The Effect of Potassium on the Electrocardiogram
Clinical and Transmembrane Correlations*

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A knowledge of molecular biology in health and disease has been a goal of the modern-day physician. Until recently, understanding of the electrocardiogram has been based mostly on the sequence and duration of the myocardial activation process. The introduction of the Ling-Gerard microcapillary electrode has permitted a study of the resting and action potential of an individual cell. Consequently, the bases for understanding of the electrocardiogram can be re-evaluated by studying the events occurring at the transmembrane cellular level during depolarization and repolarization.

The interior of the resting cell in skeletal, nerve and cardiac tissue is negative with regard to the exterior. What are the factors responsible for the membrane resting potential (MRP) and the membrane action potential (MAP)? Based largely on the study of the squid giant axon, Hodgkin* demonstrated that polarization of the cell depends largely on the ionic concentrations of sodium and potassium inside and outside the cell. These ionic concentrations produce an electromotive force which can be calculated and understood from the Nernst equation:

$$E = \frac{RT}{F} \ln \left( \frac{[I]}{[O]} \right)$$

According to this equation, the potential is directly proportional to the gas constant R, absolute temperature T, and inversely proportional to the Faraday F and proportional to ln (natural log) times the ratio of the ionic concentration inside (i) and outside (o) the cell.

Potassium ion substituted in the Nernst equation gives:

$$E_K = \frac{RT}{F} \ln \left( \frac{[K_i]}{[K_o]} \right)$$

The values for K in cat heart muscle are:

$$\frac{[K_i]}{[K_o]} = \frac{151 \text{ mEq. 1L}}{4.8 \text{ mEq. 1L}} = 31$$
$$E_K = 61.5 \log 31 = 92.6 \text{ mv.}$$
$$[K_+]$$

On the other hand, the distribution of sodium ion is opposite that of potassium because the sodium ion concentration outside the cell ([Na_o]) is much greater than inside the cell. The values for cat heart muscle from the same study are:

$$\frac{[Na_o]}{[Na_i]} = \frac{159 \text{ mEq. 1L}}{65 \text{ mEq. 1L}} = \frac{1}{24}$$
$$E_{Na} = 61.5 \log 0.042 = 24 \text{ mv.}$$
$$[Na_o]$$

In short, $K_+$ is 30 times greater than $Na_+$, while the $Na_+$ is ten times greater than $Na_+$. The ratio $\frac{[K_i]}{[K_o]}$ at $37^\circ$C creates a potential difference of 92 mv, which is in accord with the measured resting membrane potential in most mammalian cells.

Normal Membrane Resting Potential (Electrical Diastole)

Hoffman and Cranefield* have schematized the ionic source of the transmembrane potential utilizing electrical symbols...

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(Fig. 1A). A battery \[\text{V} \] represents the electromotive force generated by different concentrations of Na\(^+\) and K\(^+\). A variable resistor \[\text{R} \] represents the variable resistance to outflow of K\(^+\) and the inflow of Na\(^+\). Note that the resistance to the outflow of K\(^+\) is less than the resistance to the inflow of Na\(^+\), so that the outside of the cell membrane develops a positive charge due to potassium ion. Notice that the calculated resting potential is 92 mv. while the actual potential recorded is 90 mv., demonstrating close agreement between theory and observation.

In order to understand the genesis of the membrane resting potential (MRP), a fundamental concept is that the "leakage" or egress of potassium (K\(^+\)\[\rightarrow\]K\(^+\)) is the major determinant of the positive charge on the outside of the cell membrane (Fig. 2A). From the Nernst equation, an increase of the extracellular potassium concentration should decrease the transmembrane resting potential making the cell less excitable. This was first demonstrated for the squid axon by Hodgkin\(^5\) who showed the preponderant effect of potassium on the transmembrane potential. This observation has been made in mammalian hearts as well.\(^4\) Other ions (E, in Fig. 1A) have considerably less effect upon the MRP.\(^4\)

**Membrane Action Potential**

**(Electrical Systole)**

After electrical stimulation of the heart cell, rapid reversal of charge occurs, the outside of the cell becoming negative, the inside of the cell becoming positive (Fig. 1B). In order to present these changes in more detail, we have assembled a composite picture of the time sequence of the MAP, electrocardiogram and ionic movements (Fig. 2A, normal). It is important to emphasize that the actual transmem-

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**Figure 1:** An electrical model of the excitable cell.
brane flow of ions during the action potential depends on the permeability or resistance to flow of the ions during the various phases. The nature of the repolarization process is less well understood. As previously stated, a great deal of this knowledge comes from the giant squid axon. The sequential schema to be presented in this report is a composite of studies reported in different preparations both nerve and muscle. The electrical charges, inside and outside the cell, in electrical systole and diastole, are related to the movements of Na+ and K+ ions during the classical four phases (0-4) of the action potential and to a single QRS-T complex.

