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Intramyocardial Current Flow in Acute Coronary Occlusion in the Canine Heart

GARY J. ANDERSON, MD, FACC, JOSEPH REISER, PhD, WILLIAM B. GOUGH, PhD, CHARLES C. NYDEGGER, MD

Philadelphia, Pennsylvania

Data from numerous experimental infarction studies indicate that rapid myocardial cell depolarization following ischemia causes the flow of injury currents. These currents were measured in the canine myocardium by monitoring voltage gradients across infarct boundaries using silver chloride plunge electrodes, followed by placement of a 100 Ω resistor between the electrodes and again measuring the voltage gradients. Current flow was calculated from these measurements with the following results: 1) TQ currents developed within 15 seconds after occlusion and persisted for 120 to 150 minutes, often attaining a magnitude of 1 μA. 2) ST currents also developed within 15 seconds and attained 2 to 3 μA within 15 to 30 minutes, then usually subsided to some degree. 3) T currents were biphasic and attained 2 to 5 μA. Initially, current flowed from normal to ischemic myocardium but usually reversed within 30 minutes after occlusion. 4) The current flow was often disproportionate to the voltage gradient between 120 and 180 minutes after occlusion, possibly indicating electrical uncoupling of the infarcting cells from normal cells.

These data indicate that intramyocardial current flow develops early after acute coronary occlusion. These currents may be sufficient to induce reexcitation.

One hundred years ago Burdon-Sanderson and Page (1) showed that injured myocardium was electrically positive relative to the normal myocardium during electrical systole, a phenomenon now known to cause ST segment elevation. Fifty years later, Nahum et al. (2) suggested that this apparent elevation was actually due to baseline (TQ) depression. Subsequent studies by Wolferth et al. (3) and others (4–6) attributed ST and TQ segment shifts to ischemia-induced changes in cellular depolarization and repolarization. These changes cause voltage disparities between ischemic and normal myocardium, resulting in current flow which is seen as the TQ and ST segment changes. Although it was shown (7) that the normal myocardium has disparate repolarization with concomitant current flow, the ischemic process seems to enhance these voltage disparities (5,8–12), thus increasing the driving force for current flow. Under ischemic conditions, systolic and diastolic current flow could reach magnitudes sufficient to induce excitation of cells lying within the pathways of this current (13). Kléber et al. (14) and Janse et al. (15) recorded epicardial voltage maps in isolated pig hearts after coronary occlusion and generated "current maps" by computer analysis. Their data indicate that current densities might exceed 1 $\mu A/mm^3$.

In this paper we describe our methods and results of recording current across an infarct boundary. These data indicate that large currents rapidly develop after acute coronary occlusion and flow across the boundary.

Methods

Surgical procedures. Mongrel dogs weighing 25 to 35 kg were anesthetized with intravenous sodium pentobarbital (30 mg/kg body weight) and respiration was maintained using a Harvard respirator. The heart was exposed through a left lateral thoracotomy and suspended in a pericardial cradle. The left anterior descending coronary artery was dissected free from the epicardial surface distal to the first large diagonal branch. The sinus node was identified and either crushed or injected with formalin. Bipolar stainless steel electrodes were implanted in the atrial muscle and pacing was performed at 120 beats/min. The electrocardiogram and aortic pressure were monitored by conventional means. A Honeywell Visicorder and a Tektronix oscilloscope with Polaroid photography were used for permanent data storage.

Electrode preparation and implantation. The silver-silver chloride electrodes used for voltage and current measurements

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Address for reprints: Gary J. Anderson, MD, Likoff Cardiovascular Institute, Hahnemann University, 230 North Broad Street, Philadelphia, Pennsylvania 19102.

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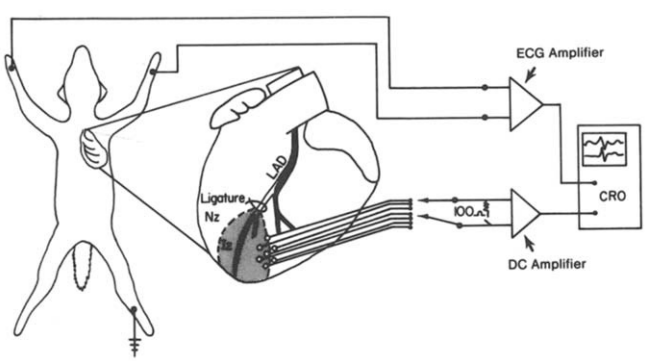
were prepared before surgery from 1 cm pieces of 20 gauge silver wire soldered to braided copper wire. The solder joints were painted and covered with shrink tubing, and silver chloride was applied to the distal 5 mm of each wire. Between 7 and 21 of these electrodes were used in each procedure.

