Intramural Depolarization Potentials in Myocardial Infarction

A Preliminary Report

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By means of small intramural electrodes, potentials at multiple depths within the ventricular wall were recorded in myocardial infarction and in normal hearts. In 41 animals with coronary artery occlusion, electrocardiographic and histologic correlations indicated that coronary QS waves may represent negative potentials transmitted from viable intramural muscle as well as from the cavity. Coronary QR waves were obtained over transmural infarcts containing a mixture of viable and dead tissue, but not over purely subendocardial lesions. In the normal ventricle, positive depolarization potentials greatly predominated over negative potentials. Clinical applications are discussed.

The most significant electrocardiographic feature of myocardial infarction is the presence of a surface QS or QR wave, either of which is believed to indicate myocardial death. In view of their clinical importance, these pathologic signs warrant more thorough experimental investigation than has been reported to date. Current theories concerning the origin of QS and QR waves are derived entirely from studies of potentials on the ventricular surfaces and in the ventricular cavities; potentials within the myocardium, or what may properly be called “intramural” potentials, have been recorded previously on rare occasions but never in myocardial infarction.

In the present study, new evidence regarding intramural activity is being obtained by means of a “plunge” electrode which makes it possible to record tracings from minute areas within the ventricular wall. This specially designed electrode, in conjunction with cinematoelectrocardiographic and histologic examination of the ventricles, has been employed thus far in a total of over 100 dogs with normal cardiac function or with experimentally produced myocardial infarcts, bundle branch block, ventricular extrasystoles or tachycardia. The following preliminary report is concerned primarily with the relationship between intramural and epicardial depolarization potentials as observed in 41 instances of myocardial infarction. In addition, the distribution of potentials within the normal ventricle is described in order to explain certain findings associated with abnormal surface Q waves. Intramural studies of bundle branch block and ventricular arrhythmias, as well as additional observations on normal and infarcted ventricles, will be reported in subsequent communications.

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**Materials and Methods**

Myocardial infarcts were produced in 41 dogs by ligating the left anterior descending coronary artery about halfway down its course. An interval varying from two days to five months followed the initial operation, after which each animal was reanesthetized and routine limb and precordial tracings were made. The chest was then opened, artificial respiration maintained with an electric pump respirator, and the heart widely exposed by an incision described elsewhere.

**Electrocardiographic Equipment and Technique**

Intramural and cavity leads were recorded by “plunge” electrodes made of tempered silver the diameter of a fine needle and insulated throughout their length except at the chloride-coated tip which formed the recording surface. Effort was made to minimize the size of the recording surface so that it would register potentials from highly localized points. Each electrode was accurately marked at 5 mm. intervals; when the electrode was plunged into the myocardium, the markings made it possible to determine the depth of the tip within 1 to 2 mm. Epicardial leads were recorded from a cotton electrode with a somewhat larger surface than that of the plunge electrode.

In each animal, a plunge electrode was introduced into the cavity of the exposed left ventricle; this lead was used as a reference and was recorded simultaneously with epicardial or intramural leads from selected sites. As many as four or five plunge electrodes were used in each heart, and intramural tracings from each electrode were taken at several measured depths from the surface. Current of injury, caused by insertion of the plunge electrode, normally attained a minimum after about five minutes. Epicardial and intramural tracings were obtained from normal control tissue as well as from the margins and central portions of the infarct. The position of all electrodes was verified post mortem.

The possibility that the presence of a plunge electrode might induce focal block in the surrounding myocardium, thereby rendering the intramural tracings unreliable, was investigated by the following simple experiment: A cotton electrode was fixed to the epicardial surface of the ventricle. The plunge electrode was then inserted obliquely into the ventricular wall so that its recording tip lay in the myocardium almost 1 mm. beneath the surface electrode. If perifocal block, or any other depolarization abnormality, were induced by the plunge electrode, simultaneous tracings from the surface and intramural electrodes should be dissimilar; that is, the abnormality would be recorded by the plunge electrode and not by the surface electrode. It was found, however, that the depolarization waves recorded simultaneously from the two electrodes were practically identical in almost every instance except that, as expected, the R wave in the intramural lead was slightly lower than the surface R wave. The width of the QRS complexes of both leads was identical, thus demonstrating the absence of block in the region of the intramural electrode. Indeed, in all experiments subsequently performed on normal hearts, the depolarization complexes in simultaneous cavity, intramural and epicardial leads were always of equal width. On the rare occasions when perifocal block or other abnormalities were caused by the plunge, they were recognized without difficulty and always disappeared after a short interval or after reinsertion of the electrode.

In order to determine whether the electrodes registered primarily local potentials, a variety of experiments was performed. For example, in normal tracings from epicardial or plunge electrodes situated a short distance from the auriculoventricular groove, the P wave usually was absent or very small. The plunge electrode was further tested by recording intramural leads from one ventricle before and after the entire contralateral ventricle was cut away; little or no change in the deflections registered by the electrodes was noted. In bundle branch block, on the other hand, plunge electrodes in the blocked ventricle often recorded deflections 2 to 3 mm. in amplitude, representing electrical activity in the opposite unblocked ventricle. It was thus demonstrated that the electrodes registered predominantly, although not exclusively, local events. This conclusion may be reached on theoretic grounds by application of Poisson’s integral which states that the electromotive force is inversely proportional to the cube of the distance between the electrode and the depolarizing cell. The potentials of cells in immediate contact with the recording tip therefore affect an electrode many times more forcibly than potentials as little as a few millimeters distant from the tip.