Membrane Action Potential in the Normal Cell (Fig. 2A)

Phase 0 is a period of rapid depolarization potential, correlated in time with the QRS complex. This phase is associated with the rapid intracellular inflow of the positively charged external Na+ ion which may be the ionic explanation for the rapid development of negativity on the outside of the cell.6,7

Phase 1 is a period of fairly rapid decrease of the potential to near zero, which varies in different species from positive to negative. Our schematic picture (Fig. 2A) depicts a positive intracellular charge which is in accord with most mammalian hearts. A decrease of sodium influx (Na+,->K+) occurs, and a relative increase of potassium efflux (K+,->K+) occurs, resulting in a near balance of ionic flow.

Phase 2 represents approximately zero transmembrane potential associated with near equilibrium of Na+ and K+ flux. This phase is concomitant with the ST segment of the electrocardiogram. Note, however, that there is a slight slope of the MAP related to progressive decrease of Na+ and increase of K+ ion flux. The ascending limb of the T wave is possibly also related to the late part of this phase, but this is not

Figure 2A: Schema for the normal myocardial cell. Figure 2B: Schema for hyperpotassemia. Figure 2C: Schema for hypopotassemia.
explicable on the basis of an increasing slope of the MAP. For such an increasing slope should produce an isoelectric or negative component in the surface electrogram or an inverted T wave; indeed this occurs in mammalian preparations. However, we have chosen to depict the T wave as upright for clinical electrocardiographic correlation. This upright wave has been explained by the recovery phase proceeding from epicardium to endocardium producing a positive charge on the epicardium and most precordial leads.

Phase 3 is a period of rapid increasing negativity in the transmembrane potential associated with a rapid extrusion of K⁺ and a marked decrease in the Na⁺ influx. In our schematic figure, these events are related to the summit and descending limb of the T wave although the experimental results are variable. There is evidence from Wilde's experiments in the isolated turtle heart that the efflux of K⁺ during an artificially stimulated beat is pulsatile and takes a longer period of time than the rapid steady influx of Na⁺ in phase O. This time of K⁺ efflux correlates with the greater duration of repolarization as compared with depolarization.

Phase 4 is a period of electrical diastole. It is associated with after potentials and, when present, the U wave of the electrocardiogram. One theoretic explanation for the U wave, as shown in Fig. 2A, is the slightly decreased efflux of K as compared with MRP. The other possibility, according to Shanes, is the reverse, namely, that Na⁺ efflux and the K⁺ influx occur during the early part of diastole and possibly during late systole. This ionic reversal restores the Na⁺ : K⁺ extra- and intracellular ratio. However, knowledge of the transionic movements during the early part of phase 4 is incomplete.

With regard to the foregoing discussion and our schematic figure (2A), it should be pointed out that the data is incomplete and somewhat conflicting. For example, as Hecht states, Na⁺ flux has not been measured in cardiac muscle. Based on micro-injection of ions in the giant squid axon, Shar and associates have demonstrated lack of correlation between bioelectric events and ionic gradients. Hence, changes in conductance and permeability of the membrane itself may have to be invoked to explain the MAP.

Based upon the quantity of charges transferred on excitation or depolarization a

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**NORMAL**

**NON-PACEMAKER CELL**

VENTRICULAR FIBER

**PACEMAKER CELL**

PURKINJE FIBER

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**DIASTOLIC DEPOLARIZATION**

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**MAP**

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**INSIDE CELL OUTSIDE**

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**+- K⁺**

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**Figure 3:** Normal "non-pacemaker" and "pacemaker" cells. The length of the arrow indicates the rate of potassium egress from the cells.
minimum of from 10 to 12 nM of Na+/cm²/beat⁴ is required. The efflux of potassium from the cells during repolarization is of the same magnitude as the influx of sodium during depolarization.⁵ Using the present biochemical techniques, one would therefore not expect to detect a change in the potassium and sodium concentration in the blood draining the heart during repolarization and depolarization.

