Quantitative Analysis of the Electrocardiographic Pattern of Hypopotassiumemia

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Electrocardiographic patterns typical of hypopotassiumemia and compatible with hypopotassiumemia were defined on the basis of the number of electrocardiographic signs of hypopotassiumemia present in 2 leads (generally leads II and V3). In 50 hypopotassiumemic patients a good correlation was found between the electrocardiographic pattern and plasma potassium concentration. Appearance of the electrocardiographic signs of hypopotassiumemia was not prevented by disturbance of other plasma electrolytes or by blood pH.

Electrocardiograms of patients with low concentrations of extracellular potassium frequently show characteristic abnormalities that disappear after administration of potassium salts.1, 2 Regression of the electrocardiographic pattern of hypopotassiumemia during administration of potassium is characterized by a gradual increase of T-wave amplitude, decrease of U-wave amplitude, and diminution of S-T segment depression in the standard limb and precordial leads without any change in Q-T or other components of the Q-U interval.1 This sequence of regression suggests that the converse, the evolution of the hypopotassiumemia pattern, consists of a progressive decrease of T-wave amplitude, increase of U-wave amplitude, and S-T segment depression in the standard limb and precordial leads. Accordingly, a schematic construction of 5 patterns, representing 5 stages in the evolution of the electrocardiogram in hypopotassiumemia, has been made.1 At that time no attempt was made to analyze the electrocardiographic signs of hypopotassiumemia in a quantitative manner or to correlate these signs with the concentrations of extracellular potassium.

During the past few years we have gained an impression that in a majority of patients with hypopotassiumemia, electrocardiograms can be correlated with the concentration of extracellular potassium. However, since others3-7 have failed to find a correlation between the electrocardiogram and serum potassium level, it was thought that a new investigation might be helpful. We made an attempt to develop quantitative criteria for objective evaluation of the electrocardiographic changes in these patients. We also considered certain factors other than the potassium concentration that may influence the electrocardiogram of patients with hypopotassiumemia.

This paper presents the results of the correlation between the electrocardiogram and plasma potassium level in 50 patients with hypopotassiumemia.

Methods and Material

Fifty adult patients with plasma potassium levels below 3.5 mEq./L were selected for the study. Description of patients whose electrocardiograms we studied is presented in a separate communication,8 which also contains the methods and results of the plasma electrolyte studies. Patients were subdivided into 3 groups on the basis of plasma potassium concentration: group A consisted of 17 patients whose plasma potassium concentrations were between 2.0 and 2.7 mEq./L, group B of 13 patients with concentrations from 2.71 to 2.98 mEq./L, and group C of 20 patients with concentrations from 3.0 to 3.49 mEq./L.

Twelve-lead electrocardiograms were recorded in each instance immediately after the blood was drawn for determination of plasma electrolytes. Potassium chloride infusion was then begun. Potassium was administered at a rate of 8 ml per minute

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This work was aided by a grant from the Eli Lilly Company of Indianapolis, Indiana, and a grant from the National Institutes of Health, grant 141 (C6); and was done during Dr. Surawicz's tenure of a Research Fellowship of the American Heart Association and while Drs. Braun and Crum were trainees, National Heart Institute, National Institutes of Health.

750 Circulation, Volume XVI, November 1957
in a concentration of 60 mEq./L of 0.45 per cent saline. In 5 patients for whom sodium chloride was contraindicated, potassium was given as a solution of 60 mEq./L of distilled water. The average dose of 34 mEq. (range 21 to 60 mEq.) was given in an average time of 71 minutes (range 45 to 120 minutes). During intravenous administration of potassium chloride, electrocardiograms were recorded at intervals of 2 to 5 minutes. In each case electrocardiograms were also frequently recorded during the subsequent hospital course.

Methods of measurement of the intervals from the onset of QRS to the apex of T wave (Q-T), the end of T wave (Q-T), and the apex of the U wave (Q-U) have been described previously.\(^9,10\) Methods of differentiating between T wave and U wave in doubtful cases have been described elsewhere.\(^1,11\)

**RESULTS**

**Correlation with Plasma Potassium Concentration.** After a careful inspection of all electrocardiographic tracings, it was found that an analysis of 2 leads of each electrocardiogram was sufficient for the purpose of this study. One limb lead and 1 precordial lead, the lead with the greatest U-wave amplitude, were chosen for analysis. The limb lead of choice was usually lead II, but occasionally lead III or aVF. The precordial lead of choice was usually lead V\(_3\), but occasionally lead V\(_2\) or V\(_4\). This choice was based on previous observations that the largest U wave in hypopotassemia usually is present in leads V\(_2\) and V\(_3\), while the possibility of both the U-wave and T-wave patterns of hypopotassemia being registered in the same lead is greater in the limb leads.\(^1\)

Detailed analysis of 50 electrocardiograms was carried out with regard to the following 3 signs: amplitude of the U wave exceeding 1 mm.; amplitude of the U wave exceeding the amplitude of the T wave in the same lead;* and depression of the S-T segment of 0.5 mm. or more. These 3 signs will be designated as positive signs of hypopotassemia. Since an analysis of 2 leads was made in each instance, a given electrocardiogram could contain a maximum of 6 positive signs. All electrocardiograms were grouped with regard to the number of positive signs of hypopotassemia that they contained. Representative electrocardiograms in each category are illustrated in figures 1 to 7.

