Reprinted from AMERICAN HEART JOURNAL, St. Louis
Vol. 61, No. 3, Pages 303-314, March, 1961 (Printed in the U. S. A.)

The electrocardiogram in normal and some abnormal conditions

In revived human fetal heart and in acute and chronic coronary occlusion

D. Durrer, M.D.
P. Formijne, M.D.
R. Th. van Dam, M.D.
J. Büller, M.D.
A. A. W. van Lier, M.D.
F. L. Meyler, M.D.
Amsterdam, Netherlands

Nearly 55 years ago a telephone wire connecting Einthoven's laboratory with the internal clinic, made it possible to register electrocardiograms from patients. After some time this connection was severed by the clinician. It must have been a strange idea indeed that a machine could give information about the patient not detectable from direct contact with the patient. In many respects this interruption may be considered a symbolic action. Electrocardiography as a part of physiology, and electrocardiography as a part of clinical medicine had to go a separate way for a long time before reunion took place.

The group I represent here is nearly completely composed of persons interested in clinical medicine. Our work started in 1947, with the study of the transmural and intramural potentials in the dog and the goat. But our main target, the human heart, was not accessible. Only in the last year did we find a method suitable to investigate the exposed heart of the human being in a satisfactory way.

Experimental approach

A. Heart. The explorer of the electrical aspects of the heart is faced with many difficulties. How can he accomplish his main purpose, the unraveling of cardiae excitation, in such a way that his approach does not change the phenomena he wants to investigate? Two lines of approach are possible. One means is exposition of the heart by thoracotomy. Probably the complexes registered from the exposed heart are not identical with the complexes from the heart in the intact thorax. The second approach is the Langendorff perfusion of the isolated heart, a method which for the human heart was used for the first time by Zbyszewski[1] and perfected by Boden and Neukirch.[2]

B. Electrodes. Three kinds of electrodes were used. (1) Differential electrodes to record local phenomena. This type of

From the Department of Cardiology and the Department of Internal Medicine, University of Amsterdam, Wilhelmina-Gasthuis, Amsterdam, Netherlands.
These investigations were supported by grants from the Netherlands Organization for Pure Research (Z. W. O.).
Received for publication Nov. 8, 1960.

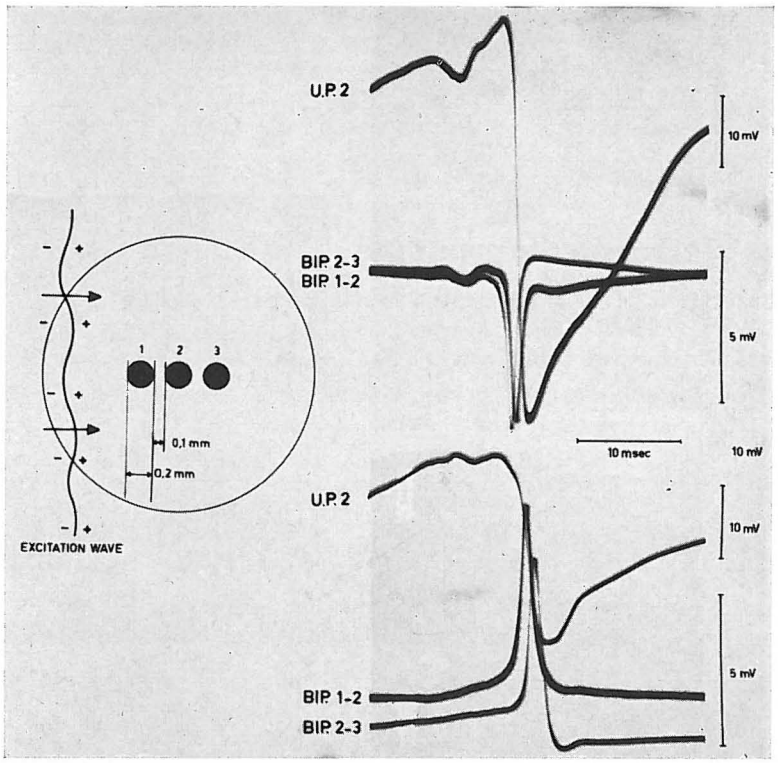

Fig. *1*. Three terminals, *1*, *2*, *3*, a distance of 0.1 mm. apart, were placed on the epicardial surface of the heart, in a region in which the excitation wave progresses from terminal 1 to 3. A point on the fast portion of the intrinsic deflection in unipolar complex from the middle terminal coincides with the point of intersection of the bipolar complexes.