Normal Impulse Formation

In a myocardial cell there characteristically exists a continuous minus 90 m volts transmembrane potential during the electrical diastolic period. However, a pacemaker cell is characterized by its inability to maintain a constant resting potential which is called a diastolic depolarization potential (Fig. 3). Following each cycle of repolarization, the potential falls at an increasing rate until threshold is reached, at which time a propagated impulse arises. In a normal automatic cell,⁶ this progressive fall of the resting membrane potential can be attributed to a decrease in the transmembrane permeability of potassium, thereby progressively decreasing the ejection of potassium from the cell.⁷ The transmembrane potential is reduced, reaching a point at which depolarization occurs, hallmarked by a sudden cellular inrush of sodium.

Hyperpotassemia

Membrane Resting Potential

(Electrical Diastole)

According to the Nernst equation augmentation of extracellular potassium causes a marked decrease in MRP as shown in Fig. 2B. This has been well shown for various mammalian species and clearly in the rabbit by Gettes and co-workers.⁸ A clinical example of this concept is presented by Walker,⁹ who described two cases of implanted electrical pacemaker failure. After the oral administration of potassium, the electrical pacemakers became functional. The explanation proposed was that an elevation of extracellular potassium decreased the transmembrane potential. With a decreased transmembrane potential, the cell membrane is partially depolarized, therefore requiring less of an external stimulus for complete depolarization. In other words, the threshold stimulus is decreased.

Membrane Action Potential

(Electrical Systole)

Phase 0: the MAP is decreased in voltage (Fig. 2B). The diminished MAP decreases the upstroke velocity of the action potential and widens the duration of this phase. This event correlates with the slowing of intraventricular conduction and the widened QRS complex.¹⁰

Phase 1, 2 and 3: with slight hyperpotassemia, the increased steepness of phase 2 and 3 correlates with the elevated ST segment and tall, peaked T wave. The increased slope of the transmembrane potential in this phase does not fully explain the tall, peaked T wave. However, hyperpotassemia increases the rate of repolarization manifested by a shortened QT interval. Assuming that rapid repolarization produces a more compact wave front, a greater summation of dipoles would occur and a taller T wave inscribed (Fig. 4). With increased hyperkalemia, the slope of phase 2 becomes greater, and the ST segment elevates further. From the standpoint of the transionic gradient, egress of potassium (K⁺→K⁺) reaches a maximum in phase 3. Note the increased extrusion of K⁺ during repolarization is opposite to what would be predicted from the Nernst equation. As an explanation, Hoffman and Cranefield¹¹ have postulated that an elevated K⁺ increases the permeability of the cell for the passage of potassium:

"A simple hypothesis for the mechanism of repolarization may be formulated as fol-
REPOLARIZATION

NORMAL

HYPERPOTASSEMIA

FIGURE 4: A schematic hypothesizing a mechanism for the configuration of the T wave in cases of normal and elevated serum potassium.

lows: during phase 2 the potential gradient permits outward K movement, but K permeability is low, perhaps lower than in diastole. As the concentration of K rises outside the fiber, it enhances K permeability. When a certain level of outside K is reached (which would ordinarily correspond to a certain ratio of K_i to K_o and therefore to a certain membrane potential), K is artificially increased, the expected result would be an increase in the slope of phase 2 and decrease in the slope of phase 3.

"... The hypothesis that the change in potential which occurs in phase 2 of the recovery process is analogous to the depolarization observed during diastole in a pacemaker cell, and that the change in phase 3 is an active regenerative repolarization which begins when a certain level of membrane potential is reached, is a very attractive one. On the basis of such a hypothesis a change in the duration of the ac-

PACEMAKER CELL

purkinje fiber

NORMAL

HYPERPOTASSEMIA

M.A.P.