All electrocardiograms were registered on a Brush recorder operated at a paper speed of 125 mm. per
second. This rapid paper speed yields deflections five times broader than those in standard tracings, thereby greatly facilitating examination and comparison of depolarization waves. Power was supplied through the amplifying system of a Sanborn Polyviso. The indifferent electrode was connected to Wilson's central terminal for all experiments. All direct leads were recorded at × 20 attenuation with the sensitivity adjusted so that 20 millivolts corresponds to a 15 mm. deflection. Although actual comparative tests have shown that the Brush Recorder is less sensitive than oscillographic equipment, the former was found to be completely satisfactory for the present study.

Cinematographic Electrocardiographic Technic

In 19 of the 41 instances of experimental myocardial infarction, the motion of the left ventricle was photographed simultaneously with direct epicardial or intramural leads. This recently developed technic is described in detail elsewhere. By recording at fast camera speeds under high magnification, the precise movements of ventricular muscle associated with a specific electrocardiographic pattern can actually be visualized. Thus the cinematographic electrocardiographic technic yields a close correlation between mechanical and electrical events in the ventricle.

Histologic Examination

After the desired electrocardiographic and cinematographic observations had been made, the experimental animals were sacrificed and relevant portions of the heart subjected to careful histologic study. The plunge electrodes were left in situ until after the tissue was carefully cut, fixed, and prepared for the microtome. Microscopic examination of the stained sections often revealed clearly the tracts made by the plunge electrodes. Since the intramural tracings had been recorded at measured distances from the epicardial surface, it was thus possible to identify the precise bit of tissue from which each tracing was derived. All epicardial, intramural and cavity electrocardiograms obtained during the experiments were appropriately located on an enlarged microphotograph of the section, allowance being made for shrinkage of tissue. The microscopic findings were then correlated with the cinematographic and electrocardiographic data.

Intramural Potentials in the Normal Ventricle

By the "plunge" technic described, 35 observations on intramural potentials at various depths of the free ventricular walls were made in 23 dogs with normal hearts. On eight occasions, normal potentials were recorded from various depths of the left papillary muscle. Since the right papillary muscle is smaller and less accessible than its counterpart, investigation of the former was not undertaken. Finally, in 14 normal ventricles, electrical activity throughout the septum was recorded with a specially designed electrode. The results of these studies are summarized here because of their pertinence to the subsequent discussion of myocardial infarction.

The Free Ventricular Walls

Consistently, a rapid diminution in the size of the R wave and a striking growth of the S wave occurred as the electrode was plunged deeper into the wall of the normal ventricle (fig. 1). In some tracings from as little as 3 mm. below the epicardial surface, the R wave was absent or almost indistinguishable and a deep S or QS wave appeared. In the majority of animals, the inner half of the wall of both ventricles yielded pure QS deflections. Findings in the left and right ventricular walls were similar, except that the outer zone of positivity appeared to involve a greater proportion of the right ventricle than of the left.

The phenomenon of negativity within the normal ventricular wall was further explored by eliminating all or part of the outer zone of positivity. Portions of the epicardial and underlying muscle were severely burned in 23 dogs and actually excised in five dogs, after which the surface was subjected to electrocardiographic study. When compared with leads from the normal surface, tracings from the burned epicardium or newly exposed muscle consistently exhibited marked lowering of the R waves. In five instances the R wave was completely replaced by a pure QS wave. These findings confirm the results obtained by Bellet and Johnston, who produced similar burns and recorded potentials from the new surface and immediately subjacent tissue.

Intramural potentials recorded from all depths of the left papillary muscle in normal hearts were consistently negative. However, an embryonic R wave or slur was often distinguished at variable points on the downstroke of the QS wave. The intramural deflections recorded from the left papillary muscle were of
greater amplitude than those from the neighboring cavity.

*The Interventricular Septum*

The septum was explored with a curved electrode which was slightly thicker than the plunge electrode, composed of the same tempered silver, and insulated throughout its length. The electrode was pushed into the septum; this phenomenon served to localize the position of the electrode, since no current of injury occurs in cavity leads.

As the septum was traversed from right to left, the following sequence of electrocardiographic events was observed: A small R wave followed by a deep S wave was recorded from the right septal surface. The R wave grew larger as the electrode was drawn deeper into the septum, attaining maximum amplitude in tracings from approximately halfway between the left and right septal surfaces. Subsequent tracings showed a progressive diminution in the size of the R wave until, when the electrode neared the left septal surface, the R wave disappeared and was replaced by a QS deflection.

![Image of epicardial, intramural, and cavity leads from normal left ventricle of dog.](http://circ.ahajournals.org/)

*Fig. 1.* Epicardial, intramural and cavity leads from normal left ventricle of dog. Magnification ×6.2. Tracings recorded at 125 mm. per second paper speed, attenuation ×20. Sensitivity: 20 mv. equal 15 mm.