electrode consists of two electrodes lying very close together, for example, 0.1 millimeter apart. (2) Small tipped unipolar electrodes for extensive exploration of the epicardial and endocardial surfaces of the heart. (3) Intramural needle electrodes.

Apparatus. A four-channel high-fidelity oscillograph with separate recording and viewing tubes was used.

Intrinsic deflection and local excitation. Our previous investigations[3,4] have shown that the electrical effects of local excitation can be best studied by means of differential electrodes. It can be demonstrated, however, that the electrical effects of local excitation can frequently be discovered in the unipolar records. A differential electrode with three terminals at a distance of 0.1 millimeter was placed on the epicardial surface on an area where the excitation process spreads from 1 to 3 (Fig. 1). The complexes between 1-2 and 2-3 are very similar. The intersection of bipolar complex 1-2 with complex 2-3 signals the arrival of the excitatory wave at terminal 2, coinciding in the unipolar record with a point on the rapid part of the intrinsic deflection. For the measurement of time relations, only the rapid portions in the complexes are used.

Contrary to the opinion of some investigators, we found that the location in the QRS complex of the electrical effects caused by local excitation is not constant. It may differ in complexes from different areas of the heart (Fig. 2). The effects of local excitation are represented by a fast deflection which may occur near the middle of the downstroke of the R, near the top of the S. On the ascending limb of the S it may appear as a negative going potential. In some areas, mainly on the posterior wall, we even found the effects of local excitation on the ascending limb of the Q.

Total excitation of dog heart

Total excitation of the heart of the dog, the experimental animal commonly used, is now rather well known.[3,5-7] I will comment on only a few points. During the study of the sinus node and A-V node, we were impressed by the sensitivity of these structures to pressure of the exploring electrode. Even slight pressure on the sinus node caused disappearance of the multiphasic electrical activity, specific for these structures. The introduction into the sinus node of a needle electrode of the type we used caused a complete disappearance of multiphasic activity.

Specific tissues of heart. The electrical activity of the main branches of the bundle of His can be seen as multiphasic deflections preceding the cavity potential.

The pattern recorded in the subendocardial branches of the Purkinje system is somewhat different; mostly only one or two spikes are found. We could find no appreciable delay between the spikes caused by activity of the Purkinje fiber and the beginning of the myocardial depolarization complex after the Purkinje depolarization.

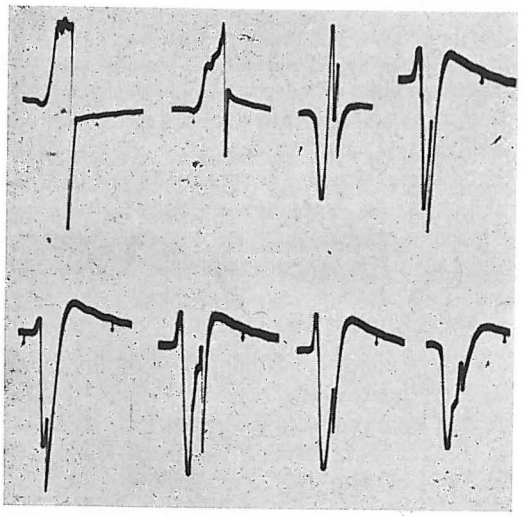

Fig. 2. Different locations of intrinsic deflection in QRS complexes. Unipolar complexes from different regions of the revived heart of a 7-month-old human fetus. The effect of local excitation can occur in the downstroke connecting top R with nadir S, near the top of the S, on the ascending limb of the S and ascending limb of a QS complex registered from the posterior side.