DIASTOLIC

DEPOLARIZATION

INSIDE

OUTSIDE

CELL

CELL

K^+

FIGURE 5: "Pacemaker" cells in cases of normal and elevated serum potassium. In hyperpotassemia, compared with the normal, the diastolic depolarization potential is decreased, depicted by a shorter arrow at the beginning of diastole. In hyperpotassemia, potassium is ejected from the cell at a more constant rate thereby prolonging the diastolic depolarization time.
EFFECT OF POTASSIUM ON THE ELECTROCARDIOGRAM

Figure 6: A case of hyperpotassemia and hypercalcemia.

There is a rough correlation between extracellular K+ and the electrocardiogram. It is to be noted that the transmembrane action potential resulting in the electrocardiogram is determined by the ratio of extracellular K+ to the transmembrane action potential.

Figure 7: "Pacemaker" cells in cases of normal and decreased serum potassium. In hypopotassemia the egress of potassium from the cells is decreased, thereby decreasing the diastolic depolarization time.
[K+] = 30

This means that a small change
in the denominator, [K+]", has a marked
effect on the transmembrane potential and
hence, is best correlated with the changes in
the electrocardiogram. The imperfect cor-
relation between the extracellular potassium
and the electrocardiogram may be the
result of the heart's variant susceptibility
to its total chemical environment of which
potassium is only a component, although a
major one.17

An approximate correlation between
serum K+ and the electrocardiogram in
hyperkalemia may be described thusly:18

Serum K (mEq/L)

5.5 - 6.6

Tall, narrow, and
peaked T waves typi-
cally occur in the hori-
Zental plane (precordial
leads) with little change
in vector direction so that the T wave
remains inverted in V1.19 Since comparable
T waves occur in many
states besides hyper-
kalemia, such as brady-
cardia, left ventricular
diastolic overload pattern,
subendocardial ischemia,
hyperthyroidism, normal athletes
especially after exercise, etc., the diagnosis
of hyperkalemia is strengthened by the
presence of a terminal conduction defect,
producing an S wave in leads 1 and V-6.
The ST segment may become elevated and
indistinguishable from the ST segment of
injury as seen in myocardial infarction or
pericarditis (see pseudoinfarction section).

6.7 - 6.9

The QRS widening
includes the initial R
wave. This finding
distinguishes it from RBBB
in which the slur ri
of the QRS is usu-
ally in the terminal portion and from LBBB
in which the middle portion of the QRS
is often predominantly slurred.

Furth er de-
crease in conduc-
tion produces a
first and second
degree A-V block
and a low, wide
P wave.

Atrial arrest is
sometimes associ-
ated with an ir-
regular rate mim-
ick ing atrial fi-
brillation.

The QRS
widening is so
bizarre that
QRS and T
may not be
separated.
This stage of-
ten heralds
the onset of ventricular fibrillation or asys-
tole.

Impulse Formation in Hyperpotassemia

As previously stated, the normal diastolic
depolarization current is due to progres-
sive decreased ejection of potassium from
the cell (Fig. 5). Since hyperpotassemia
causes an increased ejection of potassium
from the cell, the slope of the diastolic de-
pol arization current decreases (Fig. 5). In
fact, in terms of its electrical characteristic,
an automatic cell can virtually be converted
into a ventricular muscle cell. This is ex-
emplified by the early occurrence of atrial
arrest in hyperpotassemia. Furthermore, it
is important to note that as the diastolic
depolarization current slope decreases, the
rate of firing of an automatic cell is also
decreased. A correlate of this concept is
that tachycardia is rarely seen in cases of
hyperpotassemia; usually a normal rate or
possibly bradycardia exists.

Figure 6 illustrates the ECG changes
seen in a clinical case of a 74-year-old
white man who had carcinoma of the blad-
der for four years treated with fulguration
and radiation. A few days prior to this
electrocardiogram, the patient showed signs
and laboratory determinations consistent with a urinary tract obstruction. On the day this electrocardiogram was taken, the following laboratory findings were reported: potassium 7.4 mEq/L; calcium 12 mg per cent; \( CO_2 \) 23 mEq/L; albumin 2.2 gm per cent; globulin 3.8 gm per cent; creatinine 6.5 mg per cent; phosphorus 7 mg per cent; pH 7.46; magnesium 2.95 mg per cent; (1.7-2.7 mg per cent). The patient expired two days later. Necropsy revealed a normal heart.

This electrocardiogram demonstrates the classic changes of hyperpotassemia and hypercalcemia.

