ANNOTATION

The Effect of Potassium and Calcium on The Electrocardiogram

The force and general behaviour of cardiac contraction can be altered in striking fashion under experimental conditions by varying the physical and chemical composition of the fluid bathing the heart muscle. Slight increases in alkalinity or acidity bring about a lengthening or shortening of systole respectively and influence the transmission of the impulse in the conduction system. The ionic content of extracellular fluid, its historical derivation from its primitive forerunner sea water, and the importance of changes in its composition to the economy of the individual have been portrayed lucidly by Gamble (1942).

The three cations potassium, calcium and sodium must be present in fairly inflexible concentrations if the heart is to beat normally; magnesium and the anion content of extracellular fluid may be important also but they are beyond the scope of this review. As might be expected from their effect on cardiac muscle, potassium and calcium when present in abnormal amounts, produce changes in the electrocardiogram, the former dramatic and specific, the latter less ostentatious but none the less characteristic. The individual contribution of sodium to electrocardiographic changes is less well understood but, as will be explained later, a low sodium content (hyponatraemia) appears to potentiate the abnormalities caused by excessive potassium. Significant changes in the serum concentration of one electrolyte are unlikely to occur alone; whether variations in other serum electrolytes can be detected or not, they are likely to be present, in addition to fluctuations in intracellular ions not measurable by ordinary laboratory methods. The electrocardiogram reflects the summation of the changes in the ionic environment of the heart, and in this lies its chief application in the management of electrolyte imbalance (Merrill *et al.*, 1950).

Potassium—Hyperkalaemia (hyperpotassaemia)

Abnormally high serum potassium levels are found in renal insufficiency especially when oli-

guria is present, in untreated Addison's disease and conditions associated with excessive vomiting, haemoconcentration and shock. Although the body stores of potassium are reduced in diabetic acidosis and coma, high serum levels are found frequently before treatment is begun because of the mechanisms mentioned above.

Heart muscle is susceptible in some way to potassium not shared by skeletal muscle. This fact has been demonstrated convincingly in dogs whose limb muscles continue to twitch vigorously at serum concentrations of potassium sufficient to cause cardiac arrest (Winkler *et al.*, 1939).

Clinical experience tends to support this observation. With excessive or increasing concentration of potassium in the serum, rapid and dramatic changes in cardiac rhythm, for example, transition from sinus rhythm to a state resembling ventricular flutter, may be recorded graphically without apparent change in the state of the somatic muscle (Levine *et al.*, 1951).

The earliest electrocardiographic signs of potassium intoxication are an increase in amplitude and pointing of the T waves and a shortening of the QT interval.* The changes may be subtle and inconspicuous and their first appearance may be overlooked unless especially sought for or unless a control electrocardiogram is available for comparison. The sequential changes may be summarized as follows (Merrill *et al.*, 1950):—

1. Changes in ventricular activation: Tall pointed T waves and first shortening and later lengthening of QT interval. R waves become lower and S waves deeper across the precordium. ST segment is depressed in characteristic fashion.
2. Intra-auricular block: Low, wide P waves progressing to auricular fibrillation or standstill.
3. Auriculo-ventricular block: Prolonged PR interval, possibly progressing to higher grades of auriculo-ventricular block.
4. Intra-ventricular block: Bundle branch block or diffuse intra-ventricular block progressing to ventricular standstill.
5. Ectopic rhythms: Ventricular premature or escape beats progressing to ventricular tachycardia and an undulating ventricular pattern re-

* In this paper the symbol QT implies a correction for heart rate.

sembling flutter, and finally ventricular fibrillation.

Fig. 1 illustrates the typical electrocardiographic changes of severe potassium intoxication in a man aged 65 with uraemia resulting from chronic glomerulonephritis. At the time of this tracing (Fig. 1a) the serum potassium was 11.5 milliequivalents per litre (mEq./L.)* and serum sodium 112 mEq./L. No evidence of auricular activity can be seen. There is diffuse intra-ventricular block with low R waves and deep, wide S waves in leads V₂ to V₆. The ST pattern is characteristic; the S wave becomes continuous with the upstroke of T, no ST segment proper being identifiable. The T waves are tall and pointed and the QT interval prolonged. The standard and unipolar limb leads reflect the changes in the chest leads. When the electrolyte imbalance was corrected the electrocardiogram returned to its original form which, of course, is grossly abnormal from pre-existing disease (Fig. 1b). This case has been reported fully elsewhere (Merrill *et al.*, 1950).

No explanation in electrophysical terms is available for the development of deep S waves across the precordium in advanced potassium intoxication. Its resemblance to marked clockwise rotation of the heart is not supported by clinical observation.

Ventricular arrhythmias are a feature of severe cases (Fig. 2). They often present a bizarre pattern and are identical with many records obtained from the dying heart. A detailed analysis of such arrhythmias has been made elsewhere (Levine *et al.*, 1951).