Electrode placement was accomplished by temporarily occluding the exposed left anterior descending coronary artery until a visibly cyanotic area appeared, usually within 30 to 60 seconds. Electrodes were then placed on both sides of the border between cyanotic and normal myocardium 2 to 3 mm from the boundary, and several electrodes were placed along the boundary. The number of electrodes in the three areas depended on the total number used, but at least two electrodes were always placed in the ischemic and normal zones, and at least three in the border zone (Fig. 1). After electrode placement, the ligature was released for at least 30 minutes to allow the ischemic myocardium to return to normal.

Electrical recording. Each electrode was connected by way of the braided copper wire to a switching network that allowed voltage measurements to be made between any two electrodes and permitted a resistor to be connected between the two electrodes while voltage was being monitored. Voltage measurements were made using a differential direct current amplifier and a Tektronix storage oscilloscope.

Myocardial current measurements were made by using a parallel resistance technique in which a 100 Ω resistor was connected between two of the electrodes. This resistance was therefore placed parallel to the myocardium, and the current produced by any myocardial source was divided between the 100 Ω resistor and the myocardium depending on relative resistances. If a resistance equal to myocardial resistance was used for the external shunt resistor, the current flow through the resistor would be exactly equal to the current flow through the myocardium. Myocardial tissue *resistivities* range from 160 to 800 Ω-cm (16,17); myocardial *resistance* depends on the geometry of the tissue through which the current flows, but given an interelectrode distance of 4 to 5 mm the resistance would be approximately 100 Ω. Thus, a 100 Ω resistance was chosen for the shunt resistor. In this analysis we neglected the resistance arising at the electrode-tissue interface, but, by carefully applying the silver-silver chloride layer, we kept this resistance as low as possible. Similarly, electrode polarization could produce baseline errors but measurements were made quickly and the silver-silver chloride layer is quite resistant to polarization. In the normal zone, polarization could be observed as a baseline shift, but this rarely occurred.

Figure 1. Diagrammatic representation of signal acquisition and display. Electrodes were implanted in the wall of the left ventricular normal zone (NZ) and ischemic zone (IZ), as well as in the visual border zone. A switching system was used to select bipolar electrograms and a second switch was used to insert the 100 Ω resistance across the electrodes. CRO = cathode ray oscilloscope; DC = direct current; ECG = electrocardiographic.



Experimental procedure. After the electrodes were placed and an interval of at least 30 minutes had elapsed, injury currents were assessed by measuring ST segment elevation (80 ms after the QRS complex) and TQ segment changes. When these shifts had decreased to baseline, the left anterior descending coronary artery was acutely ligated and measurements begun. Measurements were made between every contiguous pair of electrodes in two steps as follows: 1) A pair of electrodes was connected to the differential amplifier and one cardiac cycle was stored on the oscilloscope (this constituted the voltage recording), and 2) the 100 Ω resistor was switched across the two electrodes and one cardiac cycle was again stored on the oscilloscope. The two tracings were then photographed. These two steps were repeated for every pair of contiguous electrodes, a process that required approximately 5 to 10 seconds per pair. This process was repeated for the duration of the experiment (150 to 300 minutes).

Data analysis. These methods result in a series of Polaroid photographs of each pair of electrodes for the duration of the experiment, from which current flow can be calculated. Current flow is determined from the tracing made with the 100 Ω resistor using the conversion factor (from Ohm's law) of 1 μA = 0.1 mV. Because this method measures extracellular current, which is equal in magnitude but opposite in direction to intracellular current, an inverting amplifier was used. Thus, a positive deflection on the recording signifies an intracellular current flow in the indicated direction.

Data reduction was performed on a Hewlett-Packard calculator (model 9820) and digitizer (model 9864A) from the Polaroid photographs. Data were then graphically displayed on a Hewlett-Packard X-Y plotter (model 9862A).

A total of 29 experiments were conducted, 12 emphasizing TQ current data, 12 emphasizing ST and T wave data and 5 experiments creating TQ and ST segment maps. Mapping was done using 27 to 40 electrode pairs with a 5 mm interelectrode distance. The heart was removed after the experiment and the electrode positions were verified relative to the visible boundary.

Results

TQ current. The development of diastolic (TQ) current across the ischemic boundary was prompt after coronary ligation (Fig. 2A). A shift of TQ current was usually noted within 5 to 10 seconds after ligation and progressive increments were seen through 2 to 15 minutes. In 9 of 12 experiments, near maximal TQ current was attained within the first 2 minutes after occlusion; in the other 3 experiments, the maximal TQ current was attained within 15 minutes.