**The QRS Changes**

The QRS is slightly broadened with the terminal vectors directed to the right, posterior, and superior; note that S waves are present in V-2, V-6 and aVF. As the serum potassium level increases the initial QRS vector forces are also increased in duration and changed in direction, simulating at times myocardial infarction. Note in this case that the Q waves present in standard leads 2, 3 and aVF are approximately .02 to .03 seconds in duration. Since hyperpotassemia decreases the rate of ventricular depolarization, the prolonged QRS complex would be expected to terminate rightward, posterior and superior. Interestingly enough, this is the location of the last portion of the heart to be depolarized normally — the crista supraventricularis and the basal portion of the heart.

**T Wave Changes**

The T wave changes of hyperpotassemia, that is, the presence of tall peaked T waves over the precordium, mimic the electrocardiographic changes in myocardial ischemia, sinus bradycardia, diastolic overload of the left ventricle and etc. However, hyperpotassemia has the following changes not usually present in the above: 1) narrow-based T wave; 2) no change in the T wave axis in the horizontal plane, note in this case the flattened T wave in V-1; 3) presence of an S wave in V-6; 4) absence of U waves; U waves are rarely present in hyperpotassemia, frequently present in sinus bradycardia, myocardial ischemia and diastolic overload of left ventricle.

It should be pointed out that potassium transport across the cell membrane is one of the major determinants for the inscription of the T wave. Therefore, at times, the above differential diagnosis is difficult to make electrocardiographically.

**The ST Segment and QT Interval**

In this case, the corrected QT interval and ST segment are shortened. The specific shortening of the ST segment is classic and almost pathognomonic for hypercalcemia. However, digitalis also shortens the ST segment. Usually, digitalis displays the classic sagging of the ST segment with an ST segment vector directed to the right. From basic experimental studies, hyperpotassemia also shortens the ST segment and QT interval. However, from a practical clinical standpoint, this slight shortening is not readily seen in a single electrocardiogram.

Little experimental work has been done with ECG changes in hypermagnesemia. However, the data indicates that all electrocardiographic changes present in hyperpotassemia qualitatively but to a lesser extent quantitatively can be produced by hypermagnesemia.

The interesting electrocardiographic clinical point in this case is that hyperpotassemia is usually associated with chronic renal disease which lowers the serum calcium and prolongs the ST segment. The presence of a shortened QT interval and ST segment and the electrocardiographic changes of hyperpotassemia decrease the differential diagnostic possibilities.

**Hypopotassemia**

**Membrane Resting Potential**

(External Diastole)

According to the Nernst equation, a decreased concentration of extracellular potassium results in an increase in the membrane resting potential which is called hyperpolarization (Fig. 2C). However, the transmembrane resting potential does not in-
crease to the extent calculated by the Nernst equation. This observation may be attributed to an extracellular leak of potassium that would be expected to occur after a period of hypokalemia. Consequently the extra-to-intracellular ratio of potassium returns to normal.

Membrane Action Potential (Electrical Systole)

Phase 0. The voltage of the action potential is usually increased resulting in an increase of QRS amplitude (Fig. 2C). Occasionally, the upstroke velocity is increased shortening the duration of this phase. Uncommonly, the QRS is widened; this is explained by hyperpolarization which delays conduction and overcomes the small increase in upstroke velocity.

Phase 1 is not appreciably changed.

Phase 2 is shortened in duration and increased in slope. This is reflected in a shortened ST segment. Since the action potential is greater, this phase may be more positive, manifested by an ST segment depression. Contrary to the Nernst equation, potassium permeability during systole is inversely proportional to the electrochemical driving force. From the practical standpoint, as a first approximation, the rate of potassium efflux during systole is proportional to the serum potassium concentration (see section on Correlation between Serum Levels in Hypokalemia and the Electrocardiogram). Therefore, in hypokalemia one would produce a more positive phase 2 (Fig. 2C). In summary, for reasons unknown, the decreased $K_+^+$ causes a decreased efflux of potassium from the cell ($K_+^+\rightarrow K_0^+$) maintaining a more positive intracellular charge and therefore a negative extracellular charge and ST segment depression. Prinzmetal and colleagues state that hyperpolarization of the MRP is another reason for the depressed ST segment (see section on Mild Myocardial Ischemia and Hypokalemia).

