranging from a
decrease of 4 per cent to an increase of 17 per cent. Q-Tc showed an average increase of 4.9 per cent, the changes ranging from a decrease of 6 per cent to an increase of 15 per cent. The changes are probably not significant and can be explained in part by the fact that the more nearly normal configuration of the T waves after administration of potassium allowed more accurate determination of the Q-aT and Q-T duration (page 811). In all cases the T wave showed a tendency toward positivity in the left ventricular epicardial leads. In other words, when it was originally low positive it became higher positive; when it was diphasic, the voltage of the negative phase decreased while that of the positive phase increased; when it was negative, its voltage decreased.

In the five cases of hypopotassemia in which calcium was injected, Q-aTc could be measured accurately only in two cases; these showed a decrease of 26 per cent and 27 per cent respectively. Q-Tc could be determined only in four cases, and in these it showed a decrease ranging from 18 per cent to 29 per cent and averaging 25 per cent. The amplitude and configuration of T were very little influenced.

The U Wave and the Q-aU and Q-U Durations

In our study of 100 normal cases we found that the duration from the beginning of QRS to the apex of the U wave (Q-aU duration) became longer with a falling heart rate. The duration from the end of T to the apex of U remained approximately constant (0.10 second) at all heart rates. The interval from the beginning of QRS to the end of U (Q-U interval) showed a much greater increase with falling heart rate than Q-aU. Women had longer Q-aU and Q-U intervals than men at all heart rates. In this paper we have expressed the observed Q-aU and Q-U intervals as a percentage of the normal values for the heart rate and sex found in our previous study. These percentages are designated as the “corrected Q-aU and Q-U intervals” or Q-aUc and Q-Uc.

Of the 25 cases of hypocalcemia (tables 2 and 4) no U waves were visible in the registered leads in two thirds of the cases. In the seven cases where U was visible, the apex of U could be measured accurately only in three cases while the end of U could be measured accurately only in four cases; in the other cases the results of the measurements were provided with a question mark. In the cases where it could be determined accurately, Q-aU ranged from 100 per cent to 110 per cent and averaged 104.4 per cent of normal; if the cases with question marks are included, the lower range becomes 84 per cent and the average 103.3 per cent. The distance between the end of T and the apex of U ranged from 0.02 to 0.08 second.
with an average of 0.056 second in the cases without question mark, and from 0.0 to 0.9 second with an average of 0.05 second in the entire material. The average value for this distance is accordingly less than the lowest value observed in normal persons, namely, 0.06 second. We see, therefore, that the apex of U in hypocalcemia occurs approximately at the expected normal time, and that its distance from the end of T becomes shorter because of the prolonged Q-T interval. It is probable also that the reason why the U wave could not be seen in the majority of the cases was that it was masked by the end of the T wave. When we determined the relation of the expected time of appearance of the end of T to the expected time of appearance of the apex of U in these cases, we found that the apex of U would have appeared before the end of T in 5 of the 17 cases. The interval Q-Uc in the four cases where the end of U could be measured accurately ranged from 98 per cent to 107 per cent with an average of 103 per cent, and from 80 to 110 per cent with an average of 102 per cent in all cases. This indicates that not only the apex but also the end of U appear at the expected normal time in hypocalcemia.

In our cases of hypopotassemia without hypocalcemia (tables 1 and 4) the U waves were always of normal amplitude or elevated, and the Q-aU and Q-U intervals could be measured accurately in nearly all cases. The Q-aU interval averaged 94 per cent, while the Q-U interval averaged 96 per cent of normal. This means that in hypopotassemia the apex as well as the end of the U wave appears slightly earlier than normally. As the end of T

[Diagram]

Fig. 8. (A) Observation 10, table 3A. Lead II, retraced from figure 5 of Engel, Martin and Taylor. Sprue with diarrhea and tetany, before and after administration of calcium. Depressed, sagging S-T segment, diphasic (minus-plus) T waves and elevated U waves, merged with T. After calcium, shortening of S-T and Q-T and separation of T from U. (B) Observations 8 and 9 of table 3A. Lead V1, retraced from figure 5 of Reynolds, Martin and Homann. Chronic nephritis and uremia with hypocalcemia and hypopotassemia. Depressed, prolonged S-T segment, negative T wave merged with elevated U wave. After administration of potassium (second row) the depression of S-T disappears, the T wave becomes upright and the U wave lower, but the duration of all components is unchanged. After administration of calcium (third row), shortening of S-T and Q-T and separation of T from U.

apparently occurs at the normal time, the interval between the end of T and the apex of U is shorter than normal, that is 0.02 to 0.11 second with an average of 0.073 second.

In the cases of hypopotassemia with hypocalcemia (tables 2, 3, and 4) the U wave was more or less elevated in all cases. The Q-aU interval had an average of 103 per cent while the Q-U interval averaged 100 per cent of normal. These normal average values are to be expected, as we have seen that hypopotassemia tends to shorten while hypocalcemia tends to prolong slightly the Q-aU and Q-U intervals.
The interval between the end of T and the apex of U ranged from 0.02 to 0.10 second with an average of 0.06 second. Due to prolongation of Q-Tc in these cases, this interval is less than in pure hypopotassemia.

After administration of potassium the U wave became lower in all cases, and in two cases it became completely invisible. In the 13 cases where U could be measured before and after potassium, the changes of the Q-aTc interval ranged from a decrease of 10 per cent to an increase of 19 per cent, with an average increase of 0.15 per cent. The change of the Q-Uc interval in the 10 cases in which it could be measured both before and after potassium ranged from a decrease of 9 per cent to an increase of 14 per cent, with an average decrease of 0.5 per cent. The conclusion can thus be made that administration of potassium has no influence on the Q-aU and Q-U intervals. The changes of the distance from the end of T to the apex of U ranged from a decrease of 0.08 second to an increase of 0.02 second, with an average decrease of 0.016 second.

