Observations on D. C. and Very Low Frequency Components of the Electrocardiogram. (31397)

WALDEMAR J. WAJSZCZUK* AND JÓZEF K. CYWINSKI (Introduced by Ulrich C. Luft)
IVth Department of Internal Medicine, Medical Academy, Warsaw, Poland

The purpose of this report is to describe the recording of direct current and very low frequency components of the electrocardiographic curve and to emphasize the significance of such measurements. Our studies on this subject resulted in the development of a technique which permitted recording relative shifts of the slow segments of the electrocardiogram, *i.e.*, T-Q (also called base-line) and S-T segments or J point and their quantitative measurements(1).

It has been suspected(2) that not everything that appears as S-T segment elevation or depression is a true elevation or depression as measured in absolute voltage values from the base-line, usually assumed to be the zero potential line, of the recording. A concept of true base-line voltage changes and their theoretical explanation has been offered(3). This concept was supported with results of biochemical studies on myocardial cells(4). Further experimental studies supplied data for the formulation of a theory explaining the causes of relative shifts of the segments of the electrocardiogram(5,6). Support and correlation with the resting and action transmembrane potentials of the myocardial cells was supplied(7). The need for studies of low frequency components of electrocardiograms has been again pointed out recently(8).

Materials and methods. The preliminary studies reported here served primarily to work out a suitable and simple method which would permit recording and measuring the direct current and very low frequency component of the electrocardiogram quantitatively. The second purpose of these studies was to assess the sensitivity of the method in various experimental situations involving electrolyte imbalance in the hearts under study. The recordings were performed upon the exposed canine and rabbit hearts *in situ* in normal conditions, under the influence of ischemia and local application of 5% KCl and NaCl on the epicardium as well as intramyocardially, and after mechanical injury of the heart under the electrode. The electrodes used were commercially available laboratory type calomel electrodes. In order to avoid their movement over the epicardium the electrodes were connected to the heart surface by cotton threads soaked in Ringer's solution and sutured subepicardially. The recording and reference electrodes were identical. It appeared extremely important that the neutral, grounding electrodes of the system be exactly the same type of electrodes as used for the recordings. The introduction of any other electrodes, particularly of the polarizing type, caused a battery effect in the circuit between the calomel electrodes and the others (even when using bipolar leads between 2 calomel electrodes) and produced a drift in the recording. It was also necessary to disconnect all other metal recording electrodes and to avoid any other contact between the preparation and grounded equipment, since all these conditions can cause false drifts in the tracing. Only if all these precautions are observed can the segmental shifts be accepted as originating in the heart.

The zero-voltage reference line was obtained by short-circuiting the two recording calomel electrodes. This was done every few minutes during the experiments to check for drift during normal conditions and induced segmental shifts were measured from this level which is indicated as an interrupted line in the illustrations.

When electrolytes were applied to the heart the zero-voltage reference line did not change even in the presence of major shifts in the segments of the electrocardiogram, nor when 2 electrodes of the bipolar lead arrangement were immersed each in a different concentration of the same electrolyte or in solutions of different electrolytes (*i.e.*, KCl and

* Present address: Dept. of Physiology, Lovelace Foundation for Medical Education and Research, Albuquerque, N. M.