In tracings recorded 5 mm. below surface, the R wave is small and is followed by a large S wave. Muscle 11 or 15 mm. below the surface yields no R wave. Hence it appears that positive potentials normally prevail only at and immediately beneath the surface of the ventricular wall. S-T segment elevation indicating current of injury is due to trauma by plunge electrode.

except for a segment of about 1 mm. in the middle which formed the recording surface. By passing this electrode through the heart from one ventricular surface to the other, it was possible to record successively from one cavity, from the adjacent septal surface, from various points within the septum, and finally from the opposite septal surface and adjacent cavity. Current of injury always appeared when the electrode was pushed into the septum; this phenomenon served to localize the position of the electrode, since no current of injury occurs in cavity leads.

As the septum was traversed from right to left, the following sequence of electrocardiographic events was observed: A small R wave followed by a deep S wave was recorded from
As the left cavity was entered, current of injury vanished and the QS wave persisted. These findings support the concept that most of the septum is actually a part of the left ventricle.7

Comment

The striking feature observed in intramural studies of the normal ventricles is the unexpected predominance of negative over positive potentials. With the exception of a relatively thin shell on the epicardial surface and in the middle and right side of the septum, all portions of the ventricular musculature yielded essentially negative deflections. Predominantly positive depolarization potentials were found to prevail in only about 20 per cent of the ventricular muscle of the normal heart. In contrast, when an impulse traverses a two-dimensional muscle strip, 50 per cent of the tissue yields predominantly negative deflections and the remaining 50 per cent is predominantly positive. Hence the ventricular myocardium apparently does not behave electrically in the same manner as a simple muscle strip. The distribution of potentials in the auricles, on the other hand, is consistent with the behavior of a simple muscle strip.4,8

Until more is known concerning the electrophysiology of cardiac muscle, the apparent difference in mode of auricular and ventricular depolarization cannot be adequately explained. Among the factors which may be pertinent are: (1) The auricular wall is sufficiently thin to act electrically as a two-dimensional structure, while the thicker ventricle must undergo three-dimensional depolarization.1 (2) The auricles possess no specialized conducting tissue, whereas the Purkinje system penetrates deeply into the ventricular wall. Hence the depolarization wave may enter the ventricular myocardium at a relatively superficial intramural level rather than at the endocardium. (3) The auricular depolarization wave travels at a constant rate of speed. The velocity of the ventricular depolarization process, as determined in the present study by comparing the times of onset of the intrinsic deflections in leads from multiple intramural levels, is greater in the inner half of the ventricular wall than in the outer portion. This finding may be related to the penetration of the Purkinje system into the ventricular wall, or to as yet undiscovered biochemical and/or enzymatic differences within the ventricular myocardium.

The Coronary QS Wave

Current concepts concerning the significance of the coronary QS wave are based primarily upon the experimental studies of Wilson and his associates.9 These workers found that regions of transmural infarction, whether acute or chronic, yielded almost identical QS waves in leads from the epicardial surface and the subjacent cavity. Furthermore, pressure on the epicardium failed to elicit current of injury in surface leads. As interpreted by most commentators, Wilson's fundamental findings signify that the negative potential of the cavity is passively transmitted unaltered through a transmural "hole" or "window" of infarcted tissue. Thus, epicardial or precordial QS waves generally are believed to occur over regions of through-and-through muscle death.

Thirty-five of the 41 instances of experimental myocardial infarction included in the present study were shown histologically to involve tissue at all levels from the ventricular cavity to the epicardial surface. A correlation of observations in these transmural lesions indicates that two types of QS waves may be recorded from the surface of either acute or chronic infarcts. The first type of surface QS wave appears to be derived entirely from the negative cavity potential, as suggested by Wilson, and may therefore be called the cavity type of surface QS wave or, more conveniently, the surface "QSc" wave. The second type of surface QS wave evidently is at least partially determined by electrical activity in the ventricular wall; hence it will be tentatively termed the mural type of surface QS wave, or simply the surface "QSm" wave. The distinctly dif
different pathologic situations responsible for
"QSc" and "QSm" waves have been demonstrated by three methods: (1) Cinematographic and electrocardiographic exploration of the epicardium; (2) intramural leads from multiple levels, and (3) histologic examination of the infarcted region.

**Cavity-Type QS (QSc) Surface Wave**

1. Cinematographically, epicardial regions yielding QSc waves were seen to protrude or balloon while normal portions of the ventricle were in systole. This phenomenon, most apparent in profile views of the heart and in lesions of relatively recent origin, indicates absence of contraction of the infarcted area. Electrocardiographically, the entire ventricular complex including the surface QSc wave was identical in timing, magnitude and configuration with simultaneously recorded cavity leads. The QSc waves in both epicardial and cavity tracings exhibited early onset and gently rounded contour; the S-T segments were always isoelectric and failed to show current of injury when the surface was traumatized by pressure with a sharp electrode or by application of a 10 to 15 per cent solution of potassium chloride; the T waves were slightly positive and did not change when the surface of the infarct was heated. Further evidence of muscular inactivity was obtained by stimulating the QSc area with a sharp applicator or with an interrupted current of threshold intensity; no response occurred, although either of these procedures consistently elicits extrasystoles when applied to normal ventricular muscle.