The effect of administration of calcium on the Q-aU and Q-U intervals could be followed only in the four cases where the U wave was measurable before as well as after calcium. The changes of Q-aUc ranged from a decrease of 7 per cent to an increase of 4 per cent, with an average decrease of 0.5 per cent. The changes of Q-Uc ranged from a decrease of 5 per cent to an increase of 5 per cent, with an average increase of 0.25 per cent. The distance from the end of T to the apex of U showed an increase of 0.01 to 0.09 second with the average being 0.052 second.

**THE SECOND HEART SOUND AND ITS RELATION TO THE T AND U WAVES**

A phonocardiogram was available only in 11 of the 25 cases of hypocalcemia described in table 2 and summarized in table 4. From these tables, it is apparent that in hypocalcemia the second heart sound begins much earlier than normal with respect to the T wave but
only slightly earlier with respect to the U wave. This sound begins from 0.01 to 0.10 second (on the average 0.061 second) later than the expected end of T for the heart rate and sex; this is 0.054 second later than in normal subjects. We must conclude, therefore, that in hypocalcemia the mechanical systole is prolonged, but not as much prolonged as the Q-T interval.

In the eight patients with pure hypopotassemia in which the heart sounds were registered (table 4), the second heart sound began on the average 0.015 second later than in normal persons in relation to the apex of T, 0.017 second earlier in relation to the end of T, but only 0.008 second earlier in relation to the expected Q-T duration. In relation to the apex of U, it began 0.01 second later than in normal subjects. In hypopotassemia with hypocalcemia, the relation of this sound to the T wave is like that found in pure hypocalcemia. In our case of hypopotassemia with hypercalcemia the distance from the apex and end of T to the beginning of the second sound had the highest values encountered in any of our cases.

In the five cases of hypopotassemia with phonocardiograms, where potassium was given, the relations of the second heart sound to the electrocardiogram at the lowest potassium level were compared with those at the highest potassium level and the most normal configuration of the electrocardiogram. It was found that the beginning of the second sound at the higher potassium level appeared on the average 0.004 second later with respect to the apex of T, 0.002 second later with respect to the end of T, and 0.005 second later with respect to the apex of U. These are insignificant changes. However, in three of our observations (table 3B, observations 2, 3, and 4), infusion of potassium caused relative normalization of the electrocardiogram, but the patients died a short time after the last tracing was taken. If we substitute for these preterminal trac-

**Fig. 11. Observation 8, table 3B.** Uremia due to obstruction of ureters in uterus carcinoma invading the bladder. The heart sounds (HS) are superimposed on lead V₅. (A) Serum potassium = 5.8, sodium = 143, calcium = 4.4, chloride = 79, carbon dioxide = 29.2, mEq per liter. Pattern of hyperpotassemia with peaked, "tent-shaped" T waves. (B) Four weeks later, two days before death. Serum potassium = 3.0, sodium = 130, calcium = 3.15 mEq per liter. Pattern of hypopotassemia with hypocalcemia. Depressed, prolonged S-T segments. Merging of T and U, with apex of the T plus U wave probably formed by U.
gressively later without any significant change in the heart rate. The question whether the changes of the second heart sound are caused by the administration of potassium alone, or also by the infusion of fluids in previously dehydrated patients, cannot be answered satisfactorily at the present time. Another possible source of error in the determination of the time relations of the second heart sound is that the rapid vibrations comprising the beginning of this sound were usually difficult to identify during the height of hypopotassemia but very easily seen after administration of potassium. Accordingly we may not have compared quite the same phenomena before and after potassium administration.

The effect of calcium administration on the second heart sound could be observed in a satisfactory manner only in one case (table 3B, observation 6 and fig. 7). In this case the second sound appeared 0.05 second later with respect to the apex of T, 0.01 second later with respect to the end of T, and 0.02 second later with respect to the apex of U. In another case (observation 7) there seemed to be no change in the relationships, but the T and U waves could not be differentiated exactly. In observation 8 of table 3B the second sound appeared 0.10 second earlier with respect to the apex of T, 0.09 second earlier with respect to the end of T, and 0.03 second earlier with respect to the apex of U when hypocalcemia developed, but in this case the serum potassium concentration also showed a drop from 5.8 to 3.0 mEq per liter, so that it is impossible to say which of these two factors had the greater role in provoking these changes.

**Other Electrocardiographic Observations**

The predominant cardiac mechanism in hypopotassemia was sinus rhythm; the heart rate in the cases shown in table 2 ranged from 46 to 120, averaging 82. Administration of potassium caused, on the whole, a slight increase in the heart rate, corresponding to an average decrease of 0.05 second in the R-R interval. Of greater importance is the presence of various cardiac arrhythmias in all of our own patients who showed a serum potassium level of less than 2.6 mEq per liter. One case (observation 2) showed an upper nodal rhythm, one case (observation 5) atrial nodal rhythm, one case (observation 7) ventricular premature beats partly appearing as bigeminal rhythm and one case (observation 3) both atrial and ventricular premature beats, at times alternating with sinus beats. In all cases the arrhythmia disappeared upon administration of potassium.

The P waves were taller at the height of hypopotassemia in eight of our personal cases. The P-R interval was slightly longer at the height of hypopotassemia in three of the eight cases, but did not exceed 0.19 second at any time. The duration of the QRS interval showed no measurable changes except in observation 5 of table 3B, which was discussed on page 805.

**Discussion**

One of the most important results of this study is that the duration of the Q-T interval, corrected for the heart rate and sex, is not prolonged in cases of pure hypopotassemia and is not influenced by administration of potassium. This conclusion is corroborated by our finding that the components of this interval (the QRS complex, the S-T segment and the T wave) all have a normal duration in pure hypopotassemia.