The initial time course showed rapid development of TQ current in which intracellular flow was from the ischemic zone to the normal zone. This early phase lasted 30 to 60 seconds, after which time TQ current slowly increased fur-

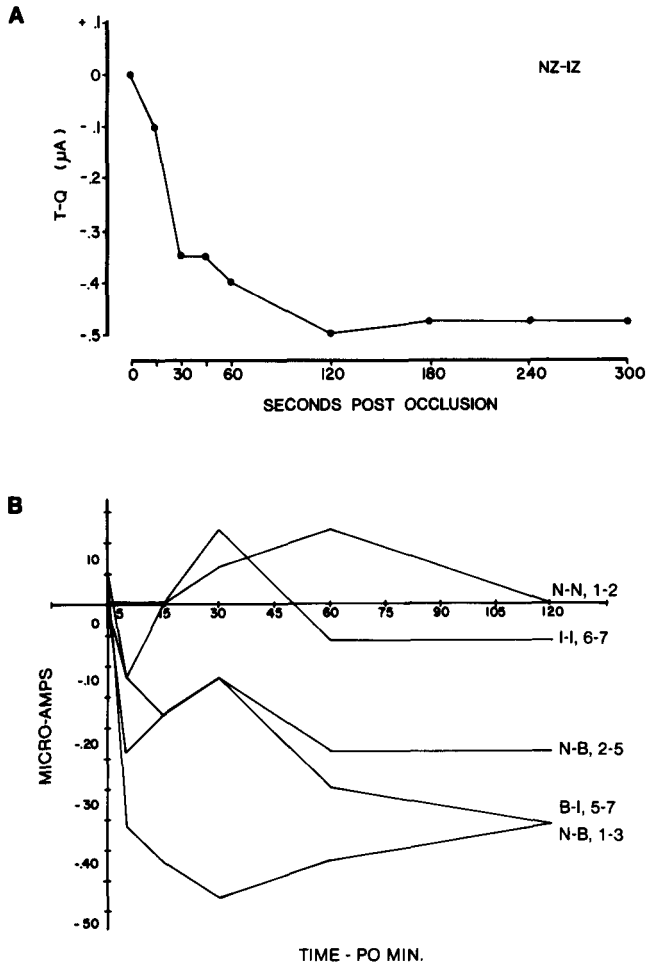


Figure 2. A, Development of TQ current after acute coronary occlusion between electrodes in the normal (NZ) and ischemic (IZ) zones. Within 15 seconds after occlusion, current flow develops between the two zones and attains maximal values by 120 seconds, flowing intracellularly from ischemic to normal zones. **B,** Changes in TQ current over 120 minutes after acute occlusion. Five of 14 recorded pairs are shown. Within 5 minutes, current develops in most recorded leads. Current flow is greatest in those leads with one electrode in the border zone (see electrode pairs N-B/2-5, B-I/5-7, and N-B/1-3), and is less in the ischemic pair (I-I/6-7) and normal pair (N-N/1-2). B = border zone; I = ischemic zone; N = normal zone.

ther or stabilized (Fig. 2B). The responses observed after coronary occlusion in different electrode pairs between ischemic and border zones were usually greater than 1.0 μA and indicated intracellular current flowing to the normal zones. Maximal TQ currents were recorded between electrode pairs in normal and infarct zones (-0.51 ± 0.39 μA; n = 18), between electrodes in border and infarct zones (-0.43 ± 0.44 μA; n = 36) and then between pairs in normal and border zones (-0.22 ± 0.39 μA; n = 36).

ST current. In 12 experiments, ST current was measured employing the electrode configuration shown in Figure 1, where 14 pairs can be obtained. After acute occlusion, a shift in the ST segment appeared within 15 seconds (Fig. 3A). ST segment shifts were not uniform across the visual boundary and showed considerable variation in amplitudes even though electrode pairs were adjacent. A typical example of the time course of ST segment shifts and their respective current recording is shown in Figure 3B. The greatest ST segment currents were observed in electrode pairs bridging the border-normal zones or border-ischemic zones. Although in most experiments ischemic areas showed marked positive ST segment changes indicating intracellular current flow from normal to ischemic zones early after coronary occlusion, there was usually a rapid return of the ST segment toward isoelectric levels with a concomitant reduction in current. The lowest current values were found in the ischemic-ischemic and normal-normal zone electrode pairs.

In 5 of 12 experiments, ST segment alternans developed early (<30 minutes) after occlusion (Fig. 3C); of 168 electrode pairs, 20 electrode pairs in 5 experiments showed ST segment current alternans. Of these 20 electrode pairs, 13 recorded alternans between the border-ischemic zone electrodes or ischemic-ischemic zone electrodes. Alternans was observed in four pairs between a border and normal zone and in three pairs between electrodes within the presumed normal zone. In 3 of the 30 electrode pairs the alternans resulted in a reversal of the current flow so that one cardiac cycle was associated with current flow in the opposite direction to that of the subsequent cycle. This reversal of current flow, when observed, was usually of short duration, lasting 5 to 15 minutes.