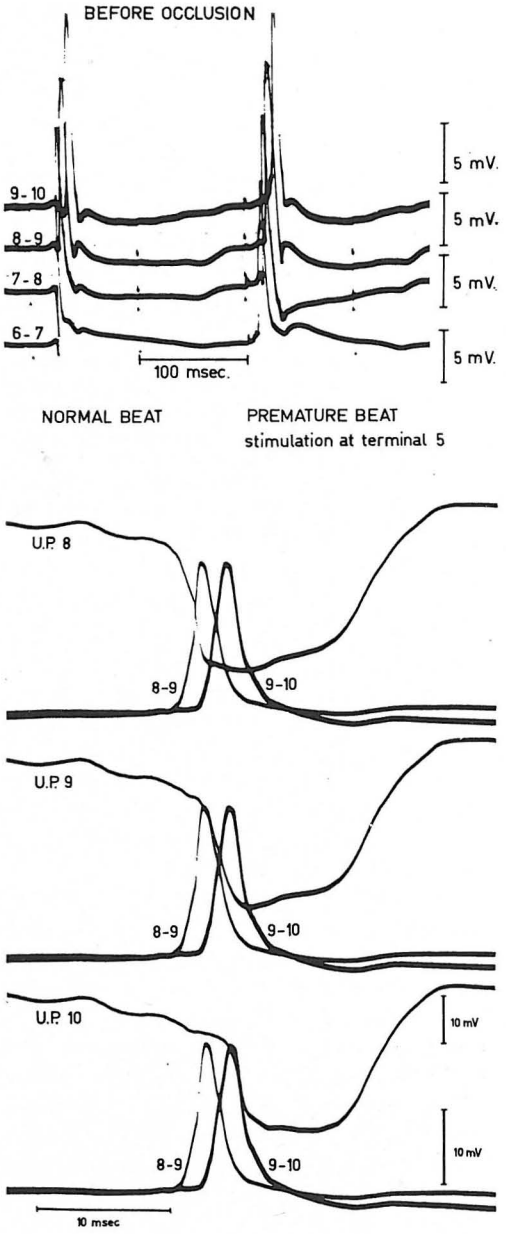

Fig. 3. *Top:* Bipolar complexes during normal beat, followed by premature beat caused by stimulation of terminal 5, situated in the subendocardial layer. *Bottom:* Bipolar complexes in outer layers of ventricular wall with unipolar complexes from the terminals between which the bipolar complexes were recorded. The intrinsic deflection in unipolar complex 8 is synchronous with the fast portion in upstroke of bipolar complex 8-9. In unipolar complex 9 the intrinsic deflection is synchronous with the intersection of the downstroke in 8-9 and the upstroke in 9-10. In unipolar complex 10 the intrinsic deflection is synchronous with the downstroke in 9-10. The duration of the bipolar complexes is approximately 5 milliseconds.

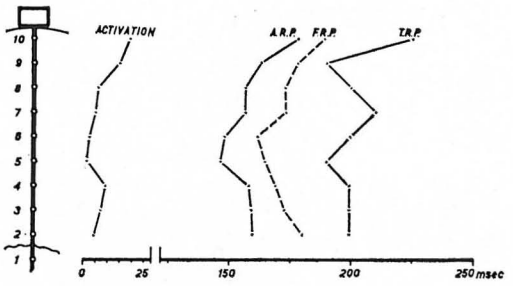

Fig. 4. The time of activation in the intramural layers was measured by the time of occurrence of the intrinsic deflection in unipolar and bipolar records. *A.R.P.* is the absolute refractory period. *T.R.P.* is the total refractory period, the duration until cardiac excitability has regained the diastolic level. *F.R.P.* is the functional refractory period, the period after which the myocardium is capable of conducting a propagated excitation wave. The time course of F.R.P. rather closely follows activation time.

The Purkinje system distributes the excitatory wave in 5 to 10 milliseconds to all subendocardial parts of the ventricles.