As mentioned in the introduction, in most of the reports describing a prolonged Q-T duration in hypopotassemia the U wave was not adequately differentiated from the T wave and the Q-U duration was measured instead of the Q-T duration. The Q-U duration in normal persons is 40 per cent to 70 per cent greater than the Q-T duration. As we found the Q-U duration to be normal in hypopotassemia, we would expect that measurement of Q-U instead of Q-T would give only very high values for the corrected Q-T duration. The apparent Q-T duration determined in this way would depend on the heart rate; it would increase from about 140 per cent at a heart rate of 100 to about 170 per cent at a heart rate of 45. The values of the apparent Q-T calculated by measuring Q-U instead of Q-T in the cases of table 3A actually lie within this range. A gradual increase in the apparent Q-T duration with increasing hypopotassemia reported in some cases could have been simulated either by a decrease in the heart rate or by an increase in the voltage of the U waves. Such an increase would cause the duration of these waves to appear longer, as the normally almost isoelectric terminal section of U would then be more easily separated from the level U-P interval. To be sure, this explanation applies only as long as the apparent Q-T interval is between 140 per cent and 170 per cent.

The lesser degrees of Q-T prolongation (values of 110 per cent to 140 per cent) reported in hypopotassemia cannot be explained by measurement of Q-U instead of Q-T, and must, therefore, correspond to a true prolongation of Q-T. In these cases factors other than hypopotassemia must be held responsible for this prolongation. One of these factors is hypocalcemia, as we have seen in the present study. Many of the conditions in which hypo-
potassium occurs (for instance, diarrhea, vomiting and renal insufficiency) are often also accompanied by hypocalcemia.* However, a prolongation of Q-T, which ranged from 105 per cent to 140 per cent and, therefore, could not have been caused by inclusion of a U wave, was found in a considerable number of hypopotassemia cases which had a serum calcium above 4.0 mEq per liter.21 It is possible that in some of these cases the total serum calcium was normal but the ionized calcium was low. Almost one-third of the group had acidosis and another one-third had renal insufficiency, and Q-T may be prolonged in these conditions independently of the serum calcium level.22, 23, 29 (pers. obs. 33a, 33b) In the present study we have attempted to include only cases of hypopotassemia accompanied by as few as possible additional metabolic alterations in our table 1. Cases of familial periodic paralysis and those of potassium depletion with fixation of potassium due to infusion of potassium-free dextrose solutions seemed to answer these requirements best.

Our measurements failed to show any changes in the duration of the T wave in hypopotassemia. It can be readily understood that the inclusion of the U wave in the Q-T interval will cause the impression of a broadening and rounding of the shape of the T wave which has been described as accompanying the prolongation of Q-T.8, 9, 10, 28, 32 According to our own measurements and those of other investigators, the duration of the S-T segment is unchanged in hypopotassemia.

The instances in which the S-T segment appeared to increase in length proportionately to the Q-T interval23 can probably be explained by difficulties in determination of the onset of the T wave in the cases with descending and sagging S-T segments, since, as mentioned in the section on the S-T segment, this segment terminates in such cases in the nadir of the negative or negative-positive T wave without any visible change in slope. If the duration to the nadir of such a T wave is measured as S-T, high values will be obtained. The possibility of some other factors causing S-T prolongation in some of the reported cases can, however, not be entirely ruled out.

According to our measurements, the duration of QRS showed no appreciable change during development or regression of hypopotassemia in almost all of the cases which were studied. One of our cases (observation 7 of table 3B, and fig. 5) had exhibited a right bundle branch block pattern, but as this pattern remained unchanged after administration of potassium it is probable that it was present even before the appearance of hypopotassemia. Another case (observation 5 of table 3B, and fig. 6) developed a peculiar slurring at the foot of the descending limb of R which we considered as belonging to the QRS group and which increased the duration of QRS to about 0.12 second. This case was discussed on page 805, where two similar cases from the literature were also mentioned. Recently two cases showing a similar pattern during diabetic acidosis associated with hypopotassemia were reported.14a In these cases the slurring became less pronounced or disappeared completely with disappearance of acidosis although the serum potassium level continued to decrease; this indicated that the changes of QRS were more related to acidosis than to hypopotassemia. A slurring of the ascending branch of the S waves in all standard limb leads appeared at the height of hypopotassemia in one case of familial periodic paralysis and was interpreted as right bundle branch block with a QRS duration of 0.20 second.14 In this case the apparent slurring could have corresponded to a very steep ascending S-T segment, but this cannot be decided definitely as the precordial leads were not registered. A pattern which was interpreted as an intraventricular conduction disturbance appeared in calves raised on a potassium-free diet.20 In the cases which showed the above-mentioned changes of QRS and in which chest leads were taken, the slurring was confined entirely to the terminal portion of QRS while the intrinsicoid deflection appeared at an approximately normal time. It is possible, therefore, that the pattern may not represent an intraventricular conduction disturbance but rather a terminal slowing in the depolarization process in each heart muscle element. At any rate, the QRS changes described above are rare in hypopotassemia and seem to appear only at very low serum potassium values or in combination with other factors such as acidosis.

Measurements of the duration of the U wave could not be undertaken since in the vast majority of the cases of hypopotassemia the U wave begins before the end of the T wave and the onset of U thus cannot be determined accurately. The apex of the U wave and the end of the U wave were found to appear slightly earlier than in normals, but the difference is very small.

Our studies have, therefore, led us to the conclusion that pure hypopotassemia causes no appreciable changes in the duration of any of the components of the ventricular electrocardiogram. The most characteristic changes
are those of the voltage and configuration of these components; they consist of a "sagging" of the S-T segment, and elevation of the U wave. These changes in persons showing a normal initial electrocardiogram and in typical unipolar leads from the anterior epicardial surface of the left ventricle are represented schematically in figure 12 which was constructed to scale for a heart rate of 60.