Occasionally ST segment elevation occurred before TQ shifts. However, in most experiments the TQ and ST changes had similar time courses.

T currents. Changes in peak T currents were often biphasic and developed an early positivity (<5 minutes) followed by reversal and negativity appearing at 15 to 30 minutes after occlusion (Fig. 4). This biphasic response may not have been recorded in some experiments because the first postocclusion current recording was not completed until 15 minutes after occlusion. When early recordings were made, maximal T currents observed several minutes after occlusion were approximately $+2$ to $+3$ μA. Positive current values indicate intracellular current flow from normal to ischemic zones and negative values indicate intracellular current flow from ischemic to normal or border zones. The highest initial values were recorded in border-normal and border-ischemic zones. When both electrodes were located in the normal zone, T current flow was nearly zero, similar to ST and TQ currents in this zone.

Correlation between electrogram and current values. In all experiments, we plotted the current values obtained with the voltage shifts of the ST segments. During the first 60 minutes after occlusion, the response of the ST current closely paralleled the ST segment bipolar electrograms. However, beyond 60 minutes after occlusion, changes in the voltage electrograms were dissimilar and not pro-

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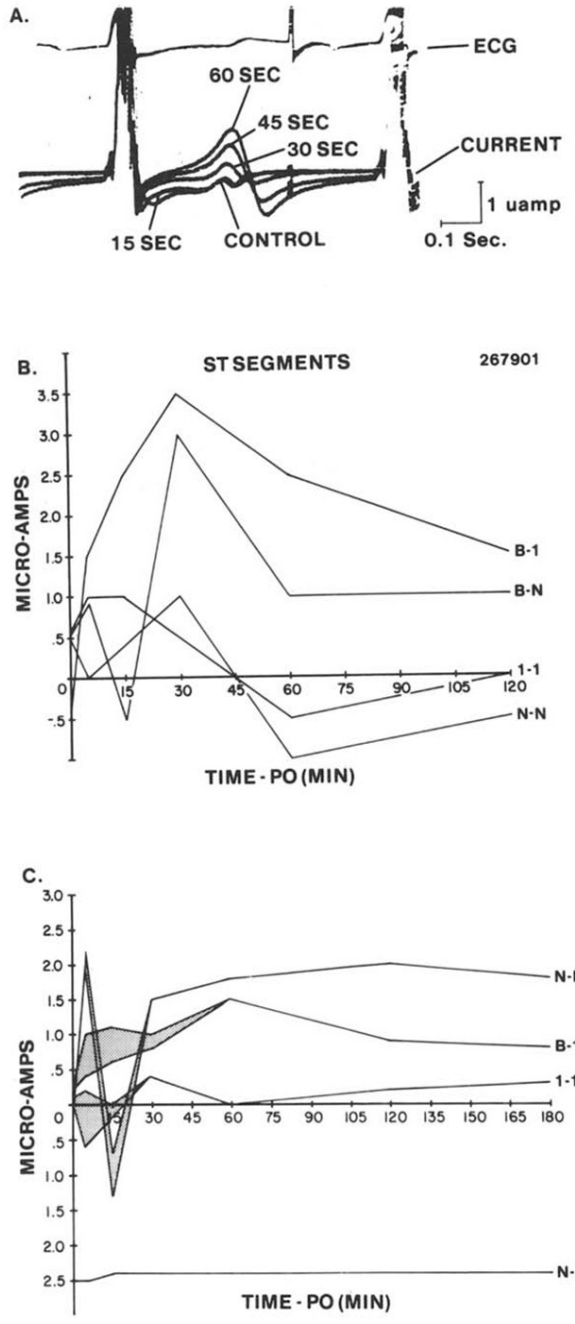

Figure 3. A, ST and TQ current recorded from an electrode between normal and ischemic zones before occlusion and every 15 seconds after occlusion. Although the J point has shifted within 15 seconds after occlusion, the TQ segment is superimposed at 15 and 30 seconds. At the 45 and 60 second recordings, the TQ segment has begun to shift (downward deflection before the second QRS complex). **B,** Time course of ST current in one experiment using four electrode pairs for 120 minutes after acute coronary occlusion. The largest currents were observed in pairs in which one electrode was within the border zone (B-I). Current values were significantly less when both electrodes were in normal zones or ischemic zones. **C,** In this experiment a biphasic response was observed and showed positive current followed by negative current. This reversal of current flow was frequently observed in these pairs. ST alternans (**shaded areas**) was observed in 3 of 19 pairs in this experiment. The development of alternans was prompt (< 5 minutes) and persisted for 60 minutes in one electrode pair (B-I). The border electrode was common to both the normal-border zone pair (N-B) and border-ischemic zone pair (B-I). B = border; ECG = electrocardiogram; I = ischemic; N = normal; PO = postocclusion.