The 2-lead electrocardiograms of each patient were submitted for inspection to several experienced observers who were asked to separate the tracings into 3 groups: electrocardiograms typical of hypopotassemia, compatible with hypopotassemia, and nondiagnostic of hypopotassemia. It was found that electrocardiograms designated as typical of hypopotassemia usually showed at least 3 positive signs, while the electrocardiograms designated as compatible usually showed 1 or 2 positive signs. Thus, we defined a tracing typical of hypopotassemia as an electrocardiogram containing 3 or more positive signs in the 2 analyzed leads. A tracing was defined as compatible with hypopotassemia if the electrocardiogram contained any 2 positive signs or only 1 positive sign related to the U wave. Nondiagnostic tracings showed either no positive signs of hypopotassemia or only a depression of the S-T segment in 1 of the 2 leads. Typical electrocardiograms were most commonly encountered in group A, less commonly in group B, and seldom in group C (fig. 8). The only 4 electrocardiograms with 6 positive signs occurred in group A. Electrocardiograms designated as compatible with hypopotassemia and the nondiagnostic electrocardiograms were most commonly encountered in groups B and C. Thus, in group A with the lowest potassium levels, 13 patients (78 per cent) had typical, 2 patients (11 per cent) compatible, and 2 patients (11 per cent) nondiagnostic electrocardiograms. In group C with the highest plasma potassium level, 2 patients (10 per cent) had typical, 9 patients (45 per cent) compatible, and 9 patients (45 per cent) nondiagnostic electrocardiograms.

**Correlation with Plasma Concentration of Electrolytes and with Blood pH.** The average plasma potassium concentration was lowest in
patients with a typical electrocardiographic pattern (2.64 mEq./L.), higher in those with a compatible electrocardiogram (3.01 mEq./L.), and highest in patients with nondiagnostic tracings (3.22 mEq./L.). The average concentrations of sodium, chloride, calcium, and average blood pH were nearly identical in all 3 groups.

Modification of the Pattern by Other Electrocardiographic Abnormalities. In each of the patients an attempt was made to determine whether the electrocardiographic abnormalities observed in the presence of hypokalemia were due to hypokalemia alone or to some unrelated factors. In 44 patients the nonhypokalemic electrocardiographic pattern was available for the comparison with the hypokalemic pattern. In 27 patients the nonhypokalemic electrocardiogram was normal, 10 showed left ventricular hypertrophy and "strain," 4 a varying degree of lowering and inversion of T wave and depression of the S-T segment, 2 "ischemic"-pointed and inverted T waves, and 1 a pattern of acute myocardial infarction.

Plasma potassium levels of patients with left ventricular hypertrophy and "strain" pattern who had electrocardiograms typical of or compatible with hypokalemia were generally higher than plasma potassium levels of patients with a normal electrocardiographic pattern in the same groups. In 3 patients depression of the S-T segment and a low T wave in lead II, and in 2 patients a tall U wave in lead V1 persisted after plasma potassium became normal. Thus, the presence of left ventricular hypertrophy and "strain" pattern may exaggerate certain features of the hypokalemia pattern. Depression of the S-T segment and lowering or inversion of the T wave due to factors other than hypokalemia also exaggerated the electrocardiographic pattern of hypokalemia. This relation was suggested by the fact that the only 2 patients in group C who were considered to have the typical pattern of hypokalemia showed S-T and T abnormalities with normal plasma potassium level after correction of potassium deficiency. In 1 of the 2 patients with deeply inverted pointed T waves presence of this abnormality appeared to obscure some of the typical signs of hypokalemia. The same was also true of the elevation of the S-T segment in 1 case of acute myocardial infarction; here the presence of a high U wave amplitude
FIG. 2. Electrocardiograms typical of hypokalemia with 5 positive signs. A., Left. An electrocardiogram of a hypertensive patient following treatment of diabetic acidosis with large amounts of insulin, saline, and glucose intravenously. Plasma K+ 2.5, Na+ 139, Ca++ 5.35, Cl− 115, HCO3− 18 mEq/L, pH 7.30. Note the depression of the S-T segment and the tall U wave in both leads. The amplitude of the U wave exceeds the amplitude of the T wave in lead V3. The negative T and the positive U are merged in lead II, but in lead V3 there is a kink between the 2 waves. Q-aT interval measures 0.26 second (expected Q-aT 0.25 second), Q-T interval 0.29 second (expected Q-T 0.31 second), and Q-aU interval 0.38 second (expected Q-aU 0.40 second). A., Right. The electrocardiogram after administration of potassium salts and feeding. Plasma K+ 5.2, Na+ 136, Ca++ 4.3, Cl− 92, HCO3− 25 mEq/L, pH 7.36. Note the disappearance of the U wave and of the depression of the S-T segment in lead V3. B., Left. An electrocardiogram of a debilitated patient with a cerebrovascular accident and 3 weeks of anorexia. Plasma K+ 2.5, Na+ 141, Ca++ 5.1, Cl− 92, HCO3− 33 mEq/L, pH 7.51. Note the depression of the S-T segment and the diphasic, poorly defined T wave merged with the U wave in both leads. The amplitude of the U wave in lead V3 exceeds 1 mm. In lead II, the amplitude of the U wave is less than 1 mm, but is greater than the amplitude of the T wave. The third complex in lead V1 is an atrial premature beat and a merging of the P wave and the U wave can be seen. The Q-aT and the Q-T interval could not be measured. The Q-aU interval measures 0.46 second (expected Q-aU 0.47 second). B., Right. The electrocardiogram after oral administration of potassium for 2 days. Plasma K+ 3.2, Na+ 149, Ca++ 4.85, Cl− 97, HCO3− 29 mEq/L, pH 7.50. Note the increase of the T wave and the decrease of the U-wave amplitude.
permitted the classification of the electrocardiogram as compatible with hypopotassemia (fig. 5).