The question of the presence of intramural extension and the degree of intramural extension of the Purkinje network is not solved. In previous experiments, we gave only indirect evidence for the existence of an intramural network of the inner layers of the ventricular wall in the dog. For many years we looked for evidence of electrical activity of the Purkinje system in the left ventricular wall, but never found it. We did find it, however, in the goat. Here we could record Purkinje activity preceding the muscular depolarization complex in bipolar intramural records at different intramural layers, even in the subepicardial layers. The intramural extension of the Purkinje network is proved conclusively by Meyling and Ter Borg.[8,9]

Intramural excitation. In the outer layers of the ventricular wall the excitatory process progresses with nearly constant velocity, approximately 50 cm. per second, toward the epicardial surface. The region in which depolarization takes place appears to be very sharply defined. The electrical effects caused by this wave can be represented by a polarized surface. The distance between sources and sinks is 1 mm. maximum. The drop in potential across this wave is at least 15 mV. (Fig. 3).

Ventricular septum. The ventricular septum is activated from both sides.[10-12] No functional boundary between the portion supplied by the right and left bundles can be demonstrated.[10] The basal regions of the septum are activated latest in the cardiac cycle; therefore, the excitation wave in the ventricular septum progresses in an apico-basal direction.

The excitatory process in both ventricles progresses toward the posterobasal region, which is activated latest in the cardiac cycle.

Repolarization. The pathway of the repolarization process cannot be investigated with the methods so successfully applied in the analysis of the depolarization process. Opening of the thorax changes the T waves. Because of the gradual character of the repolarization process the arrival of this process at the exploring terminals cannot be identified. We have tried to follow the pathway of the repolarization process, using the duration of the functional refractory period (F.R.P.) as a measure of the time necessary to restore cardiac excitability. At the end of the F.R.P. the myocardium resumes its ability to propagate an excitatory process. Since we could prove that at this particular moment the stimulating requirements are one and one-half times the diastolic level, the duration of the F.R.P. can be measured readily from strength interval curves.[13] The duration of the total refractory period, however, cannot be determined accurately. The duration of the F.R.P. shows slight differences in the successive layers of the ventricular wall: up to ± 15 milliseconds. It can be seen (Fig. 4) that the end of the F.R.P. follows more or less closely the pathway of depolarization.

Intact human heart

The clinical cardiologist is mainly interested in the excitatory process of the normal and pathologic human heart. Even in this era of cardiac surgery, adequate analysis of the human heart is difficult, and mostly impossible. An extensive analysis of the human heart during operation takes such a long time that the safety of the patient may be jeopardized. Therefore, we used the Langendorff perfusion of the revived human heart.[1,2]

Reviving. We immersed 3 fetal hearts, each 7 months old, in a large container and

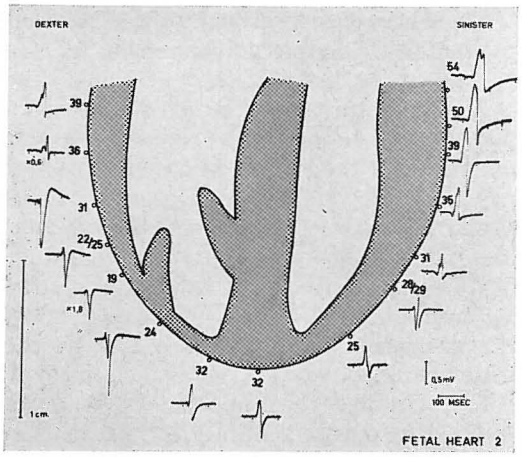

Fig. *5A*. Sagittal section of the ventricles just to the left of the ventricular septum. The numbers indicate the time of arrival, in msec., of the excitatory wave at the epicardial surface. Reference: beginning of ventricular depolarization.

used as reference electrode a large one situated at least 8 cm. from the heart. Therefore, the potential fluctuations of the reference electrode are very small in comparison with those of the exploring electrode, and the records may be called "unipolar." The perfusion fluid had no oncotic pressure, so that slight swelling of the heart, caused by interstitial edema, occurred. Boden's and our own experiments support the conclusion that the excitatory process of the heart in situ and that of the isolated heart are very similar. Records were made from 100 or more points in all hearts, and after the experiment these points could be identified on the epicardial surface of the heart.