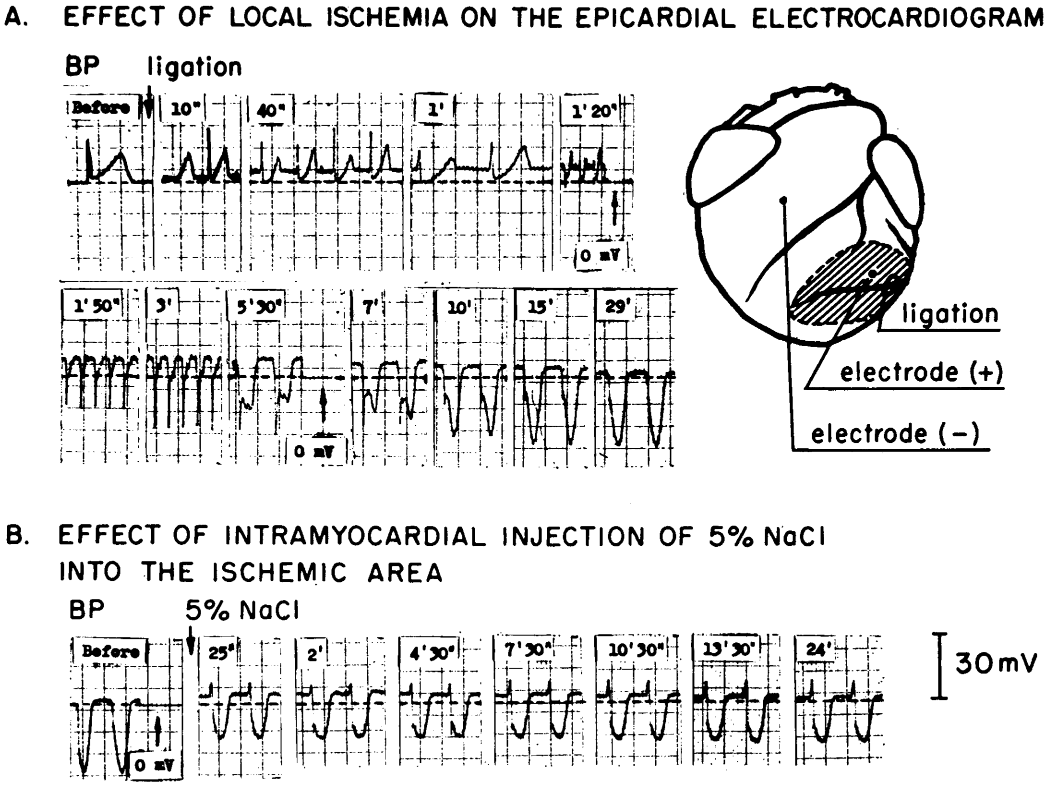

FIG. 1. Effect of local ischemia and subsequent intramyocardial injection of 5% NaCl on epicardial electrocardiogram recorded from bipolar lead. Localization of electrodes and area of ischemia are indicated on drawing of the heart. Note reappearance of R deflection after injection of NaCl. Zero-voltage reference line is indicated in this and following illustrations as a dashed line and arrows with 0 mV description. Paper speed—10, 25, 50 mm/sec.

NaCl). On the other hand, a flow of current was observed in the above-mentioned tests when the circuit was closed through the various electrolytes and the voltage could be measured between the recorded line and the zero-voltage reference line. Drift of the latter was negligible over experimental periods of up to 2 hours.

Epicardial electrocardiograms were recorded in a bipolar (BP) electrode arrangement in which both active electrodes were placed on the epicardium and the reference electrode under the skin on the leg of the animal (Fig. 1).

In another electrode arrangement, which we call unipolar (UP), one of the 2 electrodes was grounded and the electrocardiograms obtained in this manner were designated as UP-LV (unipolar from the left ventricle, when the electrode on the right ventricle was grounded) and UP-RV (with the electrode on the left ventricle grounded).

S-T segment and J point are defined according to accepted electrocardiographic criteria. In the absence of P waves in our recordings the T-Q segment is that part of the tracing immediately preceding the QRS complex, commonly referred to as the baseline. Shifts of both S-T and T-Q segments were measured in negative or positive voltage values from the zero-voltage reference line as defined above.

The recording system included a SIEMENS' Cardirex 7 electrocardiograph to which a high input impedance cathode follower was added to match the electrode circuit resistance of about 1 megohm. This arrangement was also free of drift.

Results. The recordings obtained from the epicardium of rabbits and dogs under normal

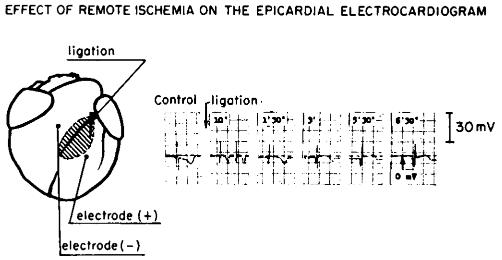

FIG. 2. Effect of ischemia of the portion of heart muscle between the electrodes on the epicardial electrocardiogram recorded in bipolar lead. Paper speed —25, 50 mm/sec.

conditions did not reveal any significant displacement of the T-Q, S-T segment or J point.