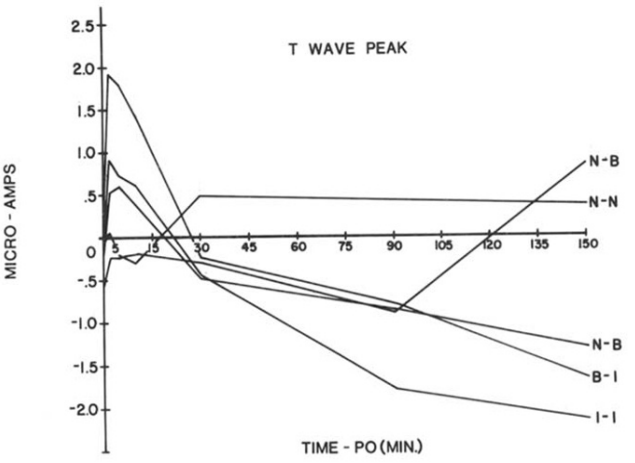

Figure 4. Peak T current after acute coronary occlusion. The earliest noted change was peaking of the T current within 5 minutes after occlusion. A biphasic response usually was noted with reversal of T current by 30 minutes and gradually increasing negative current thereafter (intracellular current from ischemic to normal tissue). One electrode pair (N-B) showed reversal again (not shown) which may have been due to perfusion from a collateral vessel. Abbreviations as in Figure 3.

portional to changes in the recorded current. We also noted that the voltage of the electrogram might decrease even though the current being recorded increased. The response observed in both the electrogram and the current in the normal zone (Fig. 5, upper left) was near parallel and changed little after occlusion. However, in the electrode pair in the normal-border zone (Fig. 5, upper right), the response was nonparallel. In that pair, both voltage and current decreased between 30 and 60 minutes. In contrast, after 60 minutes current increased as voltage further decreased. In the ischemic-ischemic pair of electrodes (Fig. 5, lower right), voltage and current increased during the first 15 minutes after occlusion and then decreased until 60 minutes. From 60 minutes to 120 minutes, voltage increased from 1.2 to 5.9 mV and current increased from -0.4 to $+0.9$ μA, indicating a disproportionately greater increase in current than in voltage. This finding was commonly observed in our experiments and the most consistent finding was that the current recorded after 60 minutes often increased as the bipolar electrogram showed decreasing voltage potential differences. This phenomenon, although often observed at 60 minutes, was greater at 120 minutes and maximal at 180 to 240 minutes.

Isocurrent maps. In the course of plotting ST current, we noted that some regions of the myocardium were consistently current sources (intracellular current flows away from a source toward a sink) and other areas were current sinks. Therefore, we plotted the directions of current flow between electrodes and considered each electrode relative to the sum of the current flow traveling either toward or away from it. One such experiment is illustrated in Figure 6. In the control period the current source is located in the