With progressive development of the hypopotassemia pattern the normally ascending S-T segment becomes at first horizontal (patterns I-II), then progressively more descending (patterns III-V). As long as the T wave still remains upright the S-T segment may develop an upward concavity and assume the "sagging" configuration considered typical of hypopotassiumia (pattern IV). If the T wave becomes inverted, the concavity of S-T becomes directed downward (pattern V). The T wave becomes progressively lower as hypopotassiumia develops. In pattern I it is lower than normal, but still exceeds the voltage of the U wave in the same lead. In pattern II the T wave becomes lower than the U wave. In pattern III, T becomes diphasic and of low voltage, with an initial negative phase which is lower than the final positive phase. In pattern IV the negative phase is higher than the positive phase. Finally T becomes completely negative (pattern V). At some time the voltage of a diphasic T wave may become so small that it becomes practically isoelectric and the ventricular complex seems to consist entirely of an S-T segment and a U wave (pattern III). The U wave shows a progressive increase in voltage with increasing hypopotassiumia. We have never seen any changes in the direction of the U wave in pure hypopotassiumia.

The fact that U waves were found only in 42 per cent to 55 per cent of the cases in a large series of persons with low serum potassium can be explained if we assume that in these studies only U waves which were clearly separated from the T waves were recognized as such.

The maximal changes of each of the three components of the ventricular complex (S-T, T and U) influenced by hypopotassiumia appear in different leads. The elevation of the U wave is most pronounced in the leads which show the highest upright U waves in normal subjects, that is, in leads V2 or V5. Lead aVR, which shows negative U waves normally, usually shows accentuation of these negative U waves. Accordingly, CR leads were found to show higher U waves than V leads. Lead aVL as a rule shows the lowest voltage of U in hypopotassiumia and is, therefore, useful in recognizing the true duration of the T wave and of the Q-T interval. The changes of the T wave and the S-T interval, on the other hand, are greatest in leads showing the greatest positive area of QRS. These are the left ventricular epicardial leads and in vertical hearts leads II and III, in horizontal hearts leads I and II.

The most typical pattern of hypopotassiumia is characterized by an S-T segment and T wave of opposite polarity to a U wave of increased voltage. The total appearance was compared...
with a letter "S" lying on its side. 25a This pattern appears most frequently in leads which show normally the combination of a relatively low T wave and a relatively high U wave, that is, in the precordial leads V3, V4, and V5. In the precordial leads situated further to the left, the U wave is usually very small and, even if markedly elevated in comparison with its normal size, may still remain absolutely small and therefore inconspicuous. In the precordial leads situated further to the right, the T wave usually remains positive and in many cases merges with an elevated positive U wave. These leads show frequently a huge positive T-plus-U wave, the apex of which probably corresponds neither to the apex of T nor to the apex of U, but to a point situated somewhere between them. In the limb leads, which reflect electrical events of a larger area of heart muscle than the precordial leads, the possibility of both the U-wave and the T-wave patterns of hypopotassemia being registered in the same lead is greater than in the precordial leads. In vertical hearts the characteristic pattern appears predominantly in leads II, III and aVF, while in horizontal hearts it appears usually in leads I, II and, with reversed polarity, in lead aVR.

The magnitude of the changes of each of the three main components may be independent of that of the other two; it is in general proportional to the degree of hypopotassemia, but may vary greatly from person to person. In some cases the U-wave changes predominate while the S-T and T-wave changes do not exceed those of pattern I. This is theoretically most likely to occur in persons who normally show high T and U waves. In other cases the S-T and T changes are very pronounced while the U waves are only slightly increased in voltage. This is likely to occur in persons showing low T and U waves and a tendency to a horizontal course of S-T prior to the appearance of hypopotassemia. The processes which modify the hypopotassemia pattern may have been present before the onset of hypopotassemia or they may appear simultaneously with the development of hypopotassemia or following it. In any case the electrocardiogram will be affected by the combination of changes due to the hypopotassemia and to other factors.

Any attempt to classify the electrocardiographic pattern of hypopotassemia according to the severity of the condition must take into consideration the factors mentioned above. The patterns represented in the figure 12 of this paper were constructed deliberately in such a way that the changes of the S-T segment, of the T wave and of the U wave develop simultaneously and in a constant relation to each other. Many other patterns could be constructed if combinations of S-T and T of one pattern with U of another pattern were used. The number of different patterns of hypopotassemia found in the precordial leads facing the epicardial surface of the left ventricle is accordingly much greater than indicated in figure 12. For future studies it may become useful to describe these patterns as consisting of S-T, T and U changes of different degree, corresponding to the changes represented in the four patterns of figure 12.

One method of expressing the severity of the hypopotassemia pattern numerically might consist of measuring the distance between the apex of T and the apex of U. In the normal pattern this distance would be negative; in pattern I it would have small negative values, in pattern II these values would be positive. In patterns III and IV the distance would be measured from the apex of U to the negative apex (nadir) of a diphasic T wave. The values would be increasingly positive in patterns II through V. The highest positive difference in any one of the limb or precordial leads would be used. The disadvantage of this method is that it would measure the absolute differences in millimeters or millivolts, and these would be influenced by extra-cardiac factors such as the distance of the heart from the chest wall and presence of edema, pericardial or pleural effusion and similar influences. One way to avoid this influence could be to express the difference not in absolute values but as a percentage of the highest QRS amplitude. It should be emphasized that this method can be used only if the electrocardiogram definitely shows one of the hypopotassemia patterns described above; applied to other electrocardiographic patterns, it will give misleading results. We have not yet applied this method on a large scale, but we expect to do so in future studies.

Since the same pattern found in two different individuals may represent a considerably different degree of the deviation from the initial pattern of these individuals, no conclusion regarding the se-
verity of hypokalemia can be made without the
knowledge of the electrocardiographic pattern pre-
ceding the development of the changes due to the
hypokalemia.