2. Intramural tracings from various levels of regions yielding surface QSc waves consistently exhibited ventricular complexes indistinguishable from those in epicardial and cavity leads. Furthermore, when the cavity potential was deliberately altered as by the production of bundle branch block, the intramural and epicardial tracings promptly registered changes identical with those in the cavity lead. Finally, at no time was a current of injury elicited by insertion of the plunge electrode into the substance of the infarct, although extreme elevation of the S-T segment always is observed when these electrodes are plunged into normal muscle. Failure to produce injury current at any level of an infarct from epicardium to endocardium appears to constitute definitive evidence of uniform through and through muscle death.

3. Histologic examination of infarcted regions yielding surface QSc waves showed complete loss of normal muscle. From epicardium to endocardium, the region consisted of a homogeneous scar of necrotic or fibrotic tissue, depending upon the age of the infarct (fig. 2). The preceding observations confirm and supplement the work of Wilson. In transmurally infarcted regions devoid of viable muscle, the negative depolarization potential recorded at the surface must be transmitted unmodified from the subjacent cavity. Hence the cavity type of surface QS wave completely conforms to accepted theory concerning the genesis of the QS wave of myocardial infarction.

**Mural-Type QS (QSm) Surface Wave**

1. Cinematographs of the surface of infarcts yielding QSm waves unexpectedly revealed distinct muscular activity. In at least four such lesions, each older than 11 days, active contraction was demonstrated by outlining the QS area with Janus green; the outlined region was clearly seen to wrinkle and shrink during ventricular systole. A number of infarcts exhibited systolic contractions of QSm areas at the periphery, while QSc areas over the center of the lesion showed characteristic ballooning.

Surface electrocardiograms containing QSm waves differed from leads exhibiting QSc waves in several significant respects: (a) Mural-type surface QS waves often were readily distinguished from the QS wave in simultaneously recorded cavity leads; the former frequently started later, presented a more abrupt downstroke, were sometimes deeper, exhibited a sharp tip, and occasionally were notched by the presence of a small embryonic R wave or merely by a slight slur. These differences between surface and cavity deflections must represent the electrical activity of surviving muscle within the infarcted region. (b) Elevated S-T segments following QSm waves, indicating current of injury, frequently occurred spontane-
ously in infarcts of less than two or three days duration, and could be produced in older lesions by mechanical or chemical trauma. (c) The T waves in surface leads containing QSm waves usually were higher than those in simultaneous cavity leads and increased in amplitude when the infarct was heated. Neither current of injury nor T-wave changes could be produced by dead muscle. The presence of viable muscle was further demonstrated by the frequent occurrence of extrasystoles when surface regions yielding QSm waves were stimulated with a sharp applicator or an electric current.

2. Intramural muscle directly subjacent to surface regions yielding QSm waves also showed unmistakable evidence of electrical activity. In tracings from these regions, the intramural QS waves differed in size, shape and magnitude from QS waves recorded at other intramural injury resulting from trauma by the electrode in chronic infarcts, and from trauma combined with spontaneous resection of the freshly infarcted tissue in acute lesions.

3. Histologically, regions of transmural infarction presenting the mural type of surface QS wave were found to include irregularly dispersed islands of surviving muscle surrounded by areas of necrotic tissue in recent infarcts and by fibrotic scar tissue in older lesions. Both
the location and the quantity of surviving muscle varied in different infarcts. Occasionally, certain layers of the myocardium consisted entirely of necrotic or fibrotic material, but patches of surviving muscle tissue always were present at some levels of infarcted regions from the epicardial layer of the normal ventricular wall. Presumably, therefore, surviving muscle at deeper intramural levels would contribute to the negativity of the surface QS wave; con-

which surface QSm waves had been recorded during life (fig. 3).

The preceding histologic findings provide an anatomic basis for the mechanical and electrical activity observed in regions yielding surface QSm waves. Depending upon their location and quantity, the patches of viable muscle persisting within the infarct undoubtedly influenced the appearance of the epicardial electrocardiogram. As previously shown, negative potentials prevail in all but a relatively thin epicardial layer of the normal ventricular wall. Presumably, therefore, surviving muscle at deeper intramural levels would contribute to the negativity of the surface QS wave; con-

versely, viable muscle in the superficial layers may account for the embryonic R wave and slurring of the QSm occasionally observed in the present series of experiments. Thus the coronary QS wave apparently sometimes results entirely from transmission of the negative cavity potential, as described by Wilson and confirmed in the present study, and sometimes represents a variable mixture of intramural

Fig. 3. Electrocardiographic and histologic appearance of section of left ventricle with 17 day old infarct. Fibrous tissue appears white or grayish-white, surviving muscle dark grey or black. Path left by plunge electrode is shown by arrow. Magnification X10.

Surface QS wave appears superficially similar to the QSc deflection in figure 2. However, current of injury obtained in surface lead upon application of pressure, and at intramural levels establishes presence of viable muscle within infarcted region. Note that QS waves in leads from surviving muscle 4 mm. and 6 mm. below surface differ from surface QS wave as well as from cavity QS. These findings indicate that surface QS deflection is of mural type (see text).
FIG. 4. Subendocardial infarct 26 days old. Magnification $\times 5.7$. Arrow shows approximate location of plunge electrode. Mallory's connective tissue stain: blue, connective tissue; red, surviving muscle.