Phase 3 has a decreased slope which may be due to a diminished rate of potassium efflux as explained in phase 2. Sodium influx is not significantly changed. These events result in a broad, flattened T wave.

Phase 4 is a diastolic period characterized by a slow return of the action potential to the MRP level. A U wave is produced juxtaposed to the T wave. In summary, the less than normal efflux of potassium in phases 2, 3 and 4 is represented in Fig. 2C by smaller arrows than the normal in Fig. 2A.

Correlation between Serum Levels in Hypokalemia and the ECG

Surawicz and associates have written an excellent paper on this theme. If the ECG reflects the changes in the transmembrane potential, a correlation should exist between the ECG and intra-and extra-cellular potassium ratio. Since, as previously mentioned in this report, there is a 30/1 ratio between $K_+^+$ and $K_0^+$ concentration, a slight change in $K_0^+$ should produce a marked change in this ratio. An alteration of serum potassium concentration from 4.0 to 2.0 mEq/L corresponds to a decrease of 50 per cent. Such a profound decrease of myocardial cell potassium has not been published. In cats, one of the lowest reported myocardial potassium levels has been 15 per cent of normal. In rats subjected to potassium depletion, only minimal changes in myocardial potassium result. Isolated turtle hearts perfused with solutions containing low and high potassium concentration show little effect on the intracellular potassium concentration. Hence, both theoretically and experimentally, the potassium gradient of the myocardial cell membrane is largely determined by the extracellular potassium. Soloff and co-workers found a better correlation between the ECG and the intracellular potassium rather than the extracellular potassium. However, they used the potassium of the red blood corpuscle as an index of myocardial cell potassium. The relationship between the RBC and the intracellular myocardial potassium deserves more study.

An approximate correlation between the ECG and the serum potassium in hypokalemia is described as follows:
EFFECT OF POTASSIUM ON THE ELECTROCARDIOGRAM

Serum K (mEq/L)

3.0 - 3.5

The T wave is slightly flattened and broadened and a U wave appears. These changes are seen earliest in the horizontal plane, especially in lead V-3. There is prolongation of the corrected Q-U interval. The Q-T interval is normal but if prolonged other diagnoses must be considered, such as myocardial ischemia, hypocalcemia, etc.

2.7 - 2.9

Further flattening of the T wave occurs and the U wave becomes taller than the T wave. The U/T ratio becomes greater than 1.

2.6 - 2.0

ST segment depression occurs resembling an injury current.

There is no direct correlation between the T wave, the U/T ratio and the serum potassium level until the amplitude of T wave falls below 1 mm. This is best noted in the precordial leads with the highest U wave. Left ventricular hypertrophy often produces U waves and depressed ST segments in the left precordial leads. In the presence of both left ventricular hypertrophy and hypokalemia, the ST segment becomes depressed in leads V1-V3. Although the amplitude of both the P wave and QRS increases slightly in hypokalemia, these changes cannot be used diagnostically. After the administration of potassium chloride, the P and QRS amplitude decrease. However, Surawicz points out that a similar decrease occurred after the infusion of saline.

Impulse Formation in Hypokalemia

Hypokalemia decreases the efflux of potassium from the cell thereby increasing the slope of the diastolic depolarization potential (Fig. 7). Consequently, the diastolic time decreases and the heart rate increases. In the presence of hypokalemia, this increased rate of depolarization of automatic cells may be one of the mechanisms for the existence of multiple atrial and ventricular premature contractions and paroxysmal atrial tachycardias which have been observed in cases of hypokalemia (see section on Arrhythmias and Hypokalemia).

Arrhythmias and Hypokalemia

In the isolated rabbit's heart, a decreasing concentration of potassium in the perfusate produced premature systoles followed by coupling and ectopic tachycardias. The appearance of partial or complete A-V block were premonitory to terminal ventricular fibrillation. Repolarization is a period of partial polarization and hyperex-

Figure 8: A case of severe hypokalemia.
citability called the vulnerable period. Since hypokalemia prolongs repolarization, a longer period of hyperexcitability exists and may be one of the mechanisms responsible for ectopic arrhythmias (see section on Impulse Formation and Hypokalemia).