Some authors have attempted to correlate the
electrocardiographic pattern of hypokalemia with
the level of serum potassium. They described a lowering
of the T wave at the level of 3.5 to 4.0 mEq.
per liter and a "double hump" pattern at the serum
potassium level between the 2.5 and 3.5 mEq. per
liter. The two humps (representing the T wave and
the U wave) change their mutual relations in such a
way that at the higher serum potassium levels T is
higher than U and at the lower serum potassium
levels U is higher than T. Finally, a pattern similar
to the recumbent letter S was said to correspond to
the serum potassium level of about 2 mEq. per
liter. This method does not take into account the
factors discussed in the preceding paragraphs; fur-
thermore, the absolute serum potassium level is only
indirectly responsible for the hypokalemia pattern
(see page 825).

An attempt to correlate the electrocardiographic
changes with the level of serum potassium and the
cumulative potassium balance was undertaken re-
cently; no correlation was found. The electro-
cardiograms were classified according to the ratio
of the voltages of the T and U waves. Apparently
leads with the highest U wave were used for this
purpose. One of the disadvantages of this method is
that considerable variation of the T/U ratio may
occur in the transitional zone due to the change of
the heart position during different phases of respi-
ration. T may normally vary from positive to notched,
positive-negative or negative under these conditions
and U may also change its voltage to some extent
depending on the heart position in these leads. This
method is further limited by the fact that it can be
used only for milder degrees of hypokalemia, in
which the T wave remains positive.

Bellet and co-workers subdivided the changes of
the ventricular complex observed by them in 79 cases
with hypokalemia into five patterns. Pattern 1 was
characterized by depression of S-T, accompanied
by positive T waves with lengthening of the Q-T
interval. In our opinion, this pattern in most cases
corresponds to the patterns III through V of our
figure 12; we assume that in these cases the U wave
was incorporated into the T wave. In those cases
of pattern 1 in which a distinct U wave was reported,
this pattern may have corresponded to our pattern
I in which true Q-T prolongation was present due
to other causes than hypokalemia. Pattern 2 of
Bellet and co-workers was characterized by inver-
sion of the T wave accompanied by Q-T prolonga-
tion, frequently followed by a U wave. In patterns
2a and 2c, S-T was slightly elevated or isoelectric
and followed by a terminal downward dip of the T wave,
as is seen in the late phase of myocardial infarction.
We consider that these patterns are not produced
directly by hypokalemia but are caused by con-
comitant myocardial ischemia, pericarditis or other
conditions. In pattern 2b the inversion of T was
accompanied by depression of S-T. We assume that
in this pattern the U waves were considered as T
waves, so that this pattern actually corresponds to
our pattern V.

Patterns 3a and 3c of Bellet and associates were
characterized by positive T waves of normal ampli-
tude, beginning immediately after QRS without an
isolectric S-T segment, and accompanied by a pro-
longed Q-T duration. We consider that in these
patterns the T wave was completely merged with the
U wave in the leads in which this pattern appeared;
this would correspond to a variation of our pattern
III in which the depression of S-T is of less than usual
and the elevation of U of more than usual magnitude
(fig. 4A, in leads V1 and V2 of fig. 3A and in leads II
and V2 of figure 6d). In pattern 3b a definite isoelectric
S-T period was present; this pattern was rare and observed especially in the
presence of "alkalinosis with or without hypo-
calcaemia." This pattern corresponds to the modi-
fication of the hypokalemia pattern seen in the
presence of a low ionized serum calcium and dis-
cussed later on page 825.

Pattern 4 of Bellet and his colleagues was char-
acterized by an upright but almost isoelectric T
wave, followed by a U wave. This pattern evidently
Corresponds to our patterns I or II. It may appear
even in normal persons in the transition zone of T,
and would be diagnostic of hypokalemia only
when it appears in left precordial leads as well or
when a previous normal tracing is available for com-
parison. Finally, pattern 5 of Bellet and co-workers
showed a T wave of normal amplitude and normal
Q-T duration, followed by an "unduly prominent
U wave." This pattern would correspond to our
pattern II appearing in a person with initially high
T waves and steep S-T segments.

In the recognition of the electrocardiographic
pattern of hypokalemia, there are two
main problems of differential diagnosis: First,
other factors than hypokalemia may cause
some or all of the features of the hypokale-
mia pattern to appear in a given
electrocardiogram. Second, a true hypokale-
mia pattern may be atypical or obscured
by electrocardiographic changes caused by
other factors.

Pointed, inverted T waves or diphasic
(positive-negative) T waves do not resemble
the hypokalemia pattern sufficiently to
cause any confusion even in the presence of a
depressed S-T segment. However, many clinical
conditions unrelated to hypokalemia may
present a depression of the S-T segment with a horizontal or downward course, accompanied by diphasic (negative-positive) or inverted T waves, such as are encountered in the hypopotassemia pattern shown in figure 12. If the U waves which accompany these patterns are very low or absent, hypopotassemia can be practically excluded. The higher the U wave, the greater the probability that a true hypopotassemia pattern is present.

The suspicion of a hypopotassemia pattern does not usually arise if the S-T and T changes are opposed to the main QRS deflection in all leads (as in ventricular hypertrophy and strain patterns, and intraventricular conduction disturbances). The S-T and T changes caused by diffuse coronary insufficiency are independent of the QRS direction and may sometimes resemble the S-T and T changes of hypopotassemia; the same is true of the digitalis pattern. In the latter the Q-T duration is usually shortened while the apex and apparently the beginning of the U wave appear at a normal time; therefore the end of the T wave is easily recognizable and is frequently separated from the onset of the U wave by an isoelectric segment. Accordingly, if the negative phase of the T wave is followed by a short positive phase separated from the U wave by an isoelectric interval, the digitalis pattern and not the hypopotassemia pattern is likely to be present. The unchanged Q-T duration in hypopotassemia associated with a slightly earlier appearance of the U wave cause, in almost all cases of hypopotassemia, a merging of the terminal part of the T wave with the U wave even if the latter is not appreciably elevated.