Form of epicardial complexes.[14] There are no typical patterns for the left or right ventricle. Complexes of the rS type are found near the attachment of the anterior papillary muscle of the right ventricle, but also at the anterior surface of the left ventricle (Fig. 5).

Complexes of the qR type are present on the left ventricle, on two areas, e.g., the anterolateral portion of the left ventricle and the high posterobasal area near the left atrium. But qR complexes are also found on the right ventricle, on the left lateral and high anterolateral area and the posterobasal area. These complexes show initial negativity. We may conclude that the patterns which up to now have been considered typical for the right ventricle and left ventricle are also found on some portions of the heterolateral ventricle.

The form of the epicardial complexes at corresponding anatomic areas shows a striking correspondence. I may mention the opinion of Boden and Neukirch,[2] after their experiments on the isolated human heart, that the differences in the electrocardiograms of normal persons are probably caused mainly by extracardiac factors.

The posterior and lateral surfaces of the left ventricle show Q waves, as could be expected. But also the posterior surface of the right ventricle shows initial negativity. The area showing Q waves is located, therefore, at the posterior and lateral parts of both ventricles.

These Q waves all begin at the same time in the cardiac cycle and probably at the beginning of the left ventricular cavity potential. Their depth varies. The Q is deepest about one third of the way from apex to base. The deepest Q waves all are present on the posterior attachment of the ventricular septum and near the attachment of the posterior papillary muscles of the right and left ventricles (Fig. 6).

To demonstrate this relation in still another way, a section was made in the left ventricle, parallel with the ventricular septum and just to the left of it (Fig. 5*B*).

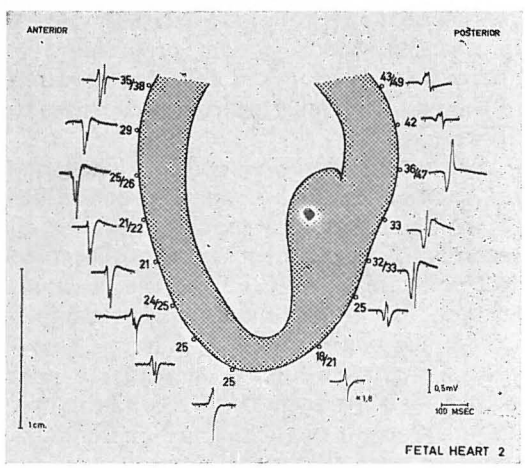

Fig. *5B*. Frontal section of the ventricles just to the left of the ventricular septum. The numbers indicate the time of arrival, in msec., of the excitatory wave at the epicardial surface. Reference: beginning of ventricular depolarization.

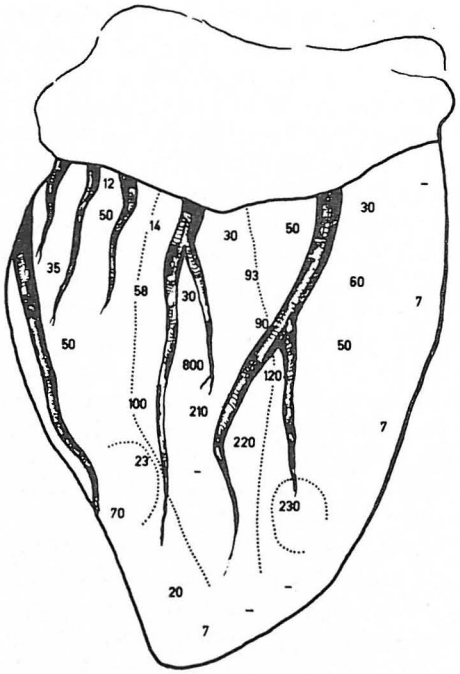

Fig. 6. Posterior view of the fetal heart. The numbers indicate the depth of the Q wave (in microvolts) in unipolar complexes from these places. Deepest Q waves are present one half of the way from apex to base, in the area overlying the posterior attachment of the ventricular septum. The attachment of posterior papillary muscles is indicated too.