Local ischemia produced by ligation of a branch of a coronary artery (Fig. 1) produced elevation of the T-Q segment and depression of the J point with development of negative T wave and complete disappearance of the R deflection. Maximal elevation of the T-Q segment appeared between 3 and 5 minutes following the ligation and was in the range of about +10 mV. The maximal depression of the J point was delayed and was in the range of —8 to —10 mV. This type of change in which the recording positive electrode was near the center of the ischemic field is illustrated in Fig. 1.

It was also noticed that local injection of 5% NaCl solution in the ischemic area produced a positive shift of the T-Q segment of +2 mV to +3 mV similar to that observed after epicardial application of this solution. Simultaneously a decrease of the negative potential values of the J point and a reappearance of the R deflection of the electrocardiogram developed (Fig. 1).

Relatively little displacement of the T-Q and S-T segments was noticed when the electrodes were placed symmetrically on opposite sides of the small area of ischemia. A small shift concerned mainly the T-Q segment and was in the range of —2 to —3 mV. Perhaps in this arrangement the effect of ischemia on both electrodes was of opposite sign and was cancelled (Fig. 2).

Local application of Ringer's solution at room temperature (22°C) in the area of the positive electrode produced a small positive displacement of the J point of the electrocardiogram in the range +2 to +4 mV and an increase of the magnitude of the T wave. The application of the same Ringer's solution at body temperature caused return of the J point to normal and transient decrease of the magnitude of the T wave. Because of the observed temperature effect other electrolyte solutions were applied at body temperature in subsequent experiments. Application of the warmed Ringer's solution (about 37°C) to the area previously influenced by application of other electrolytes in high concentration produced normalization of the tracing.

Local application of the 5% KCl solution produced immediate positive shift of the T-Q segment and a delayed and smaller negative shift of the J point which was shorter lasting (Fig. 3). Maximal shift of the T-Q segment appeared after about 2 minutes and was in the range of +15 to +20 mV. The maximum negative shift of the J point developed between one and two minutes and was in the range of —5 to —6 mV, and relatively fast return to normal followed.

Local application of 5% NaCl solution produced a positive shift of the T-Q segment (Fig. 3). The maximum shift was in the range of +4 to +7 mV and was reached after a few seconds. The accompanying S-T segment shift was in the opposite direction

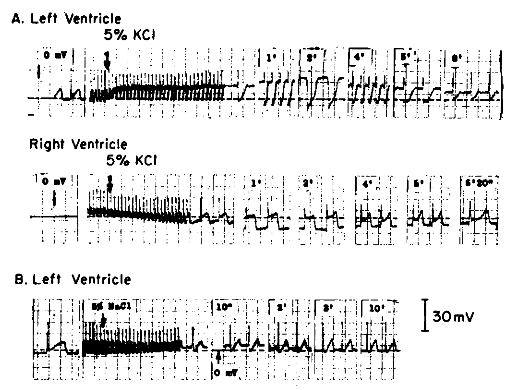

FIG. 3. Effect of application of 5% KCl and 5% NaCl solutions on epicardial electrocardiograms. Electrolytes were applied epicardially in the area of the electrode on left ventricle or in the area of the electrode on right ventricle. Electrocardiograms were recorded in bipolar leads with unchanged location of electrodes. Note difference in direction of shifts of segments and of their magnitude despite the same amount of 5% KCl applied to both ventricles. Paper speed—5, 10, 25, 50 mm/sec.

TABLE I. Changes in the Potential of the Base-Line and S-T Segment (J Point) of the BP Electrocardiogram Recorded from the Epicardium Under the Influence of Various Factors (Acting on the Left Ventricle).

	Base-line	S-T (J)	R
1. Local ischemia: a—central portion	↑ ++	↓+++	(—)
b—peripheral portion	↓	—	(+)
2. 5% KCl—on epicardium	↑++++	↓ ++	(—)
3. 5% NaCl—on epicardium	↑ +	—	(+)
4. 5% NaCl—intramyocardially	↑ +(R)	—(↓)	(+)
5. Injury with extravasation of blood	↓ ++	↑ ++	(+)

Arrows indicate direction of the shift of the base-line and S-T segment (J point); number of plus signs indicate the magnitude of shift. In the column "R" are indicated changes in the R deflection of the electrocardiogram; it disappears in 1a and 2, is vestigial in 5, reappears in 4, and is unchanged (+) in others.

and was relatively small.