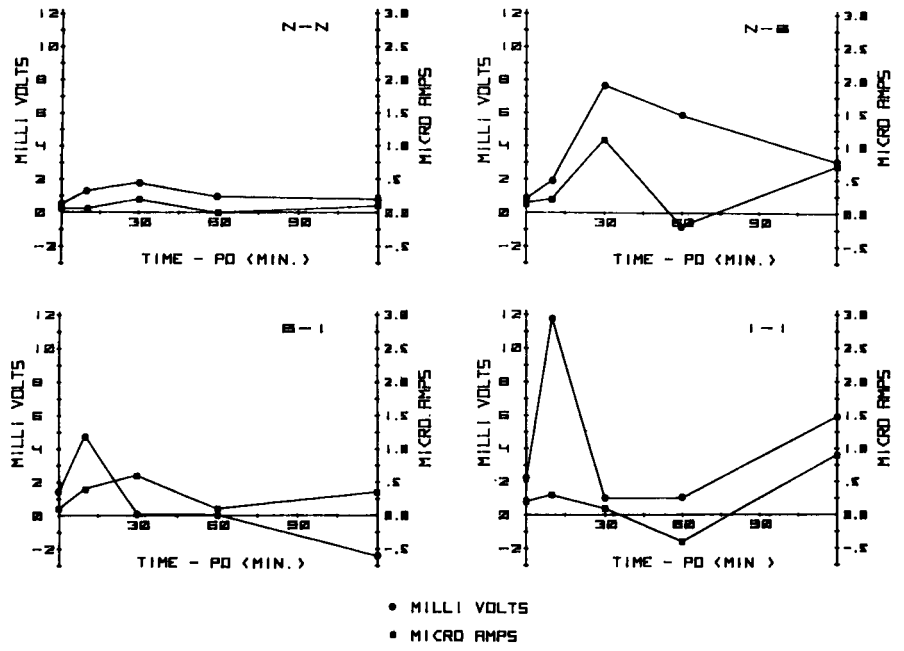

Figure 5. Relation of bipolar electrographic voltage to current in four electrode pairs following acute coronary occlusion. Note the nonparallel relation between current and voltage especially after 60 minutes in the normal and border zone pair (N-B) (see text). Abbreviations as in Figure 3.

upper right of the field and sinks were identified in two areas, the lower left and lower right fields. Immediately after occlusion, a current sink of approximately 15 μA (net) developed in the infarct zone approximately 3 to 4 mm from the visual boundary; the current source was a similar distance from the boundary in the upper left corner. The source-sink relations did not remain stable and between 5 and 30 minutes the current sink rotated to the right. However, at 60 minutes the current sink persisted in that location and the current source diminished in amplitude as the isocurrent line began to shift perpendicular to the visual boundary. In the five experiments in which extensive mapping was performed, the maximal current sources were 5 to 15 μA (net). The development of sources and sinks in all experiments was immediate and attained similar magnitudes as those shown in Figure 6. Within 30 minutes the magnitudes of these sources and sinks progressively decreased in all experiments, possibly indicating electrical uncoupling.

Relation of current to arrhythmias. Ventricular arrhythmias were observed in 20 of 36 experiments. However, by experimental design we limited the infarct size by occluding only the distal left coronary artery, and the frequency and severity of the ventricular arrhythmias were therefore reduced. Despite these precautions arrhythmias were observed. Maximal TQ current occurred in 9 of 12 experiments within the first 2 minutes and in only 1 experiment did a correlation exist between these currents and ventricular premature beats. Peak ST currents that occurred

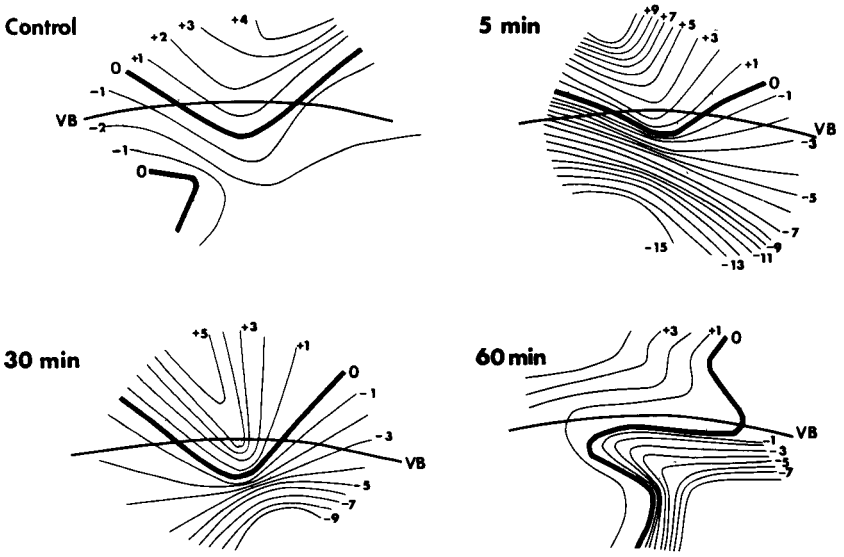

Figure 6. ST "current maps" generated by summation of the current flowing to and from each electrode with respect to 40 electrode pairs. In control, maximal source was (summed between all electrodes) 4 to 6μA and maximal sink was -2 to 3 μA. After acute occlusion, maximal source was $+11$ μA and sink was -15μA at 5 minutes and gradually subsided through the following 30 minutes. The maximal ST current sink gradually shifted to the lower right field (60 minutes) from the lower left with an associated shift in the 0 current demarcation. VB = visual boundary.

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between 5 and 15 minutes after occlusion were associated with arrhythmias in 2 of 12 experiments. When ST currents peaked between 15 and 30 minutes, arrhythmias appeared or increased in frequency in an additional two experiments. The correlation between peak T currents was higher. In 5 of 12 experiments, ventricular arrhythmias correlated with early maximal T currents occurring between 5 and 15 minutes. In 2 of 12 experiments, peak T currents arising between 15 and 30 minutes correlated with increased ventricular arrhythmias. Arrhythmias did not correlate with any of the observed peak currents in the remaining eight experiments.