Modification of the Pattern by Different Heart Rates. The electrocardiographic patterns typical of or compatible with hypopotassemia occur less commonly when the heart rate is rapid. Thus, the only nondiagnostic electrocardiograms in groups A and B appeared in patients with rapid heart rates. On the other hand, the only electrocardiograms typical of or compatible with hypopotassemia in group C occurred in the group of patients with the slowest heart rate. Electrocardiograms typical of hypopotassemia occurred in patients with R-R intervals between 0.61 and 0.88 second in

Fig. 3 Top. Electrocardiogram typical of hypopotassemia with 4 positive signs. Left. An electrocardiogram of a patient with liver cirrhosis and long-standing vomiting. Plasma K+ 2.5, Na+ 143, Cl− 102, HCO3− 20 mEq./L., pH 7.41. Note the depression of the S-T segment in lead V2. Further note that the T wave is poorly defined and partly merged with the U wave. The amplitude of the U wave exceeds the amplitude of the T wave in both leads and the U wave exceeds 1 mm. in lead V2. The Q-aT and Q-T intervals could not be measured. The Q-aU interval measures 0.44 second (expected Q-aU 0.43 second). Right. The electrocardiogram 15 minutes after potassium infusion was discontinued. Plasma K+ 3.0, Na+ 142, Ca++ 4.15, Cl− 107, HCO3− 16 mEq./L., pH 7.38. Note the more positive and the less inverted T waves in lead Vf and V3 and the decreased amplitude of the U wave. The Q-aT interval measures 0.35 second (expected Q-aT 0.27 second), Q-T interval 0.41 second (expected Q-T 0.36 second) and Q-aU 0.44 second (expected Q-aU 0.45 second).

Fig. 4 Bottom. Electrocardiogram typical of hypopotassemia with 3 positive signs. Left. An electrocardiogram of an alcoholic patient with a history of long-standing vomiting. Plasma K+ 2.4, Na+ 123, Cl− 63 mEq./L., pH 7.60. Note the merging of the T wave with the U wave in lead II; in some cycles a small notch could be seen between the 2 waves. The amplitude of the U wave in lead II appears to exceed the amplitude of the T wave. The U wave in lead V3 is tall but clearly separated from the T wave. The Q-aT interval measures 0.31 second (expected Q-aT 0.30 second), the Q-T interval 0.42 second (expected Q-T 0.38 second), and the Q-aU interval 0.47 second (expected Q-aU 0.48 second). Right. The electrocardiogram after 5 days of intravenous and oral potassium administration. Plasma K+ 5.1, Na+ 125, Ca++ 4.3, Cl− 91 mEq./L., pH 7.40. Note the changes of the T and U waves.
group C, with R-R intervals of 0.51 to 0.88 in group B, and with R-R intervals of 0.38 to 0.88 second in group A. These results were interpreted as evidence that the recognition of the electrocardiographic pattern of hypopotassemia becomes progressively more difficult with increasing heart rate. The difficulty in recognition of hypopotassemia when the heart rate is fast is due to several factors. One of these is the progressive decrease of the U-wave amplitude when the heart rate increases. Another difficulty caused by tachycardia is the frequent merging of the U wave with the preceding T or the subsequent P wave.

We found that in several cases merging of the U wave with the P wave could be recognized as such when attention was directed to the shape of the P wave. A P wave that is merged with a positive U wave begins above the baseline and ends at the baseline. This gives the P wave a prominent

Fig. 5 Top. Electrocardiogram compatible with hypopotassemia with 2 positive signs. Left. An electrocardiogram of a patient with a history of prolonged vomiting and a recent myocardial infarction with shock. The tracing was recorded shortly after infusion with hypertonic saline. Plasma K⁺ 2.8, Na⁺ 171, Cl⁻ 148, HCO₃⁻ 36 mEq./L., pH 7.61. Note the Q wave in both leads and S-T segment elevation in lead V₅. The U wave in lead V₃ is deeply inverted and is of greater amplitude than the T wave. The Q-aT interval measures 0.28 second (expected Q-aT 0.29 second). The Q-aU interval measures 0.48 second (expected Q-aU 0.47 second). Right. The electrocardiogram after potassium infusion. Plasma K⁺ 3.1 mEq./L. Note the decrease of the amplitude of the U wave.