The relative directions of shift of the T-Q and S-T segments and their magnitudes under various experimental conditions are summarized in Table I.

The shifts of the segments of the electrocardiograms described above followed changes of environment in the area of the positive recording electrode in the bipolar arrangement of the electrodes. It was observed that the same factors applied in the area of the negative electrode located on the right ventricle produced a similar influence on the electrocardiographic recordings, but the shifts were of opposite sign. In addition the voltage readings of the segmental shifts were 1/2 to 1/3 smaller than those recorded during the application of agents to the left ventricle. These differences are illustrated in Fig. 3.

Another interesting observation was made while comparing the BP leads and UP leads in local ischemia (Fig. 4).

Recordings taken with BP leads revealed an elevation of the T-Q segment in the range of +4 mV. Unipolar recordings taken from the left ventricle showed the elevation of the same segment of +1 to +2 mV only, while unipolar recordings taken from the right ventricle showed a marked positive shift of the T-Q segment ranging up to +12 mV. A similar shift of the J point was also noticed. The difference of the voltage of the T-Q segment between the recording from the left and from the right ventricle amounted to 10 millivolts indicating the higher potential level of the base-line (T-Q) segment of the recording over the right ventricle when compared with that over the injured portion of the left ventricle.

Discussion. It has been demonstrated in these experiments that using an appropriate electrode arrangement, certain displacements of the S-T segments, the J point and of the T-Q segment resulting from ischemia or local disturbances of the normal electrolyte balance can be measured with sufficient accuracy directly from the epicardium. Direction and magnitude of these changes depend upon the nature and extent of the lesion. It has been emphasized by various authors(5,7,9,11) that marked differences exist between recordings taken during severe ischemia of the myocardium or from the necrotic center of an ischemic area on the one hand and during mild ischemia or from the borders of an ischemic area on the other. The changes affecting the S-T and T-Q segments are opposite and are described as a depression of

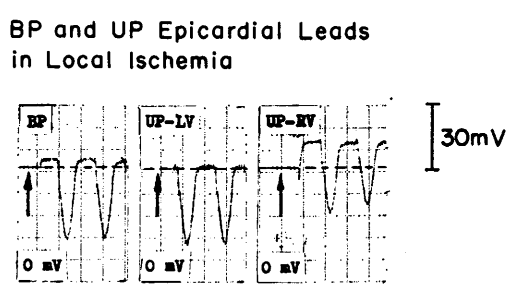

FIG. 4. Difference in voltage of T-Q segment shifts of epicardial electrocardiogram recorded with bipolar lead between 2 electrodes located on left and right ventricle and of electrocardiograms recorded with unipolar leads with the same electrodes (on left ventricle—UP-LV; on right ventricle—UP-RV). Paper speed—25 mm/sec.

the T-Q segment with elevation of the S-T segment in severe ischemia (5,7,9,11) and an elevation of T-Q with depression of S-T segment in the areas of mild ischemia(7,9,11). Measurements with intracellular electrodes revealed a close relationship between the intracellular and epicardial recordings and demonstrated that the acute ischemic state is associated with hypopolarization, while hyperpolarization develops during mild ischemia(7).

Another observation made in our experiments was that the shift of the T-Q segment differed in magnitude over different areas of the heart muscle when the same experimental conditions were applied (Fig. 3 and 4). The unipolar lead technique employed here enabled us to measure the difference of the T-Q segment shifts in normal as well as in pathologic conditions, depending upon the localization of the electrode on the heart (Fig. 4). This approach might be useful in attempts to estimate the degree and localization of myocardial hypertrophy, as well as the degree of myocardial damage.

Evidence suggesting that phenomena similar to those described here can be picked up in recordings from standard external electrocardiographic leads has been provided elsewhere (ref. 12, Fig. 2) in experiments in which the intracoronary injection of 60 μg of KCl in dogs produced a striking displacement of both T-Q and S-T segments of the electrocardiogram in Lead III. Differentiation between the relative shifts of the S-T and the T-Q segments (or rather the T-P segments for standard external leads) would be possible under these circumstances if the corresponding zero-voltage reference line were obtained, as in our method. Further correlation of the segmental shifts with the intracellular and extracellular electrolyte concentration, oxygen tension, blood flow and other parameters of myocardial function are needed before the method could be used for clinical-diagnostic purposes.