U waves are present in all normal subjects and in nearly all patients; they may reach 0.15 millivolt in the standard limb leads and 0.2 millivolt in precordial leads. Usually high U waves may appear in the absence of hypopotassemia after exercise, in bradycardia, in athletes, in hypertension, and in dying hearts. Accordingly, it is impossible to make the diagnosis of hypopotassemia only on the basis of elevated U waves not accompanied by characteristic changes of T and S-T until the more exact criteria discussed on page 820 are available.

The greatest diagnostic difficulties are encountered in patients in whom the fully developed hypopotassemia patterns, including both the T and S-T changes and the U-wave changes, are seen, but in whom no reason for loss of potassium is found and in whom the serum potassium is not low. Striking examples of this may be found in patients who are being treated at the same time with digitalis and quinidine. In these patients depression of S-T and diphasic T waves characteristic of the digitalis pattern are combined with elevated U waves which apparently also appear earlier and often show partial merging with the T waves, as in the typical hypopotassemia pattern. The similarity may become so great that the two patterns may become practically indistinguishable. In view of this similarity we have even considered the possibility that this digitalis-quinidine pattern may be due to a redistribution of intracellular and extracellular potassium similar to that found in hypopotassemia. This subject will be discussed in a separate communication.

A pattern bearing a superficial resemblance to the more advanced hypopotassemia patterns may appear in advanced hyperpotassemia. In such instances a wide S wave of a greatly prolonged QRS complex may be mistaken for a horizontal S-T segment while the greatly prolonged, rounded P wave may be mistaken for a U wave. Multiple chest leads will almost always enable the correct diagnosis, since in some of these leads the voltage and slope of the terminal part of QRS and of the P waves will be of a sufficient magnitude to make their identification certain.

The appearance of peaked P waves, A-V conduction disturbances, and ectopic rhythms while in itself not diagnostic of hypopotassemia, may serve as corroborating evidence of the existence of this condition if the other electrocardiographic criteria are equivocal.

The recognition of the true hypopotassemia pattern may be difficult in all cases in which the T and U waves are merged. In the majority of the cases in which a sufficient number of standard and unipolar leads has been registered, a definite notch or kink between the descending or ascending limb of T and the ascending limb of U is present at least in some of these leads. The best leads for the detection of this kink
are leads V₁, V₄ and aV₅. However, in some cases the merging of T and U may be complete and no kink is visible in any of the leads registered. It may be difficult to determine whether the pattern which thus results represents the hypopotassemia pattern with a Q-T interval of normal duration accompanied by merging of T and U or whether the pattern is produced by a true prolongation of the Q-T interval with an absent or invisible U wave. This variant of the hypopotassemia pattern may cause a casual observer to decide against hypopotassemia because what appears as the T wave is increased in height. Such cases require special procedures in order to decide whether the questionable wave is a T wave or a T + U wave.

The first of these procedures is the measurement of the duration of the questionable wave and of the intervals from the beginning of QRS to the onset, apex and end of this wave. After correction for the heart rate and sex,² these intervals are compared with the same values in normal persons. Such a comparison will show whether these intervals approach most closely the normal values for the T wave or those for the U wave. Normal values can be used for comparison since in pure hypopotassemia these intervals show only insignificant deviations from the normal.

The second and more complicated procedure is the registration of a phonocardiogram synchronously with the electrocardiogram. Where multiple channel electrocardiographs are not available for routine use it has been found helpful to register the precordial lead V₁ through a magnetic microphone in contact with the chest wall, to visualize the time relation between the second heart sound and the T and U waves. In none of the more than 1000 cases with normal duration of QRS studied by us in this way did the second heart sound begin later than 0.03 second before the apex of the U wave. Accordingly, the appearance of the second sound later than 0.03 second before the apex of a questionable wave proves definitely that this wave is a T wave and not a U wave. On the other hand, the appearance of the second sound earlier than 0.03 second before the apex of a questionable wave makes it almost certain that this wave is a U wave.

In none of the 1000 personal cases referred to above did the second sound begin earlier than 0.03 second before the apex of the T wave, and among all the published cases with heart sounds available to us this occurred only in one case (observation 8, table 2). This was a case of uremia with a serum calcium level of 2.4 mEq per liter, a Q-Tc of 146 per cent, and a second sound beginning 0.11 second before the apparent apex of T. The occurrence of the second sound 0.03 second before the apex of the T wave was observed in two of all the published cases (observations 7 and 9 table 2); these were cases of uremia with serum calcium respectively of 3.0 and 3.15 mEq per liter and corrected Q-T (Q-Tc) of 142 and 145 per cent. In one of our own cases (observation 8 of table 3B, a patient with uremia who showed a serum calcium level of 3.15, a serum potassium level of 3.0 mEq per liter and a Q-Tc of 130 per cent), the second sound began 0.02 second before the apex of the T wave. In none of the other observed or published cases did the second sound begin before the apex of the T wave. All four cases mentioned above were cases of uremia; in one case the serum potassium level was low, in the other three it was not measured. The U wave could not be seen in these cases, but in all of the cases the apex of the U wave would have coincided with the T wave if the Q-U interval were of normal duration. It is very likely, therefore, that, in cases of hypocalcemia with marked Q-T prolongation associated with elevation of the U wave, summation of the T and U waves causes the formation of a new apex situated between the true apices of T and U, and that this apex is measured instead of the apex of T in these cases. In none of the published cases of hypocalcemia due to hypoparathyroidism did the second sound occur before the apex of the T wave. It can thus be concluded that the appearance of the second sound before the apex of the questionable wave makes it most likely that this wave is a U wave. The exceptions to this rule are very rare and seem to be confined to cases of hypopotassemia with hypocalcemia.