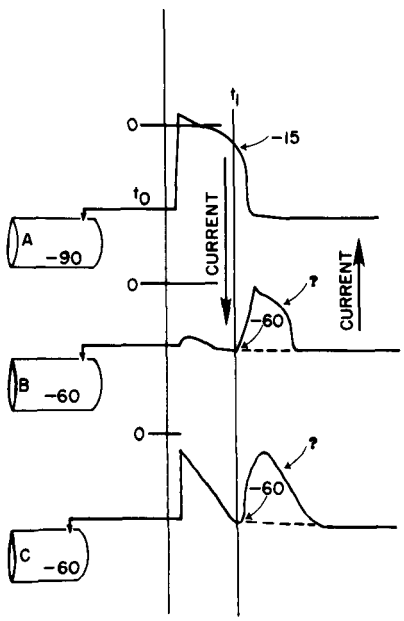
Discussion

Our studies provide electrophysiologic data indicating that TQ, ST and T currents develop rapidly after acute coronary occlusion. Current flow was observed within 10 to 30 seconds after occlusion and attained magnitudes of 0.1 to 0.5 μA during the TQ segment and 1 to 5 μA during the ST and T segments. These currents presumably develop secondary to ischemia-induced changes in the action potential, including a decrease in the membrane resting potential and shortening of phase 2 (5,6,12). Changes in both the TQ and ST-T current were noted within seconds after acute arterial occlusion; these results, similar to those of Bruyneel (18), suggest that changes in the action potential configuration occur within several beats of the onset of ischemia. Data from intracellular studies after acute arterial occlusion have shown action potential changes 2 to 5 minutes post-occlusion (5,6,12). Presumably the mechanisms for the changes noted immediately after occlusion are similar to those occurring at 5 minutes. Because the membrane resting potential decreases with ischemia, the intracellular potential of ischemic cells is positive relative to the normal (more negative) tissue. As a result, intracellular current flows from the ischemic to the normal tissue during the TQ interval (5,6). Conversely, the action potential of the ischemic tissue is shortened during electrical systole (ST interval). Therefore, during phases 2 and 3 ischemic cells are more negative relative to the normal tissue, which shows a longer phase 2 and is therefore more positive. Intracellular current during the ST segment thus flows from the normal (positive) tissue toward the ischemic tissue.

Physiologic Implications of Current Flow

Role of ST and TQ currents in reexcitation. The physiologic importance of intramyocardial current flow in infarction is unknown. This systolic current flow between adjacent cells is the normal process for impulse propagation during phase 0 of the action potential. Although the role of ST and TQ currents in acute myocardial infarction is unclear, it has been suggested as a possible mechanism for reexcitation (9,10). Han (9) states, "If neighboring myocardial fibers repolarize at sufficiently disparate rates, already repolarized fibers may be reexcited by the flow of current between these and neighboring fibers that are still depolarized." It has also been suggested (13) that "slow waves" and arrhythmias seen in hypothermia arise from high current densities generated by potential differences. Our data confirm that these currents are in the 1 μA range during both systole and diastole and suggest two possible mechanisms for reexcitation secondary to current flow (Fig. 7). During diastole, intracellular current flows from the ischemic tissue (-60 mV) to the normal tissue (-90 mV). This current tends to depolarize the normal myocardium and may represent a source for late coupled extrasystoles because the maximal voltage disparity occurs after full repolarization of the normal cell (Fig. 7A and C). Alternatively, during phase 2 of the normal zone action potential, the ischemic zone is more negative. At time t_1, the action potential in the normal zone is more positive (-15 mV) than that in the fully recovered ischemic cell (-60 mV). Therefore, intracellular current flows from the normal zone to the ischemic zone. Because of the shortened action potential in the ischemic zone (cell C), this current is depolarizing and may be of sufficient magnitude to induce reexcitation of the ischemic cell which has completed repolarization earlier. It has been shown that some cells within the infarct zone may not discharge with each beat and show 2:1 responses or marked delay in conduction. In the absence of a fully propagated action potential, the depolarizing current from the normal zone may excite this cell (cell B). Such a circumstance would arise if the ischemic cells were stim-

Figure 7. Diagrammatic representation of the relation between ischemic and normal cells and current flow during depolarization and repolarization (see text).



ulated rapidly (12) or demonstrated long time-dependent refractoriness.

It has also been suggested (9,19) that reexcitation may not occur because of electrotonic interaction between cells and the low resistance coupling between these neighboring cells. However, it should be emphasized that ischemic boundaries do not share similar properties with those of normal cells because uncoupling (20,21) occurs.