Relation of Serum Potassium Levels to Electrocardiographic Changes

When an isotonic solution of potassium chloride is injected at a steady rate by vein into dogs, the serum potassium concentration increases in linear fashion with time, and a sequence of electrocardiographic changes develops resembling closely that outlined above. The earliest abnormalities appear at a potassium concentration of about 7.8 mEq./L.; intra-auricular block develops at 9 to 11

mEq./L. and cardiac arrest at 14 to 15 mEq./L. (Winkler *et al.*, 1938).

In man the correlation is much less exact because of simultaneous variation in concentration of other electrolytes, chiefly sodium and calcium. There is adequate experimental evidence that some degree of tolerance to potassium is achieved by simultaneous administration of calcium (Winkler *et al.*, 1939). The dissociation between the clinical and electrocardiographic appearances on the one hand and the serum potassium level on the other appears to be the result more often of depressed serum sodium levels, for serum calcium values may be within normal limits. Fig. 3, reproduced from an article by Merrill, Levine, Somerville and Smith (1950), illustrates the potentiating effect of low serum sodium levels on the electrocardiogram of hyperkalaemia.

If the electrocardiogram was abnormal before potassium intoxication developed, the signs of both the pre-existing condition and of hyperkalaemia will be superimposed. However, the inverted T waves of left ventricular enlargement may be made upright by potassium, while those of cardiac infarction may be more deeply inverted (Sharpey-Schafer, 1943).

Hypokalaemia (Hypopotassaemia)

Here also exact correlation is lacking between lowered serum potassium levels and electrocardiographic changes. As Wallace (1949) has pointed out recently, relative changes from one level to another are more important than departure from the absolute level of 5 mEq./L.

Potassium depletion results from losses in urine, gastric secretion or other body fluids as in pyloric obstruction and excessive vomiting, especially in infants, and in a variety of other gastro-intestinal diseases. In diabetic coma, hypokalaemia develops from such losses and is aggravated by a poor intake, by dilution of body water with potassium-free fluids used in treatment and intracellular transfer of potassium following glucose and insulin therapy. In certain types of chronic glomerulonephritis, where tubular reabsorption of potassium is deficient while glomerular filtration is unimpaired, hypokalaemia may result (Sherry *et al.*, 1948). Intensive desoxycorticosterone ace-

*The normal serum potassium concentration is 5 mEq./L. Milliequivalents per litre are obtained by dividing milligrams per litre by atomic weight and multiplying by valency.

tate (DOCA) therapy, especially in Addison's disease and certain alkalotic states, encourages potassium losses. Finally, in familial periodic paralysis, transfers of potassium occur from extracellular fluid into the cells without loss in the urine; dramatic and widespread muscular paralyses are associated with a fall, often abrupt, in serum potassium (Gass *et al.*, 1948).

The chief electrocardiographic abnormalities occurring with hypokalaemia comprise depression of the ST segments and lowering or inversion of T waves in all chest leads, with similar changes reflected to standard and unipolar limb leads (Fig. 4); they are generally less specific and more difficult to recognize than those of hyperkalaemia. The QT interval is prolonged and when the rate is slow enough to allow them to be seen, prominent U waves may appear. The significance of the latter is not clear, but they appear to be related to the after-potentials of ventricular contraction which in turn are influenced by the potassium content of the serum. The point is discussed elsewhere (Somerville *et al.*, 1951).

Hypokalaemia is found often with concomitant changes in concentration of other cations, especially calcium. Additional electrocardiographic abnormalities may be introduced thereby. Low potassium may accompany a high serum calcium level; the QT interval may then be prolonged or shortened respectively depending on which abnormality dominates the picture. In the hypokalaemia of diabetic acidosis, Martin and Wertman (1947) found the QT interval prolonged whether the total calcium or ionized calcium fraction was low or normal.

The lack of parallelism between the depression of serum potassium concentration and electrocardiographic changes is emphasized again. The numerous and complex variables involved in hypokalaemic states such as fluctuations in pH and in blood volume and intracellular electrolyte imbalance secondary to extracellular changes, provide a ready explanation. The electrocardiogram, however, as in hyperkalaemia, reflects the summation effects of these factors influencing cardiac muscle and is a useful guide to clinical progress and management.

Calcium (Hypercalcaemia)

Elevated blood calcium is met with in hyperparathyroidism, or after excessive administration of parathormone or irradiated ergosterol. Malignant metastases in bone may cause definite but less marked hypercalcaemia.

When calcium chloride is injected intravenously at a steady rate into dogs so that there is a linear increase in serum calcium with time from the normal of 5 mEq./L., a constant sequence of electrocardiographic changes is encountered (Hoff *et al.*, 1939):

At 7.5 to 33 mEq./L. the rate slows, PR is increased, QT decreased and T waves lowered.

At 12 to 45 mEq./L. the rate increases and death may follow ventricular fibrillation.

If ventricular fibrillation does not supervene a second slowing process may develop at concentration of 35 to 95 mEq./L. wigtenthal depression of the cardiac mechanism and cardiac arrest.

In man electrocardiographic changes follow this general pattern although such high concentrations of calcium are not recorded. Clarke (1941) produced bradycardia in normals by intravenous injection to 2.5 to 5 gm. of calcium chloride. This was followed by sinus arrhythmia, shifting pacemaker, auriculo-ventricular block and extra systoles. Similar changes, with the addition of shortened QT interval were recorded in two patients with hyperparathyroidism, when the serum calcium level was 9 meq./l. (Kellogg and Kerr, 1936).