Contrary to prevailing theory, surface lead exhibits no QS deflection; only a large R wave is recorded. Current of injury obtained at 5, 10 and 15 mm. depths indicates presence of viable muscle.

FIG. 5. Epicardial, intramural and cavity leads from margin of 27 day old infarct. Magnification $\times 7.8$. Mallory's connective tissue stain. Arrow represents path of plunge electrode. Mostly surviving muscle to left; infarct to right. Hole extending to 9 mm. depth was made by plunge electrode.

Surface of margin exhibits minimal damage, yields small Q wave and relatively large R deflection. In tracings from various depths of the ventricular wall, the negative deflection is larger than in the surface lead, while the positive deflection disappears. These electrocardiographic findings indicate that the surface Q wave is not transmitted unaltered from the cavity, and the surface R wave is not transmitted from intramural muscle distant from the electrode.

(The use of color in figures 4 and 5 is made possible by a grant from Winthrop-Stearns, Inc., to the publication fund of the American Heart Association.)
and cavity potentials. If sufficient amounts of viable muscle remain within the deeper layers of an infarct, it is possible that the coronary QS wave may be derived solely from mural potentials. Such a circumstance was illustrated by the virtual disappearance of the positive deflection and the occurrence of a surface QS wave when the shell of positivity in the normal ventricular wall was experimentally destroyed.

Comment

In the present series of experiments, both the cavity and the mural types of surface QS wave frequently were recorded over different portions of the same infarct. In general, QSm waves occurred over a relatively large proportion of the surface of smaller infarcts, while QSc waves were more commonly obtained from larger infarcts. Although some large infarcts yielded only QSc waves, the majority included a zone of QSm waves over the periphery. Older lesions tended to present larger areas of QSc than of QSm waves, while the reverse was frequently true of more recent lesions. Thus the relative incidence of the two types of deflections appeared to be a function of the size and age of the infarct.

During the initial stages of the study, no distinction between cavity-type and mural-type QS waves was perceived upon inspection of epicardial tracings; this was true of leads recorded at 125 mm. per second as well as at normal paper speeds. After considerable experience had been gained, however, it was often possible to differentiate the two types of waves and, therefore, to predict the histologic findings by careful examination of the surface electrocardiogram. In the series of experiments now in progress, a “map” of each infarct is plotted purely on the basis of information gained from epicardial and intramural leads. With only occasional minor inaccuracies, the outlines of the infarct and the locations of viable muscle within its borders can thus be diagrammed before the histologic sections are made. Nevertheless, observers unfamiliar with the pertinent criteria seldom are able to differentiate QSc and QSm waves in epicardial leads. In precordial leads recorded on standard electrocardiographic equipment, the two types of QS waves usually are indistinguishable.

The Coronary QR Wave

According to current theory of the genesis of coronary QR waves, infarcted subendocardial muscle transmits the negative cavity potential to the epicardium, causing an initial downward deflection, after which overlying intact muscle contributes a positive potential, represented by the late R deflection. Thus the surface or precordial QR wave is believed to occur over infarcts limited to the subendocardial region, as well as over the margins of transmural infarcts which have their greatest breadth in the subendocardium. Since recent investigations have yielded conflicting results concerning the histologic findings associated with QR waves, these deflections were considered an appropriate subject for experimental study.

Of the 41 instances of experimentally produced myocardial infarction in the present series, six presented histologic evidence of necrosis or fibrosis only at subendocardial levels. These six infarcts extended from the endocardium through one-eighth to one-half the thickness of the ventricular wall, in no instance destroying subepicardial or epicardial muscle. Standard limb leads and multiple precordial tracings were recorded from each animal several weeks after coronary ligation, the chest was reopened, and electrocardiograms were made directly from the epicardial surface over the lesion as well as from multiple intramural levels as previously described. Contrary to prevailing theory, both the precordial and epicardial depolarization complexes were normal, as shown by comparison with tracings from normal areas of the same heart and from other normal hearts; no QR waves were obtained. High-speed cinematographs recorded simultaneously with the direct leads in three instances likewise revealed no abnormality in the appearance or contractility of the epicardium overlying the infarct. Intramural tracings from various levels of the subendocardial lesion and overlying intact tissue appeared to be within normal limits in four of the six animals (fig. 4). In no instance did the intramural leads yield evidence supporting the
current theory of the genesis of coronary QR waves.

Since QR waves were not recorded over recent or chronic subendocardial infarcts, an experiment was performed to determine if such deflections might be obtained during the earlier stages of the lesion. In 18 animals, an attempt was made to produce acute myocardial necrosis by means of burns inflicted with an electric cautery. Histologic examination established that seven of these burns were purely subendocardial, extending from the cavity through one-eighth to three-fourths of the thickness of the ventricular wall. Immediate electrocardiographic exploration of the undamaged surface over the necrotic region consistently failed to reveal a negative initial deflection. In three animals, the R wave recorded over the burn was somewhat lower and later than in normal control leads, but nothing resembling a QR wave was seen. Similar observations have previously been made by Pruitt, Barnes and Essex. Thus it appears that acute subendocardial necrosis produced by cauterization, like recent and chronic subendocardial infarction, does not necessarily produce coronary QR waves.