Fig. 6 Bottom. Electrocardiogram compatible with hypopotassemia with 1 positive sign. Left. An electrocardiogram of a patient following perforation of a duodenal ulcer and gastrectomy. Plasma K⁺ 2.9, Na⁺ 133, Ca⁺⁺ 4.25, Cl⁻ 93, HCO₃⁻ 28 mEq./L. Note the merging of the U wave with the T wave. The amplitude of the U wave in lead V₃ probably exceeds 1 mm. The Q-aT interval measures 0.21 second (expected Q-aT 0.22 second), Q-T interval 0.31 second (expected Q-T 0.30 second). Right. The electrocardiogram after 8 days of feeding. Plasma K⁺ 4.6, Na⁺ 146, Ca⁺⁺ 4.6, Cl⁻ 92, HCO₃⁻ 23 mEq./L., pH 7.36. Note the increase of the amplitude of the T wave and the decrease of the amplitude of the U wave.
Fig. 7. Electrocardiograms nondiagnostic of hypopotassemia in patients with hypopotassemia. A., Left. An electrocardiogram of a patient with pseudobulbar palsy, inadequate diet, infusions of potassium-free solutions, and steroid therapy. Plasma $K^+ 2.5$, $Na^+ 132$, $Cl^- 96$, $HCO_3^- 19$ mEq./L., pH 7.54. Note the tachycardia and the absence of electrocardiographic signs of hypopotassemia. The P wave and the U wave are merged, simulating a high-amplitude P wave. The third complex in lead V3 follows a premature beat and appears after a longer R-R interval. This demonstrates the separation of the U wave from the following P wave and shows the true amplitude of the P wave. A., Right. The electrocardiogram after potassium infusion. Plasma $K^+ 3.3$, $Na^+ 137$, $Ca^{++} 3.6$, $Cl^- 96$, $HCO_3^- 17$ mEq./L., pH 7.54. Note the decrease of the P wave amplitude, probably caused by a decrease of the U-wave amplitude. B., Left. An electrocardiogram of a patient in hepatic coma. Plasma $K^+ 2.8$, $Na^+ 125$, $Ca^{++} 3.9$, $Cl^- 68$ mEq./L. Note the absence of electrocardiographic signs of hypopotassemia. The P-R interval is prolonged and the P wave appears to be merged with the U wave, probably accounting for the high amplitude of the P wave. Note the tilted P wave in lead V3 with the onset situated farther above the base line than the end of the P wave. B., Right. The electrocardiogram after 7 days of feeding and intravenous potassium administration. Plasma $K^+ 4.5$, $Na^+ 141$, $Cl^- 77$, $Ca^{++} 4.9$ mEq./L., pH 7.44. Note that the U wave and the P wave are still merged in lead V3; the marked decrease in P-wave amplitude probably is due to the decreased amplitude of the U wave. C., Left. An electrocardiogram of a patient with cholelithiasis, vomiting, and diarrhea. Plasma $K^+ 3.0$, $Na^+ 133$, $Ca^{++} 4.5$, $Cl^- 93$ mEq./L., pH 7.37. Note the absence of electrocardiographic signs of hypopotassemia. C., Right. The electrocardiogram after 12 days of adequate diet. Plasma $K^+ 4.2$, $Na^+ 141$, $Ca^{++} 4.65$, $Cl^- 93$ mEq./L., pH 7.35. Note that the T waves have become more peaked in lead II.
wave a characteristic tilted appearance and frequently contributes to a significant increase of the amplitude of the P wave (fig. 2B and 7B). We have recognized the usefulness of the sign of a “tilted P wave” in the diagnosis of hypopotassemia after repeatedly observing a progressing descent of the onset of the P wave during administration of potassium to patients with hypopotassemia. Figure 7A demonstrates the apparent increase of the amplitude of the P wave due to the merging of the latter with the U wave.

Correlation of Individual Positive Signs and Plasma Potassium Level. Correlations between S-T, T, and U-wave abnormalities and the plasma potassium were possible in the 27 patients whose electrocardiogram became normal when the plasma potassium rose to normal.

1. S-T segment. Depression of the S-T segment of 0.5 mm. or more was present in 9 of the 27 patients. The plasma potassium level in these 9 patients ranged from 2.0 to 2.83 mEq./L. The electrocardiograms of these patients were characterized by a poor definition of the T wave in the lead with the depressed S-T segment. The T wave was considered in all these cases as a diphasic, negative-positive wave, and the positive component was usually of low amplitude. The electrocardiographic patterns were considered as typical of hypopotassemia in 8 out of 9 patients with S-T depression. It was concluded that depression of the S-T segment caused by hypopotassemia is a sign of an advanced hypopotassemia.