The third procedure for the differentiation of T and U consists of the administration of substances modifying the electrocardiogram in such a way that the pattern becomes more typical. It has been shown that in the case of an electrocardiographic pattern due to deficiency of two electrolytes, the administration of one of these will more clearly demonstrate the deficiency of the other. The almost selective action of calcium on the S-T segment makes it possible to shorten this segment by
means of an intravenous injection of 10 to 20 cc. of a 10 per cent calcium gluconate solution. The shortening of the S-T segment causes an earlier appearance of the apex and end of the T wave and a better separation of the T wave from the U wave (figs. 7, 8A). This method can be successfully applied not only in the cases of hypopotassemia showing long S-T segments, in which hypocalcemia may be suspected, but also in cases with normal duration of the S-T segment in which the T and U waves are merged (fig. 8B). The shortening of the S-T segment following calcium administration in cases with normal or high serum calcium is less pronounced than in cases with hypocalcemia, but in most of the cases it does result in separation of the T wave from the U wave. As has been pointed out previously, the action of calcium is very transient and may last for 1 or 2 minutes only; therefore the electrocardiogram has to be recorded during and immediately after the calcium injection.

The administration of potassium may also cause separation of a questionable T + U wave into its components by elevating the T wave and lowering the U wave. However, in order to be safe, this procedure can be adopted only after a thorough evaluation of the clinical data, and must be carried out very slowly and under constant electrocardiographic observation with a direct-writing instrument. This procedure is, therefore, much more laborious and time-consuming than the intravenous injection of calcium, and is seldom required for purely diagnostic purposes.

The diagnosis of the hypopotassemia pattern may be difficult in the presence of other electrocardiographic abnormalities not due to hypopotassemia. In the case of marked intraventricular conduction disturbances (bundle branch block, ventricular premature beats) the recognition of the hypopotassemia pattern is difficult since the T and U waves merge, the degree of merging being proportional to the increase in the duration of QRS. On the other hand, in the case of right bundle branch block or extrasystoles originating in the left ventricle the second heart sound occurs earlier in relation to the T wave and may even occur before the apex of T. We have found that the purest hypopotassemia pattern appears in leads in which the total area of QRS is nearest zero. For instance, in figure 5 leads V₅ and V₆ show a marked depression of S-T and a distinct kink between the low T wave and an elevated U wave, while lead V₂ does not differ in its configuration from that of typical right bundle branch block.

Marked S-T and T changes due to the currents of injury in myocardial infarction or to other factors may be expected to obscure the electrocardiographic hypopotassemia pattern. The appearance of deep inverted U waves in left precordial leads in the presence of hypopotassemia reported in two cases was probably due to the fact that the individuals who developed the hypopotassemia pattern had negative U waves in these leads previously. The recognition of the hypopotassemia pattern may be difficult in the presence of tachycardia and/or prolonged P-R interval because of the merging of the P wave with the U wave; this has been discussed earlier.

The detailed studies of the electrocardiographic pattern of hypocalcemia included in the present investigation were carried out in order to be able to evaluate the influence of hypocalcemia on the electrocardiographic pattern of hypopotassemia. Our method of measurement of the components of the Q-U interval, applied to the electrocardiograms of hypocalcemia compiled from the literature, confirmed the frequently described prolongation of the S-T segment with normal duration of the T wave, which results in a prolonged duration of the Q-oT, Q-aT and Q-T intervals, corrected for the heart rate and sex. Actual measurements of the S-T segment in the electrocardiogram of hypocalcemia have been reported previously, but the method of measurement was not defined exactly. All cases studied by us with a serum calcium lower than 4.0 mEq. per liter had a Q-aT duration exceeding the normal upper limit of 63 per cent of the expected Q-T duration, corrected for the heart rate and sex. The time of appearance of the U wave and its duration, as evident from the nearly normal duration of the Q-aUc and Q-Uc intervals, is not changed in hypocalcemia. Accordingly, the U wave is visible as a separate wave only in cases with not very marked Q-T prolongation, for example, in not very severe hypocalcemia; in the
cases with pronounced Q-T prolongation the U wave is merged with T or even completely absorbed by the latter.

The electrocardiographic pattern of hypopotassemia accompanied by hypocalcemia consists of a combination of the patterns of pure hypopotassemia and pure hypocalcemia. As a result, the hypopotassemia patterns of figure 12 become modified by a lengthening of the S-T segment. A Q-oT duration exceeding 74 per cent of the Q-T duration expected for the heart rate and sex makes it almost certain that hypocalcemia is present. Due to the prolongation of the Q-T duration without a corresponding increase of the Q-U duration the degree of merging between T and U is greater than in pure hypopotassemia. In none of the cases seen by us was this prolongation of Q-T great enough to cause a complete swallowing up of the U wave by the T wave, but such a possibility must be taken into consideration. This could have been one of the factors responsible for the apparently normal configuration of the electrocardiogram in case 6 of Currens and Crawford,7 in which an extremely low serum potassium was present with a low serum calcium.

The administration of potassium in cases with a hypopotassemia pattern modified by hypocalcemia causes the configuration of the S-T segment, the T waves and the U wave to change toward normal, but the duration of S-T remains unchanged (fig. 8B). The administration of calcium shortens the S-T duration, while the electrocardiographic features of the hypopotassemia pattern remain unchanged (fig. 8A). Hypocalcemia may cause a lowering or inversion of the T wave.1, 25, 32 and the hypopotassemia pattern may accordingly appear to be more severe as far as the T-wave changes are concerned if hypocalcemia is also present. Administration of calcium in such cases will disclose more truthfully the electrocardiographic changes due to hypopotassemia.