Hypocalcaemia

Depression of the serum calcium follows removal or injury to the parathyroid glands, an infrequent complication of partial thyroidectomy. Similar reduction with or without tetany is found with rickets, osteomalacia, pregnancy, coeliac disease, sprue and other causes of steatorrhoea, and with certain cases of renal insufficiency with phosphate retention. When tetany is produced by hyperventilation, no reduction in serum calcium may be noted although the ionized calcium fraction is depressed.

The dominant change in the electrocardiogram in hypocalcaemia is prolongation of the QT interval (Fig. 5). Other abnormalities are incon-

FIG. 1.—Electrocardiograms of a case of potassium intoxication with uraemia. Fig. 1a shows the typical changes of severe hyperkalaemia (serum potassium: 11.5 mEq./L.). When the electrolyte imbalance was corrected, the tracing returned to its original form which is abnormal from pre-existing disease (Fig. 1b).

FIG. 2.—Electrocardiogram showing ventricular arrhythmia occurring with hyperkalaemia. The pointed T waves and ST segments are characteristic. The rhythm became irregular with a lowering of serum potassium (Fig. 2c). In 2d, the tracing has improved, but the T waves are still pointed and QT is abnormally long (0.46).

FIG. 3.—Electrocardiograms obtained from four patients with serum potassium elevated to about the same degree. The changes are more pronounced when the serum sodium is also depressed than when it is normal.

FIG. 4.—Electrocardiogram of hypokalaemia obtained from a woman aged 50 with Addison's disease treated for six years with DOCA. The ST segments are slightly depressed in V4-6; T waves are low or flat, and upright U waves are present in all chest leads. The QT interval is prolonged (0.48).

FIG. 5 (Courtesy of Prof. A. Kekwick and Mr. R. Vaughan Hudson).—Electrocardiogram (chest leads) of hypocalcaemia obtained from a man with Riedel's disease of the thyroid and hypoparathyroidism. A few minutes later he developed tetany. The QT interval is prolonged (0.46) and the T waves flat or widened, especially in V4-6. While this pattern is indistinguishable from that of hypokalaemia, certain cases of hypocalcaemia can be recognized by a prolonged ST segment rather than a widened T wave.

spicuous and inconstant. Barker *et al.* (1937) investigated nine patients with hypocalcaemia, three with hypoparathyroidism following thyroidectomy and six with renal insufficiency and uraemia. They found the QT interval prolonged in all instances, and by comparing the latter with mechanical systole (the interval between the first and second heart sounds) showed disproportionate lengthening of electrical systole (QT interval). The increased QT interval of hypocalcaemia may be indistinguishable from that of hypokalaemia; in certain cases they may be differentiated by the fact that lengthening resulting

from calcium deficiency involves the ST segment, while in hypokalaemia wide flat T waves are responsible (Nadler *et al.*, 1948). Table 1 summarizes the chief effects of calcium and potassium on the electrocardiogram. As pointed out above, what the electrocardiogram records is the summation of effects of electrolyte imbalance involving intra- and extra-cellular concentrations of different ions. Changes produced thereby may reflect a combination of two abnormal patterns, for example those of hyperkalaemia and hypocalcaemia. Pre-existing abnormalities will persist or may be modified further.

TABLE I SUMMARY OF EFFECTS OF POTASSIUM AND CALCIUM ON THE ELECTROCARDIOGRAM				
	Potassium		Calcium	
	High	Low	High	Low
PR	Lengthened	—	Lengthened	—
QRS	Lengthened	—	—	—
ST	Depressed	Depressed	—	Lengthened
T	Tall, pointed	Low or inverted	Low or unchanged	—
U	—	Prominent	—	—
QT	At first, shortened, later lengthened	Lengthened	Shortened	Lengthened
Arrhythmias	Frequent	—	May occur	—

Summary

1. The main electrocardiographic changes found with hyperkalaemia are tall pointed T waves; characteristic ST segment depression; intra-auricular, intra-ventricular and auriculo-ventricular block and prolonged QT interval. In the early stages the latter may be shortened. In advanced potassium intoxication, various forms of ventricular arrhythmia may supervene.

2. In hypokalaemia the QT is prolonged, prominent U waves appear, ST segments are depressed and T waves are low or inverted.

3. Hypercalcaemia causes auricular-ventricular block, shortening of the QT interval and low T waves. Bradycardia and sinus arrhythmia may occur.

4. The main feature of hypocalcaemia is lengthening of the QT interval.

5. Abnormal serum concentrations of potassium and calcium may be present at the same time and both may influence the electrocardiogram.

6. The electrocardiogram is valuable in the diagnosis and management of electrolyte imbalance since it represents the summation of effects of ionic disturbances affecting the heart.

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ERRATUM

The Editors regret that in our April number the illustrations to Mr. D. R. K. Reid's article on Hashimoto's Disease appear in wrong order. Figure 1 should be figure 4, figure 2 should be figure 1 and figure 4, figure 2.