2. T wave. The T wave was positive and its amplitude could be determined in the precordial lead in all 27 patients. In 12 patients the amplitude of the T wave was 1 mm. or less, in 8 patients it ranged from 1.5 to 3.0 mm., and in 7 from 4.0 to 8.5 mm. The group of patients with the highest T waves and the group of patients with the medium-sized T waves had similar plasma potassium concentrations (2.95 and 3.01 mEq./L.).

The group of patients with the lowest T waves had lower average (2.63 mEq./L.) and lower range of plasma potassium concentrations than the other 2 groups. It was concluded that there was no direct correlation between the amplitude of the T wave and plasma potassium level until the amplitude of the T wave fell below 1 mm. in the precordial lead with the highest U wave. However, T-wave amplitude below 1 mm. was usually found in patients with lowest plasma potassium levels and typical electrocardiographic patterns of hypopotassemia.

3. Ratio of the U-wave amplitude to the T-wave amplitude. The analysis was limited to the U/T ratio in the precordial lead. The U/T ratio was less than 0.5 in 8 patients, between 0.5 and 1.0 in 6 patients, and more than 1.0 in 9 patients. The groups of patients with the smallest and the medium ratios had similar plasma potassium concentrations (2.94 and 3.05 mEq./L.). The group with the highest U/T ratios had a lower range and a lower average (2.52 mEq./L.) potassium concentration than the other 2. All electrocardiograms in this group were considered to be typical of hypopotassemia. It was concluded that there was no direct correlation between plasma potassium level and U/T ratio in the precordial lead with the highest U wave until this ratio exceeded 1. However, the U/T ratio of more than 1 usually occurred in patients with lowest plasma potassium levels.

4. Amplitude of the U wave. There was no significant correlation between the amplitude of the U wave and plasma potassium concentration. The U-wave amplitude was found to be related to the heart rate.
Duration of the Q-aT, Q-T, and Q-aU Interval. The present study afforded us an opportunity to check the validity of the results of previous study of this subject. The details of measurements will not be repeated and only the essence of the results will be presented. Q-aT, Q-T, and Q-aU intervals in the electrocardiograms of 42 patients were measured and expressed as a percentage of the normal expected value. Electrocardiograms of 8 patients with heart rates faster than 110 per minute were excluded because no normal values for such heart rates were available to us.

The Q-aU interval was within ±10 per cent of the expected value in 36 out of 42 patients, slightly prolonged (+16 and +17 per cent) in 2 patients, and not measurable in 4 patients.

The Q-aT and Q-T intervals will be discussed together. We subdivided the electrocardiograms of our patients into a group with normal and a group with prolonged Q-T or Q-aT intervals. The group with normal intervals (within 10 per cent of the expected value) included 18 patients with both intervals measurable before administration of potassium and 7 patients in whom one or both of these intervals became measurable only after administration of potassium. The group with prolonged intervals had Q-aT intervals ranging from +12 to +45 per cent and Q-T intervals from +12 to +33 per cent. The group consisted of 8 patients in whom the prolonged intervals were measurable before the administration of potassium and of 9 patients in whom the intervals became measurable only after administration of potassium.

Comparison of plasma potassium levels in both groups of patients demonstrated similar ranges (2.21 to 3.48 and 2.00 to 3.35 mEq./L) and almost identical average values (2.87 and 2.84 mEq./L). There was, however, a significant difference in plasma calcium concentration. The group with normal intervals had plasma calcium concentrations ranging from 3.7 to 6.6 mEq./L, with an average value of 4.76 mEq./L, while the group with prolonged intervals had plasma calcium concentrations ranging from 3.05 to 5.05 mEq./L, with an average value of 3.9 mEq./L. Plasma calcium concentrations below 4.5 mEq./L were encountered in 7 out of 25 patients with normal intervals and in 14 out of 17 patients with prolonged intervals. In 2 of the 3 remaining patients with normal calcium concentration and prolonged intervals, there was electrocardiographic evidence of heart disease of the type often associated with Q-T prolongation.

It was concluded that prolongation of the Q-aT and Q-T intervals, defined according to previously described criteria, was related to hypocalcemia but not to hypopotassemia.

Effect of Intravenous Potassium Administration in 42 Patients. The amplitude of the P wave decreased in 7, increased in 1, and remained unchanged in the remaining patients. The duration of P-R interval shortened from 0.01 to 0.02 second in 3 patients and remained unchanged in all others. The QRS voltage decreased in 36 and remained unchanged in 6 patients. The amplitude of the T wave increased in 32, remained unchanged in 6, and decreased in 3 patients. The latter 3 patients had inverted T waves. The apex of T wave could not be defined in 13 out of 50 patients with hypopotassemia for one or more of the following reasons: isoelectric T wave, diphasic T wave in all leads, or T wave merged with the U wave. After potassium administration: the apex of the T wave could be defined in all but 1 patient. The amplitude of the U wave remained unchanged in 4 and decreased in the remaining patients. The duration of the Q-aT, Q-T, and Q-aU intervals, corrected for sex and heart rate, remained essentially unchanged in all patients in whom measurements could be done before and after administration of potassium. The heart rate remained unchanged in 22, slightly decreased in 9, and slightly increased in 11 patients.