In the presence of hypokalemia, but in the absence of digitalis, arrhythmias have been produced by hemodialysis.\textsuperscript{19} Rubin\textsuperscript{19} described atrial and nodal tachycardias and ventricular premature contractions in four patients not receiving digitalis. Del Greco and Grumer\textsuperscript{9} reported one instance of paroxysmal atrial tachycardia in a non-digitalized patient. Castleman et al\textsuperscript{15} described in a non-digitalized patient the occurrence of atrial fibrillation during dialysis. However, decreasing the flow rate of the pump terminated the atrial fibrillation; therefore, they did not attribute the arrhythmia to electrolyte changes. Ectopic arrhythmias produced solely by hypokalemia have theoretical and experimental validity but the clinical evidence is inconclusive.

\textit{Mild Myocardial Ischemia and Hypokalemia}

Prinzmetal and co-workers\textsuperscript{20} have recorded transmembrane potentials in the dog's heart after blood withdrawal. ST segment depressions were obtained from islands of "mild" myocardial ischemia. From this ischemic area, the potassium content of the venous blood was less than arterial blood suggesting an increase of intracellular potassium. The sodium concentration was generally higher suggesting a decrease of intracellular sodium. These investigators state: "The increased uptake of K\textsuperscript{+} by the mildly ischemic cells may be explained theoretically as follows: in normal cells, energy is supplied chiefly by aerobic breakdown of glycogen cells for an increase in cellular uptake of glucose. Since glucose has an affinity for K\textsuperscript{+}, it carries K\textsuperscript{+} with it into the cell. Thus, the transmembrane ionic concentration gradient of K\textsuperscript{+} increases. This may well result in a state of hyperpolarization by increasing the electrical charges on the membranes of the mildly ischemic cells." In their data, the action potential shows, for example, an increased MRP from a control of minus 89 mv to minus 98 mv. Phases 1 and 2 are higher than normal (Fig. 2C). The typical ST segment depression of mild coronary artery ischemia in the dog is similar to that seen in the human with clinical angina.

Hence, these investigators believe that the ST segment depression in mild ischemia is caused by a decrease in extracellular and an increase in intracellular potassium. In further support of their concept, they demonstrated a disappearance of the ST segment depression after perfusion of the mildly ischemic area with high potassium solution.

Figure 3 illustrates a clinical case of severe hypokalemia mimicking mild myocardial ischemia as described above. This tracing is that of a 33-year-old white woman hospitalized for severe depression and inanition. The serum potassium was 1.8 mEq/L (Fig. 3A). Note the profound horizontal ST segment depressions in almost all leads. One hour after fairly rapid intravenous infusion of 40 mEq/L of potassium, the tracing (Fig. 3B) showed much less ST segment depression. The electrocardiograms taken the following day were normal. This tracing highlights the need for knowledge concerning the electrolyte concentration of the patient before interpreting the electrocardiogram. Kwocynski et al\textsuperscript{21} have recently reviewed the many different clinical conditions which cause electrocardiographic ischemic patterns in the absence of coronary artery disease.

\textit{Pseudo-Infarction Pattern}

Nora and Pelz\textsuperscript{22} have published electrocardiograms characteristic of myocardial infarction associated with hyperkalemia. Two of their cases demonstrated typical ECG changes of acute anterior myocardial infarction. A normal heart was present at one necropsy, while in the other case abnormal Q waves and ST-T segments disappeared after the blood potassium re-
turned to normal. Castleman and associates have reported cases consistent with the report of Nora and Pelz. The electrocardiograms showed acute anterolateral myocardial infarction associated with hyperkalemia. The abnormal Q waves disappeared after the serum potassium was lowered by hemodialysis. Myocardial infarction was not evident at necropsy. Abnormal Q waves associated with myocardial infarction are the result of changes in the initial portion of the QRS complex. In terms of the action potential, these changes are explained by the decreased slope of phase 0 and a decreased rate of ventricular depolarization resulting from hyperkalemia.

Levine et al have reported ST segment changes characteristic of injury currents. The electrocardiograms suggest the diagnosis of myocardial infarction or pericarditis. These ST segment alterations returned to normal after removal of excess potassium by hemodialysis. Other authors have described similar changes.