The consistent failure to obtain a negative deflection over pure subendocardial lesions, whether acute or chronic, suggests that some degree of epicardial damage is essential to the production of coronary QR waves. This conclusion is substantiated by findings in the 35 instances of transmural infarction produced during the study. In four such cases, QR waves appeared in both precordial and epicardial leads recorded over all or almost all portions of the lesion. Many of the remaining transmural infarcts presented QR deflections in precordial and epicardial leads from zones of variable width over the margins. Histologically, every region over which QR waves had been recorded was found to consist of a mixture of surviving muscle and fibrotic or necrotic tissue involving the epicardial surface (fig. 5).

Discussion and Clinical Applications

The present study of intramural, epicardial and precordial tracings in the experimental animal indicates that intramural depolarization potentials are not represented in leads facing the intact epicardium. This conclusion is derived from the following observations: (1) Although an overwhelming preponderance of intramural tissue in the normal heart is predominantly negative during ventricular depolarization, the depolarization wave in epicardial and precordial leads is normally positive. Burning or removal of the relatively thin shell of positive epicardial tissue diminishes the positivity of the surface depolarization potential.

![Diagram showing relationship between electrocardiographic and histologic findings in region of myocardial infarction. From left to right: C-type QS wave, identical with cavity QS, is recorded over region of through and through infarction. M-type QS wave occurs over region containing mixture of surviving muscle and fibrotic tissue involving the surface; compared with the depolarization wave in simultaneous cavity lead, this mural type deflection often exhibits later onset, sharper downstroke and sharper tip. S-T segment elevation. QR waves are recorded from epicardial surface consisting of mixture of surviving muscle and infarcted tissue, but exhibiting somewhat less damage than the QS zone to the left. As the amount of epicardial damage decreases, the Q wave becomes smaller and the R wave larger. Normal surface tissue over regions of subendocardial infarction yields a normal depolarization wave. (Reprinted from J. Thorac. Surg. 24: 105, Aug., 1952.)](http://circ.ahajournals.org/)

or actually changes the deflection from positive to negative. (2) If the epicardial zone of positivity remains intact, as in subendocardial infarction, the depolarization wave in precordial and surface leads remains positive. (3) If the epicardial region is damaged but contains a variable amount of surviving viable muscle, as in patchy transmural infarction, precordial and surface leads exhibit a negative deflection sometimes followed by a positive deflection. Preliminary correlations between electrocardio-
graphic and histologic findings in such lesions suggest that the degree of epicardial damage determines whether a QS or QR wave is inscribed (fig. 6).

The preceding observations suggest that the status of underlying intramural muscle is not represented in epicardial and precordial electrocardiograms. Rather, it appears that such tracings merely provide a fair representation of epicardial potentials. Whether the deeper layers of ventricular muscle consist of completely fibrotic tissue, completely normal muscle, or a mixture of both, is not revealed by leads facing the epicardium. Consequently, prognostically unimportant epicardial disturbances may yield a greatly distorted electrocardiogram although the overwhelming mass of ventricular muscle remains normal. Conversely, severe pathologic changes within the depths of the ventricular wall may fail to reveal themselves in routine tracings if the epicardium remains intact. Finally, a coronary QS wave may signify either uniform through and through muscle death, or inactivity of only the epicardial zone of positivity, or any intermediate amount of myocardial damage. Such lesions can be reliably differentiated only by means of direct epicardial and intramural leads or by histologic examination. Unfortunately, the leads employed in clinical electrocardiography are comparatively remote from the heart and seldom provide sufficient information to determine the precise pathologic situation responsible for a given coronary QS wave.

An awareness of the limitations of clinical electrocardiography may serve to minimize certain diagnostic and therapeutic errors in patients with myocardial disease. All too commonly, individuals die of myocardial lesions which the electrocardiogram has failed to reveal. On the other hand, most internists have observed patients with greatly distorted tracings who nevertheless have small hearts, adequate myocardial function, and are able to lead active lives for years or decades; as noted by Wilson, these individuals frequently are advised to restrict or eliminate their normal activities, thereby contracting "coronary disease of electrocardiographic origin." Such apparent discrepancies between the electrocardiographic and clinical picture sometimes can be explained in terms of the concept that a "pure" QS wave may occur over regions containing significant amounts of viable muscle. The application of this concept to several common clinical situations is illustrated by the following examples.

Example 1. After experiencing a typical coronary occlusion, the patient exhibited QS waves in all precordial leads from V₁ to V₄ in the third, fourth and fifth intercostal spaces. A diagnosis of extensive myocardial infarction was made. Upon fluoroscopic examination, however, the heart appeared small and the left ventricle contracted well in each of numerous views; no regions of ballooning were observed. High-speed cinemato-photographs of the fluoroscopic views confirmed the occurrence of systolic contractions in all visible portions of the left ventricle. Despite the ominous appearance of the electrocardiogram, the patient was in excellent condition. These cinematofluoroscopic and clinical findings indicate that the infarcted region contained enough viable muscle to maintain contractility. A similar situation was observed in experimentally produced infarcts which exhibited systolic contractions in regions yielding the mural type of QS wave.