Ectopic beats were present in 13 patients with plasma potassium levels ranging from 2.0 to 3.35 mEq./L. There was no relation between the presence of ectopic beats and plasma potassium concentration. The ectopic beats were supraventricular in 9, ventricular in 3, and both supraventricular and ventricular in 1 patient. After intravenous administration of potassium chloride supraventricular ectopic beats disappeared in 5, decreased in 1, underwent no change in 3, and increased in 1 patient.
The ventricular ectopic beats decreased in 2, underwent no change in 1, and increased in 1 patient. Special features of ectopic beats occurring in hypopotassemia are described in a separate study.13

Discussion

The electrocardiographic pattern of hypopotassemia can be defined with accuracy by the use of certain quantitative criteria. These are related to the U-wave amplitude, the relation between U and T amplitude, and to S-T segment displacement. Our preliminary observations indicate that this typical electrocardiographic pattern of hypopotassemia is fairly specific and that the only known clinical situation in which such an electrocardiographic pattern frequently appears in patients with normal plasma potassium is a combined effect of digitalis and quinidine.1

In our subjects there was a good correlation between the number of electrocardiographic signs of hypopotassemia and the plasma potassium concentration. Unless tachycardia is present, if the potassium concentration is below 2.7 mEq./L, a tracing typical of hypopotassemia is to be expected. All patients with plasma potassium concentrations exceeding 2.7 mEq./L showed a wide variety of electrocardiographic patterns. The presence of such a wide variety of patterns can probably be explained by 2 factors. First, normal serum potassium concentration may range from 3.50–3.72 to 5.5–5.62 mEq./L.14,15 Therefore, a hypopotassemic serum level can be expected in some individuals after a very small and in others only after a considerable decrease in potassium concentration. Secondly, there is a wide range of normal T-wave amplitudes in different individuals.16 When the T wave initially is small, a slight decrease in amplitude may cause a reversal in T/U ratio and contribute to a typical hypopotassemia pattern. A similar degree of lowering of an initially tall T will not greatly disturb the T/U ratio and may go unnoticed (fig. 7C). The normal T wave apparently was tall and peaked and the electrocardiogram showed no sign of hypopotassemia when the plasma potassium level was 3.0 mEq. L.

Our findings confirm the general experience that electrocardiographic changes diagnostic of hypopotassemia appear only with seriously low potassium levels,17 and that T-wave lowering occurs regularly only with potassium levels below 3.0 mEq./L.18 However, our observations are in contrast to those of other workers who describe a poor correlation between the electrocardiographic pattern and the severity of the hypopotassemia.3,2 Two factors may account for this disagreement: the small number of patients with potassium concentration below 2.7 mEq./L observed by these investigators, and the different methods of electrocardiographic evaluation.1

The cause of the electrocardiographic findings in hypopotassemia is uncertain. Dependence on the plasma potassium concentration is suggested by the rapidity of development of electrocardiographic abnormalities following perfusion of the isolated heart with potassium-free fluid.19 and the acute removal of potassium by hemodialysis in dogs.20 We have observed a similar rapidity during glucose infusions in normal subjects and in patients with diabetic acidosis.21 However, it has been postulated that the electrocardiographic findings in hypopotassemia are due to a change in ratio of intracellular to extracellular potassium.1,22 If this is true, the results of our study may simply indicate that the change of ratio in the myocardium is determined largely by a change in the extracellular potassium concentration. This appears probable because of the large change in ratio produced by a small change in extracellular potassium concentration. For instance, a change of plasma potassium concentration from 4.0 to 2.0 mEq./L, corresponds to a decrease of 50 per cent. Such decreases in the content of cellular myocardial potassium have not been reported to our knowledge. It has been stressed that in cats subjected to various experimental procedures the changes in the myocardial concentration of potassium were smaller than changes in the skeletal muscle potassium, and the reported results show changes of myocardial potassium of less than 15 per cent.22 Likewise, in rats subjected to experimental potassium depletion, a stability of the content of myocardial potassium has
been emphasized and compared with more variable concentrations of potassium in the skeletal muscle. Furthermore, it has been shown that the intracellular potassium concentration in hearts perfused with solutions containing low, normal, and high potassium concentrations was not significantly different. If these results of animal experiments are applicable to the human heart, one may assume that the potassium gradient across the myocardial cell membrane is largely determined by the extracellular potassium concentration.

Our findings indicate that abnormal concentrations of electrolytes other than potassium do not interfere with the identification of electrocardiographic signs of hypopotassemia. An exception may be encountered in patients with pronounced hypocalemia; here the Q-T prolongation, due to hypocalemia, causes a complete merging of the T wave with the U wave.