The term "hypopotassemia" has been used in this paper in order to designate the condition associated most commonly with the described electrocardiographic pattern. The correlation with the serum potassium level has been made because the electrocardiographic changes usually parallel this level. We are aware, however, of reports describing in some cases the lack of electrocardiographic abnormalities in spite of a definitely low serum potassium on one hand and the appearance of an electrocardiographic pattern of hypopotassemia with a normal or high serum potassium level on the other hand. In the recent review of this problem2 it was estimated that only 80 per cent of patients with serum potassium level below 3.5 mEq. per liter show suggestive electrocardiographic abnormalities. It is very likely that a better correlation could be obtained if the electrocardiographic diagnosis were improved by the routine use of the methods described in the present paper.

Up to the present time no exact correlation of the electrocardiographic pattern of hypopotassemia with either the total body potassium or the extracellular or intracellular potassium concentration could be obtained. According to our opinion, the best correlation would be expected with the potassium gradient across the cell membrane and not with the intra- or extracellular potassium concentration alone. A study of this problem by correlating the electrocardiographic pattern with the ratio of the potassium concentrations in the plasma and in the blood cells has been conducted by us for some time, but the available data are not yet sufficient for a final evaluation. Since sodium replaces the potassium in the cells if the latter is lost, the simultaneous study of the relation between the intra- and extracellular sodium concentration appeared to us imperative. Other electrolytes, and possibly the pH of the blood, may be partly responsible for the development of the pattern, but there is no established evidence for this as yet.

The lack of understanding of the precise etiology of the hypopotassemia pattern does not prevent the practical application of the electrocardiographic method for the diagnosis of the clinical manifestations of hypopotassemia. The seriousness of this condition for the patient cannot be measured by the estimation of the total body potassium loss or of the level of serum potassium, but by the amount of impairment of the function of the muscle cell. The electrocardiogram portrays
the reversible changes in the function of the heart muscle with great rapidity and exactitude, and it appears very unlikely that the response of the skeletal or smooth muscle is different from that of the myocardium. A correlation study between the degree of muscular weakness or other studies of the function of the skeletal muscle in patients with hypopotassemia and the electrocardiogram is contemplated in order to prove this assumption.

SUMMARY

1. The electrocardiograms of 25 cases of hypocalcemia, 25 cases of hypopotassemia without hypocalcemia (6 of these our own patients) and 8 cases of hypopotassemia with hypocalcemia (2 of these our own patients), as well as 1 case of our own of hypopotassemia with hypercalcaemia, were subjected to detailed examination. The components of the Q-U interval (the Q-oT, Q-aT, Q-T, Q-aU and Q-U intervals from the beginning of QRS to the origin, apex and end of T and the apex and end of U, respectively) were measured. These components were also measured in 16 cases of hypopotassemia without hypocalcemia before and after potassium administration, and in 5 cases of hypopotassemia with hypocalcemia before and after calcium administration.

2. The results of our measurements were compared with the values obtained in normal subjects for the corresponding heart rate and sex. These results are summarized in table 4. It was found that in pure hypopotassemia the duration of none of the components of Q-U deviates appreciably from the normal values. The widespread impression that Q-T is prolonged in hypopotassemia has resulted either from the inclusion of the U wave in the Q-T interval, or from the presence of other coexisting factors. Our results showed that in hypocalcemia the duration of the Q-T interval and its components is prolonged to a degree corresponding to the prolongation of the S-T segment, but the Q-aU and Q-U durations are unchanged. In hypopotassemia with hypocalcemia, Q-T and its components are prolonged as in hypocalcemia; the degree of merging between T and U increases with the increased Q-T duration. The administration of either potassium or calcium corrected only the electrocardiographic changes due to the deficiency of this particular electrolyte while the changes due to the deficiency of the other remained.

3. The phonocardiogram was taken synchronously with the electrocardiogram in all of our own patients who are included in this study. The mechanical systole in hypopotassemia is either of normal duration or shortened; in hypocalcemia it is prolonged, but not as much as the duration of the Q-T interval. The beginning of the second sound was never observed more than 0.03 second before the apex of the U wave. It was found only exceptionally (in some cases of hypocalcemia) before the apex of the T wave.

4. The typical electrocardiographic pattern of hypopotassemia consists of a progressing depression of the S-T segment, lowering and inversion of the T wave and increase in amplitude of the U wave in left precordial leads. Five typical patterns of hypopotassemia were constructed according to the degree of development of these changes. QRS changes were found only occasionally. Ectopic rhythms usually appeared in the more severe cases.

5. The differential diagnosis between the true hypopotassemia pattern and patterns similar to it, but due to other factors, was discussed. The pattern most similar to the hypopotassemia pattern is that appearing in some cases after administration of digitalis together with quinidine. The recognition of the atypical hypopotassemia patterns was also discussed. Among these the most difficult is the pattern with merging of the T and U waves without a distinct and visible kink in the merged wave. For the differentiation of this pattern from a true prolonged Q-T, three methods are recommended.

6. The degree of development of the electrocardiographic pattern of hypopotassemia is in general parallel to the decrease in the serum potassium level, but there are some exceptions. Studies are in progress to correlate the hypopotassemia pattern with the ratio of intracellular to the extracellular potassium concentration.
SUMARIO ESPAÑOL

Análisis detallado de electrocardiogramas en pacientes con hipopotasemia sin hipocalcemia reveló que el intervalo Q-U y sus componentes (Q-oT, Q-aT, Q-T, y Q-aU) tienen esencialmente la misma duración que en sujetos normales con el mismo pulso y sexo. El patrón típico de hipopotasemia se caracteriza por depresión progresiva de S-T, aplastamiento e inversión de T y aumento de U en las derivaciones precordiales del lado izquierdo. En hipopotasemia con hipocalcemia S-T y Q-T pero no Q-U, están prolongados, causando un aumento en el grado de fundición entre T y U. Tres métodos de diferenciación entre T y U's completamente fundidas y ondas T verdaderas de Q-T prolongados se describen.

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The Electrocardiographic Pattern of Hypopotassemia with and without Hypocalcemia
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Circulation. 1953;8:801-828
doi: 10.1161/01.CIR.8.6.801
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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