Example 2. An 80 year old patient with a previously normal electrocardiogram experienced a massive gastrointestinal hemorrhage followed by shock. On the day following this episode, electrocardiographic studies showed QS waves in several precordial leads as well as in leads II, III and aVF. Extensive anterior and posterior myocardial infarction was suspected despite the absence of pain or other evidence of coronary occlusion. After transfusions and other supportive treatment, the QS deflections gradually disappeared and were replaced by R waves. Several months later the bleeding recurred and a similar sequence of electrocardiographic events was observed: again, QS waves appeared and gradually were replaced by R waves. The transient occurrence of QS deflections on two occasions obviously could not have resulted from through-and-through death of cardiac muscle. A more reasonable interpretation of the findings is as follows: The patient presumably had coronary arteriosclerosis. When hypotension and shock followed hemorrhage, the blood flow to the entire heart became inadequate. The cells of the epicardial region were inactivated, so that the positive potential normally yielded by these cells was replaced by a negative potential transmitted from underlying regions. When the nourishment of the epicardium was improved by raising the blood pressure, the epicardial cells resumed their normal electrical activity, giving rise to an R wave. Hence the evanescent occurrence of QS waves may represent coronary insufficiency involving the epicardial region. This electrocardiographic phenomenon is not rare, even in the absence of shock.
Example 3. QS and/or QR deflections recorded over anterior infarcts often are replaced by R waves with the onset of a superimposed posterior infarction. Since the posterior lesion could weaken but not reverse the negative cavity potential, viable muscle within the anterior infarct must be responsible for the restoration of the precordial R wave. As hypothesized by Barker, 16 living tissue within the necrotic zone may produce positive voltages strong enough to obliterate QS and QR deflections when the posterior opposing forces are removed. Thus the QS wave originally recorded over the anterior infarct must be of the mural type.

Example 4. In patients with QS waves in all precordial leads, changes in the amplitude and direction of the T wave frequently occur either spontaneously after myocardial infarction or as a result of exercise or ischemia. Such variations in the T wave appear to be independent of variations in cavity potential and therefore may represent repolarization changes occurring in viable muscle within the infarcted ventricular wall. As demonstrated experimentally, T-wave changes could not be produced at the surface of infarcted regions containing only dead muscle, but were commonly observed over regions of patchy infarction which yielded mural-type QS deflections.

Example 5. In serial electrocardiograms recorded following coronary occlusion, QRS changes often do not occur until several weeks after the onset of S-T and T-wave abnormalities. The belated appearance of the coronary QS wave generally is accompanied by new clinical signs or symptoms, and the patient’s condition may show uninterrupted improvement. In view of the clinical picture, it is improbable that the ventricular musculature depolarizes in an entirely normal manner for several weeks after occlusion, then suddenly develops a “hole” extending from endocardium to epicardium. A more logical explanation is that the deeper layers of the ventricle become electrically inactive without producing QRS alterations; only when prolonged ischemia finally causes muscle death or severe damage in the epicardial region is the normal R wave replaced by a coronary QS wave. This explanation is consistent with the observation that necrosis following coronary occlusion begins in the subendocardial region, which is farthest from the blood supply, and extends gradually toward the epicardial surface. 19 Thus the abrupt appearance of the QS waves without associated clinical changes presumably results from inactivation of the epicardial zone of positivity rather than sudden death of the entire thickness of the ventricular wall.

Summary

Experimentally produced myocardial infarction in 41 dogs has been studied by means of multiple precordial leads as well as direct leads from the epicardial surface, from several depths within the ventricular wall, and from the ventricular cavity. Intramural and cavity tracings were obtained with a specially designed “plunge” electrode. In 19 animals, high-speed cinematographs of the left ventricle were recorded simultaneously with epicardial leads. Finally, the electrocardiographic and cinematographic findings were correlated with histologic observations of the infarcted region.

Two types of QS deflections were recorded in direct leads from the surface of transmural infarcts. Electrocardiographic, cinematographic and histologic findings associated with the first type of surface QS wave established the absence of viable tissue in the subjacent myocardium and indicated that the negative surface potential was transmitted unaltered from the underlying cavity. The second type of surface QS wave was found only over infarcted regions containing islands of surviving muscle which at least partially determined the surface potential. Depending upon the amount of viable muscle present in the underlying region, the second type of QS wave was derived almost entirely from the cavity potential, entirely from intramural potentials, or from a variable mixture of cavity and intramural potentials. The first type of QS wave occurred most frequently over large, chronic infarcts, while the second type was more commonly observed over small lesions of recent origin and over the margins of larger infarcts. Several clinical cases illustrating the occurrence of QS waves over regions containing viable muscle are described.

Coronary QR waves were found only over regions of transmural infarction composed of a mixture of viable and necrotic or fibrotic tissue involving the epicardium. This pathologic picture was consistently present whether the QR deflection occurred over all portions of the infarct or only at the margins. Chronic subendocardial infarcts and acute lesions which did not involve the epicardial surface consistently failed to yield QR waves in precordial or epicardial leads.