Alkalosis and acidosis did not prevent the appearance of typical electrocardiographic signs of hypopotassemia. A typical pattern in the presence of acidosis is illustrated in figure 2A, and has been found by others. The effect of blood pH on intracellular myocardial potassium is not known, but in striated muscle intracellular potassium content was similar in patients with acidosis and alkalosis. Abrams, Lewis, and Bellet found that electrocardiographic changes occurring in acidotic and alkalotic dogs could be correlated with changes in extracellular potassium concentration.

Conflicting data are reported by Magida and Roberts, who concluded that the electrocardiographic changes observed in dogs with hypopotassemia should be attributed to metabolic alkalosis per se. However, when their electrocardiographic illustrations are evaluated by the criteria presented in this paper, it is reasonable to conclude that the changes observed in hypopotassemic alkalotic dogs are indeed due to the hypopotassemia.

Of the several features that may obscure the typical electrocardiographic signs of hypopotassemia, tachycardia was the most common in our patients. However, even when the R-R interval is short, the presence of a tall U wave frequently can be suspected when the P wave is abnormally tall and tilted, e.g., figures 1, 2, 6a, and 6c of reference 1 and figure 2 to 5 of reference 33. In these cases, similar to the cases presented in this study, administration of potassium caused an apparent lowering and leveling of the P wave. However, it must be stated that the tilted appearance of the P wave occurs not only when P is merged with U, but also when the P wave is merged with the T wave. Thus, we have observed tilted P waves in patients without hypopotassemia in several cases with a prolonged P-R interval, supraventricular premature beats, and some other situations in which the P wave was merged with the T wave.

In our experience a false electrocardiographic diagnosis of hypopotassemia has not been common. Depression of the S-T segment, when not accompanied by other electrocardiographic signs of hypopotassemia should not lead to a suspicion of this electrolyte disturbance. In agreement with other workers, our findings indicate that S-T depression is a sign of advanced hypopotassemia, always accompanied by increase in U-wave amplitude. Tall U waves but no similarity to the electrocardiogram of a dog with hypopotassemia and no alkalosis, illustrated in their figure 3. An inspection of figures 1 to 3 of this paper permits a different interpretation of the illustrated electrocardiograms from that offered by the authors. The electrocardiogram of a dog with hypopotassemia and alkalosis in their figure 1 shows an elevated P wave that has an onset situated farther from the base line than the end, and thus is very similar to the tilted P wave observed by us in patients with hypopotassemia and tachycardia. The S-T segment is depressed and the T wave has a rounded appearance. The electrocardiogram of a dog with alkalosis but no hypopotassemia, in their figure 2, shows a smaller amplitude of the P wave, the P wave does not have the tilted appearance, the S-T segment is not depressed, and the T wave has not a rounded, but a peaked appearance when serum potassium is 5.0 mEq/L. Accordingly, we think that the illustrated electrocardiographic changes in dogs with hypopotassemia are caused by hypopotassemia and not by alkalosis.
may be present without hypopotassemia in patients with left ventricular hypertrophy and "strain" pattern. The combination of tall U waves and S-T depression in left ventricular hypertrophy and "strain" may lead to a suspicion of hypopotassemia. However, in our experience, when hypopotassemia complicates the left ventricular "strain" pattern, S-T depression was found, not only in the limb and left precordial leads, but also in leads V₁₋₃. Since an uncomplicated left ventricular hypertrophy and "strain" pattern usually shows an S-T elevation in the leads with tall T and U waves (leads V₁₋₃), the finding of S-T depression in these leads becomes a useful diagnostic sign of hypopotassemia.

We found no changes of configuration or amplitude of the P waves or QRS complexes that could be attributed to hypopotassemia. However, following the administration of potassium, there was a fairly constant decrease in QRS amplitude and a frequent decrease of P-wave amplitude.

Since excessive potassium is known to decrease the action potential of the myocardial fiber, hypopotassemia might be expected to cause increased QRS and P amplitude. However, we have not considered the lowering of amplitude as a specific potassium effect because we have repeatedly observed a decrease of QRS and P wave amplitude similar to that occurring during infusion of potassium chloride also during infusion of saline.

In our subjects, the incidence of arrhythmia was not correlated with the degree of hypopotassemia. However, many of our patients had, in addition to hypopotassemia, either heart disease or other conditions known to be associated with cardiac arrhythmias. Lepeschkin and Rosenbaum suggested that increased U amplitude facilitates appearance of premature beats, analogous to the appearance of ectopic beats when a critical height of the afterpotential is reached. In their figure 2, appearance of ventricular irritability was associated with progressive increase in U-wave amplitude.

A similar experience was recorded by Stephens: during treatment of diabetic acidosis with glucose and insulin, ventricular premature beats and bigeminy developed when the U waves became large.

Ventricular tachycardia or fibrillation has not been reported as a cause of death in patients with documented hypopotassemia, but such a possibility appears to exist.