With regard to elucidating the cause of these curious ST segment changes, basic experiments were performed in dogs by Prinzmetal et al. They found that ST segment elevation represents a more severe type of myocardial ischemia than does ST segment depression. Furthermore, severe ischemia produced by ligating a major coronary artery alters the integrity of the cell membrane. Hence, intracellular potassium leaves the cell decreasing the transmembrane ionic gradient and, in turn, the resting membrane potential (Fig. 2B). When the ischemic area is connected to an indifferent electrode, a diastolic injury current exists with T-P depression in the electrocardiogram. The T-P depression is reflected in the electrocardiogram by a relative ST segment elevation. Furthermore, during systole hyperkalemia causes an increased impermeability of the cell membrane to potassium (see section on Hyperkalemia). The loss of intracellular potassium causes a rapidly decreasing negative intracellular charge, thereby increasing the negativity of phase 2 which leads to further ST segment elevation—a systolic current of injury.

An interesting “therapeutic” application of the foregoing concept is the use of “polarizing” solution containing potassium, glucose and insulin published by Sodi-Pallares and co-workers. This solution attempts to return to normal the loss of intracellular potassium which occurs in acute myocardial infarction. Sodi-Pallares and co-workers have demonstrated that this solution abolishes the ST segment elevation of injury in both animals and man.

**Summary**

This review has attempted to synthesize contemporary knowledge regarding potassium and the ECG. We have stressed information obtained from the transmembrane resting and action potential correlating it with ionic gradients during the four phases of the single cardiac cycle. Alterations in these events occurring during the normal, hyperkalemic and hypokalemic states have been discussed. Information regarding this subject has been culled from the procedure of hemodialysis, and measurements of MRP, MAP and arteriovenous electrolyte concentrations in mild and severe ischemic states in the dog. The relationship between serum potassium abnormalities and the ECG of arrhythmias, myocardial infarction and myocardial ischemia is discussed.

**Acknowledgement:** Figure 1 is reproduced from Hoffman and Cranefield with the permission of Dr. B. F. Hoffman to whom we express our appreciative thanks. We are also grateful to Dr. E. Bajusz for permission to use data previously published in his book, *Electrolytes and Heart Disease*, S. Karger, Basle.

**Resumen**

En esta revisión intentamos sintetizar los conocimientos actuales relativos al potasio y el electrocardiograma (ECG). Destacamos las comprensiones obtenidas del potencial transmembranoso durante la actividad y el reposo, correlacionado con el gradiente iónico durante las cuatro fases del ciclo cardiaco. Analizamos las variaciones en estos fenómenos observadas en estados hipokálicos y normales. Los datos informativos sobre la materia han sido obtenidos mediante la hemólisis, valoración del MRP y MAP y concentración de electrolitos arteriovenosos en
estados isquémicos leves y graves, inducidos experimentalmente en el perro.

**Resumé**


**Zusammenfassung**

Diese Übersicht hat den Versuch unternommen, die gegenwärtigen Kenntnisse hinsichtlich des Kaliums und des EKGs zu synthetisieren.


*Complete reference list will appear in the reprints.*

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**Transient Pulmonary Densities Around Retained Iodized Oil**

Ten cases of transient densities around retained iodized oil are reported. In four, these occurred five to 14 days, in the other six, four to 35 months, after bronchography. The incidence was approximately one in 400 patients who underwent intra-tracheal instillation of iodized oil, but it may in fact be higher. A fever of short duration accompanied the condition in seven patients. None of the patients appeared to be very ill. Some of the patients had previously suffered from an allergic condition. Corticosteroid therapy appeared to have a beneficial effect.

In lung tissue removed at operation nine days to three weeks after the lesions had been visible on radiographs, in three cases no signs of massive infiltration were found. In one of these, iodized oil granulomata were present, but this was probably a different type of reaction to residual iodized oil.

**Bacterial Endocarditis After Insertion of Valvular Prosthesis**

A case of rheumatic heart disease of the double mitral lesion type is presented. The patient was operated under extracorporeal circulation with the disc oxygenator for the implant of a No. 4 Starr-Edwards valve. Postoperatively, subacute bacterial endocarditis complicated the course and the patient became severely ill. Twenty-five days after the operation, it was decided to reoperate. The valve was removed. It was covered with villous material which was cultured and grew coagulase positive *Staphylococcus aureus*. A new valve was implanted. The patient died 52 days after the second operation with acute pulmonary edema.

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