The distribution of depolarization potentials in normal ventricles has been determined by means of multiple intramural and intraseptal leads. Approximately 80 per cent of the ventricular musculature exhibited predominantly negative depolarization potentials; positive po-
tentials prevailed only in a relatively thin epicardial layer of the ventricular wall and in the middle and right side of the septum. Burning or excision of the epicardial region of positivity drastically diminished the amplitude of the surface R wave or actually produced a surface QS wave. These findings, coupled with the consistent absence of QRS abnormalities in tracings recorded over infarcts not involving the epicardial region, are believed to indicate that leads facing the intact epicardium yield a fairly accurate representation of epicardial potentials and do not reflect the status of the large mass of underlying intramural muscle. The clinical implications of this conclusion are discussed.

**SUMARIO ESPAÑOL**

Por medio de pequeños electrodos intramurales en profundidades múltiples de la pared ventricular, potenciales fueron registrados en infartos del miocardio y en corazones normales. En 41 animales con oclusión coronaria, correlación electrocardiográfica e histológica indicó que las deflecciones QS coronarias pueden ser representadas por potenciales negativos transmitidos desde músculo intramural viable como así de la cavidad. Deflecciones QR fueron obtenidas sobre infartos transmurales que contenían una mezcla de tejido viable y muerto, pero no sobre lesiones puramente subendocardiadas. En el ventrículo normal, potenciales positivos de depolarización predominan grandemente sobre los potenciales negativos. Aplicaciones clínicas se discuten.

**REFERENCES**


Intramural Depolarization Potentials in Myocardial Infarction: A Preliminary Report
MYRON PRINZMETAL, S. REXFORD KENNAMER, CLINTON MCK. SHAW, JR.,
NOBORU KIMURA, INGA LINDGREN and ALFRED GOLDMAN

Circulation. 1953;7:1-14
doi: 10.1161/01.CIR.7.1.1

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on
the World Wide Web at:
http://circ.ahajournals.org/content/7/1/1

An erratum has been published regarding this article. Please see the attached page for:
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CHRONIC DISEASE PROCEEDINGS

The complete Proceedings of the Conference on Preventive Aspects of Chronic Disease held in Chicago on March 13–14, 1951, have recently been published. Copies may be obtained from the Health Publications Institute, Inc., Raleigh, N. C. The American Heart Association was one of the participating organizations in the Conference, which was sponsored by the Commission on Chronic Illness. The Association, with the National Heart Institute, drew up a Statement on Cardiovascular Diseases, which is included in the printed Proceedings.

TRIBUTE TO FRANK N. WILSON

A tribute to the late Frank N. Wilson has been received from the International Society of Cardiology through its Secretary-General, Dr. Pierre W. Duchosal. The statement reads:

"In 1950 the International Society of Cardiology nominated Frank N. Wilson, as honorary member, the first time such an honour was bestowed. This choice reflected a tacit testimony of cardiologists the world over for the work of this savant who was the genial constructor of modern electrocardiography.

"His death deprives the cardiology world of one of its most eminent pioneers.

"The Committee of the International Society of Cardiology in the name of its member Societies extends to Mrs. Frank N. Wilson its profound sympathy."

COURSE ON CONGENITAL AND RHEUMATIC HEART DISEASE

The Cook County Graduate School of Medicine announces a two-week intensive course on "The Diagnosis and Treatment of Congenital and of Rheumatic Heart Disease in Infants and Children," presented by Benjamin M. Gasul, M.D. and Egbert H. Fell, M.D., and associates, from May 18 to May 30. A circular giving full information may be obtained from the Registrar, Cook County Graduate School of Medicine, 707 South Wood Street, Chicago.

MEETINGS

Apr. 8–12: Twenty-Ninth Annual Meeting, American Heart Association, Hotel Chelsea, Atlantic City, N. J.

Apr. 8–9: Assembly panels, Assembly meeting, meeting of the Scientific Council, American Heart Association, Hotel Chelsea, Atlantic City, N. J.

Twenty-Sixth Scientific Sessions, American Heart Association, Hotel Chelsea, Atlantic City, N. J.

Apr. 13–17: American College of Physicians, 34th Annual Meeting, Hotel Chelsea, Atlantic City, N. J.


Apr. 23–25: 1st Western Hemisphere Conference of World Medical Association, Richmond, Va. Secretary-General, Dr. Louis H. Bauer, World Medical Association, 2 East 103rd Street, New York 29.

May 3: National Meeting, American Federation for Clinical Research, Steel Pier, Atlantic City, N. J. Convention headquarters at Hadlon Hall Hotel. National Secretary, Dr. Lawrence E. Hinkle, Jr., M.D., 525 E. 68th St., Room F-611, New York 21, N. Y.

May 7–10: National Congress of Cardiology, Sevilla, Spain. Secretary, Dr. E. Benot, 3 Paseo de las Delicias, Sevilla, Spain.

May 15–16: Annual Spring Meeting, Council for High Blood Pressure, Cleveland, Ohio.

CORRECTION: In the paper entitled “Intramural Depolarization Potentials in Myocardial Infarction: A Preliminary Report,” by Prinzmetal, Kennamer, Shaw, Kimura, Lindgren and Goldman, published in the January 1955 issue of Circulation, one statement requires correction. In the next to last sentence of the foreword, it is stated: “In the normal ventricle, positive depolarization potentials greatly predominate over negative potentials.” This sentence should read: “In the normal ventricle, negative depolarization potentials greatly predominate over positive potentials.”