The application of vectorcardiography for recording of the D. C. and very low frequency components of the electrical field of the heart offers considerable advantages in view of the facility in displaying voltage differences between the starting points of various phases of electrical activity and the zero-voltage point of reference as well as their spatial displacement in relation to it.

As to the choice of leads, the use of precordial ones and even the abandoned technique of bipolar chest leads might contribute to a more precise estimation of the localization and magnitude of myocardial damage or hypertrophy because of their closer relation to the electrical field of the heart and its hypothetical center as compared to the more distant standard peripheral leads.

The importance of drift-free electrodes and recording system for registering the D. C. currents has been emphasized earlier. It has been pointed out elsewhere(6) that this type of recording requires special and expensive equipment. However, recent progress in the field of medical electronics has made available several recorders equipped with D. C. channels which would require little, if any, modification. Laboratory type calomel electrodes can be modified for this purpose, as in this study, but other drift free electrodes† are now commercially available which claim to have the characteristics required for this type of work.

Summary. The authors described an experimental method of measuring the D. C. and very low frequency components of the electrocardiograms, (relative T-Q and S-T segment shifts) using a commercially available clinical model of electrocardiograph and laboratory type calomel electrodes. Several experimental trials included observation of changes in D. C. and very low frequency components of epicardial electrocardiograms under the influence of electrolytes and local ischemia and served primarily the purpose of testing out the sensitivity of the method. The observations served as a basis for discussion of usefulness of this type of ECG analysis for further theoretical studies on the electrical field of the heart and its applicability for more precise clinical diagnosis of the anatomical state of the heart. The problem of recording equipment and nonpolarizing electrodes was discussed briefly.

† Beckman Biopotential Skin Electrodes. Beckman #650900 Tissue Electrodes. Constant Potential Electrodes C-101 and C-102 (Lexington Instrument Corp.).

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Effects of Sodium Removal on Acid Secretion by the Frog Gastric Mucosa.* (31398)

GEORGE SACHS, RICHARD L. SHOEMAKER,† AND BASIL L. HIRSCHOWITZ
Department of Medicine, Division of Gastroenterology, University of Alabama Medical Center, Birmingham

In various studies of ionic requirements of the bathing solutions for H^+ and Cl^- transport in the frog gastric mucosa, K^+ and Ca^{++} have both been shown to be essential for acid secretion(1,2) while Na^+ free solutions have been claimed to support normal secretion in the mucosa(3) and 75% substitution of Na^+ by choline was shown to be without effect(4). The results presented here show that when the intracellular Na^+ concentration is reduced to very low levels, there is significant inhibition of acid and chloride secretion which is reversed by readmission of Na^+ to the nutrient but not to the secretory side.

Methods. *Rana pipiens* gastric mucosa was mounted between 2 lucite chambers as described previously(5). The potential difference (PD) was measured with a pair of calomel electrodes with renewable KCl junctions. Resistance was calculated from the change in PD obtained by sending 10 microamps of current in either direction and short circuit current was determined as the current necessary to reduce the PD to 0 within 30 seconds. Acid secretion was determined using the pH stat method(6) and Cl^{36} tracer fluxes were measured using the Nuclear Chicago liquid scintillation counter in which quench correction was performed using the channels ratio method. The bathing solutions were of the following composition: Nutrient: Na^+ 118 mM, K^+ 4 mM, Ca^{++} 1.7 mM, Mg^{++} 0.8 mM, Cl^- 109 mM, HCO_3^- 18 mM, glucose 10 mM; secretory: Na^+ 105 mM, K^+ 4 mM, Cl^- 109 mM. In the Na^+ free experiments choline was substituted for Na^+ and in the Na^+ and Cl^- free experiments SO_4^{--} was additionally substituted for Cl^-. In all the substitution experiments the membrane was washed 4 times over a period of 5 minutes with the appropriate solutions. The substitutions were carried out either on both sides simultaneously or one side followed by the other. In the experiments where the Na^+ was readmitted, aliquots of the choline nutrient or secretory solutions were withdrawn and replaced with aliquots of the Na^+

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