Genesis of ventricular arrhythmias. The experiments of Janse et al. (15) support the hypothesis that focal reexcitation may be a cause of early arrhythmias seen after coronary occlusion in the dog. Janse et al. found that the earliest activity occurred in normal tissue and found no evidence for electrical activity bridging between the latest electrical activity of the sinus beat and the ectopic impulse (although the reentrant pathway may not have been recorded). Reexcitation of the normal myocardium may be induced by the depolarizing effects of the TQ current (from ischemic to normal zones) or induced by delayed depolarization and, hence, recovery of ischemic tissue (15,22), resulting in ischemic tissue remaining more positive than normal myocardium. Both of these mechanisms represent conditions in which the ischemic myocardium is a current source and they tend to depolarize the normal myocardium, thereby potentially leading to focal reexcitation of normal tissue.

Although the focal reexcitation hypothesis is attractive, there are detailed studies showing the relation between slow conduction and ventricular arrhythmias. Conduction delay arises soon after acute coronary ligation (23) and progressively prolongs until electrical activity bridges diastole (24,25). Conduction delay of this magnitude adds support to the belief that these early arrhythmias are reentrant in origin. The absence of diastolic electrical activity does not preclude reentry since the site for reentry may be distant to the recording site or in the endo- or midmyocardium (26,27). Our data do not support either theory for arrhythmogenesis because persistent arrhythmias were infrequently encountered as a result of the intentional ligation of the distal left anterior descending artery. This was done to induce only a small infarction, which is less frequently associated with persistence of severe cardiac arrhythmias in the dog. We did note ventricular arrhythmias in 20 experiments, but they were not associated with maximal TQ or ST currents. In 7 of 12 experiments, arrhythmias did occur early (5 to 30 minutes) after occlusion coincident with maximal T currents. Further studies are required to define if a causal relation exists.

Paradoxical current response. The finding of nonparallel or dichotomous current changes when compared with the voltage electrograms deserves comment. In most studies after acute coronary ligation and during the first 60 minutes after occlusion, the current values obtained could be predicted from the electrograms and usually showed parallel responses. After 60 to 90 minutes these relations no longer held true. Previous studies on current flow (14,15) have not identified this paradoxical current response; however, current recordings in those studies were usually limited to the early (first 15 minutes) postocclusion stage. Our studies identified these responses 1 to 3 hours after occlusion when electrical uncoupling is thought to occur (20). As electrical uncoupling of the infarct zone occurs, current values from the voltage displacement of the electrograms become less predictable.

Current Sources and Sinks

Current sources and sinks in diastole and systole are to be anticipated, knowing the effects of ischemia on the action potential. Ischemic cells show loss of resting membrane potential, shortening of phases 2 and 3 of the action potential and reduced amplitude and rate of voltage development (dV/dt)(11,12). Ischemic cells are the diastolic intracellular current source because they are depolarized. The normal zone, which is more negative, constitutes the diastolic intracellular current sink. During electrical systole, the ST current source would be composed of cells with the longest plateau and hence would remain more positive relative to the more rapidly repolarizing ischemic cells. Recent studies by Kléber et al. (14) and Janse et al. (15) and our studies indicate that current sources and sinks may be juxtaposed within 5 to 10 mm of each other. This suggests that local current densities may be sufficiently high to induce reexcitation.

ST segment alternans. In our experiments ST segment alternans was frequently seen but usually disappeared after 60 minutes of occlusion. Alternans in current may arise from true alternans of the action potential (14). It may also arise from alternans of conduction, thereby alternating the activation times and hence the potential differences between the two sites (12,22). The latter of these is unlikely because our studies failed to show marked differences or alternation of activation to the respective electrode sites. Whether or not alternans induces arrhythmias is not resolved. Downar et al. (12) suggested that alternans favors reentrant rhythm. Kléber et al. (14) also suggested that current flow due to the alternans may induce reexcitation (their Fig. 10). Russell et al. (28) noted the appearance of action potential and electrographic ST segment alternans immediately preceding ventricular fibrillation in the dog. However, despite these observations, the role of alternans is yet undetermined.

Limitations of the study. Our method of recording current permits an approximation of the amount of current that could, but not necessarily does, flow between the two recording sites. We selected a resistance of 100 Ω across the input of the direct current amplifier for current measurement. Our values were obtained in a fixed system that assumes uniform myocardial resistance; the methods used by Kléber et al. (14) and Janse et al. (15) likewise have limitations related to the assumption of a fixed and uniform tissue

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resistivity of 400 Ω-cm for computation of epicardial current maps. Both methods suffer from the limitation that the anisotropy of resistivity is not taken into account, which varies according to fiber direction (lower resistance parallel to the cell long axis). There is need for further study to delineate the process of electrical uncoupling at the infarct boundary.

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