**Summary**

In 50 hypopotassemic patients, 2 leads (generally leads II and V₃) of the electrocardiogram were analyzed with regard to the following electrocardiographic signs of hypopotassemia: (1) amplitude of the U wave greater than 1 mm., (2) a ratio greater than 1 of U-wave to T-wave amplitude in the lead with the tallest U wave, and (3) S-T segment depression more than 0.5 mm. Depending on the number of signs present in the 2 leads, electrocardiograms were termed typical of hypopotassemia (3 or more signs), compatible with hypopotassemia (2 signs, or only 1 sign related to the U wave), and nondiagnostic of hypopotassemia (no sign, or only S-T segment depression in 1 of the leads).

A correlation was found between the electrocardiographic pattern and the plasma potassium concentration. In 17 patients with a potassium level between 2.0 and 2.7 mEq./L., 78 per cent had electrocardiograms typical of hypopotassemia. In 20 patients with a plasma potassium between 3.0 and 3.49 mEq./L., 90 per cent of the tracings were either nondiagnostic of or merely compatible with hypopotassemia. In 4 subjects, 6 signs were present in the 2 electrocardiographic leads; each of these patients was in the group with the lowest potassium level.

Appearance of the electrocardiographic signs of hypopotassemia was not prevented by disturbances of concentration of other plasma electrolytes or by blood pH. Hypocalcemia and the resultant lengthening of the Q-T interval occasionally caused difficulty because of merging of the T wave with the U wave. Hypopotassemia alone did not influence the Q-aT, Q-T, or Q-aU intervals.

Recognition of the hypopotassemia pattern often was difficult in the presence of tachycardia, which causes decreased amplitude of the U wave as well as merging of the P wave
with the U wave. Attention is directed to the tilted P wave, a previously unrecognized sign of U wave prominence, which may cause suspicion of hypopotassemia, despite tachycardia.

Evidence concerned with the basic cause of the electrocardiographic signs of hypopotassemia is discussed. The plasma potassium level is considered to be the important factor, either directly or by its large effect on the ratio of extracellular to intracellular myocardial potassium concentration.

ACKNOWLEDGMENT

The authors wish to acknowledge the valuable comments and suggestions made during the preparation of this manuscript by Dr. E. Lepeschkin and Dr. E. A. H. Sims, of Burlington, Vt., and Dr. Robert Tarail, of Buffalo, N. Y.

SUMARIO IN INTERLINGUA

In 50 patientes hypokalemic 2 derivationes electrocardiographic (generalmente II e V3) esesse analyzate con respecto al sequente signos de hypokalemia: (1) Amplitude del unda U plus que 1 mm, (2) proportion del amplitudes de undas U a T plus que 1 in le derivation con le plus alte unda U, e (3) depression del segmento S-T plus que 0,5 mm. Secundo le numero de signos representate in le 2 derivationes, le electrocardiogrammas esesse designate como typic de hypokalemia (3 signos o plus), compatibile con hypokalemia (2 signos, o 1 signo relateate al unda U), e non-diagnostic pro hypokalemia (0 signos o solmente depression del segmento S-T in 1 del derivationes).

Esse trovate un correlation inter le configuration electrocardiographic e le concentration de kalium in le plasma. In un serie de 17 patientes con nivellos de kalium de inter 2,0 e 2,7 mEq/l, 78 pro cento habeava electrocardiogrammas typic de hypokalemia. In 20 patientes con nivellos plasmatic de kalium de inter 3,0 e 3,49 mEq/l, 90 pro cento del registraiones esesse non-diagnostic o solmente compatibile con hypokalemia. In 4 subjectos, 6 signos esesse presente in le 2 derivationes. Omne iste patientes esesse in le gruppo con le plus basse nivellos de kalium.

Le presentia del signos electrocardiographic de hypokalemia non esesse prevenite per disturbationes del concentration de altere electrolytos in le plasma o per le pH del sanguine. Hypoalceemia e le resultante prolongation del intervallo Q-T causava certe difficultates in alunc casos a causa del fusion inter unda T e unda U. Hypokalemia sol non influentiava le intervallas Q-aT, Q-T, o Q-aU.

Le recognition del configuration de hypokalemia esesse frequentemente difficile in le presentia de tachycardia, que causa non solmente un reduction del amplitude del unda U sed etiam un fusion del undas P e U. Es signalate le phenomeno del basuculate unda U, un previemente non recognoscite signo de prominentia del unda U. Isto pote causar suspicion de hypokalemia in respecto del presentia de tachycardia.

Es discutite materiales concernite con le causa fundamental del signos electrocardiographic de hypokalemia. Le nivello de kalium in le plasma es considerate como le factor saliente, o directemente o indirectemente in consequentia de su grande effecto super le proportion extra- a intracellular in le concentration de kalium myocardial.

REFERENCES


11 SURAWICZ, B., and LEPESCHKIN, E.: Methods of a differentiation between a true and an apparent prolongation of the electrocardiographic Q-T interval. Program, Scientific meeting of the American Heart Association, April 3–4, 1954.


21 SURAWICZ, B.: Unpublished observations.


32 MAGDA, M. G., and ROBERTS, K. E.: Electrocardiographic alterations produced by an increase in plasma pH, bicarbonate and sodium as compared with those seen with a decrease in potassium. Circulation Research 1: 214, 1953.