The relation of the Q and the papillary muscle is evident. It is probable, therefore, that two factors, at least, contribute to the genesis of the Q wave: (1) excitatory wave in the ventricular septum progressing in an apico-basal direction, and (2) activation of the papillary muscles from their bases to apex.

Epicardial excitation pattern. The time of occurrence of the intrinsic deflection, if well developed, was measured in all records. All measurements were corrected to the beginning of the Q at the posterior surface. The times of arrival were grouped in 5-millisecond intervals. The first epicardial break-through occurs at the area trabecularis. At each 5-millisecond interval an enlargement of the epicardial area activated is seen. The anterior and posterior attachments of the ventricular septum appear to form no boundary for the epicardial excitation wave. Epicardial excitation occurs latest in the posterobasal region of both ventricles.

Elsewhere we described epicardial excitation as a double envelopment of the surfaces of both ventricles.[14]

Many years ago, Lewis[15] published a figure representing his considered view on excitation of the human heart. It is evident from Fig. 5*A* that there is a remarkable similarity between Lewis' considered view and our findings.

These conclusions are valid only for the 7-month-old fetal heart. We hope to repeat these experiments in the adult heart in the near future.

Let us now turn to abnormal excitation. Because of our clinical interest, we studied the changes occurring during acute coronary occlusion and in myocardial infarctions, 4 to 14 weeks old.

Acute coronary occlusion

Epicardial excitation pattern. In the ischemic area, all epicardial complexes show S-T elevations and abnormal Q waves. In contrast, epicardial excitation of the normal tissue surrounding the ischemic area remained constant up to 12 hours after the beginning of occlusion, i.e., up to the end of the experiment.

The epicardial surface of the ischemic area is activated late, up to 50 milliseconds, in the cardiac cycle. This delay is caused

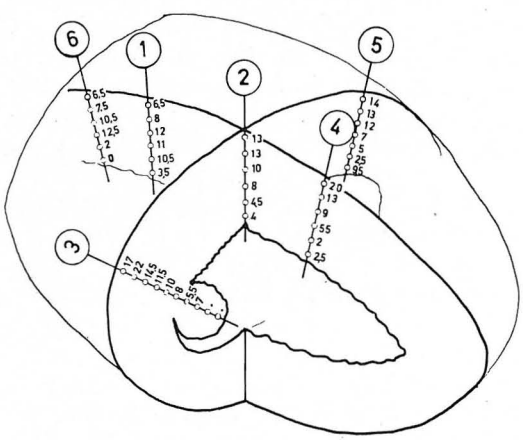

Fig. 7. Coronary occlusion during 2-3 hours. Spatial view of two cross sections of the left ventricle. The numbers at the epicardial surface indicate the needle electrodes. The smaller numbers at the intramural terminals indicate the degree of S-T shift measured (in mV.) immediately after ventricular depolarization. Needle electrodes *2*, *3*, *4*, and *5* have the highest degree of S-T shift in the subepicardial layer.

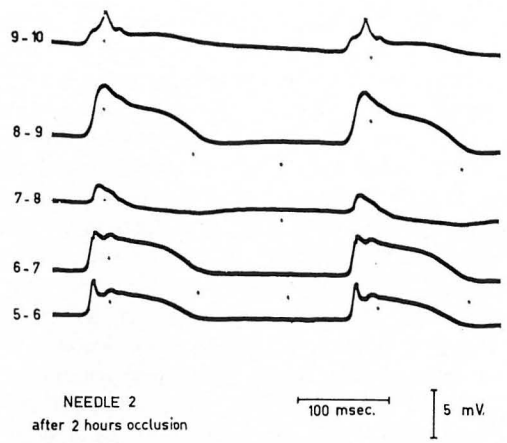

Fig. *8*. Intramural bipolar complexes 2 hours after beginning of coronary occlusion. The complexes show a large reduction in voltage and are notched. The S-T shift present points to the presence of a gradient of injury, making the outer layer positive in respect to the inner one.

by the decrease in conduction velocity of the excitatory process in the ischemic area.

The occurrence of premature beats during coronary occlusion is well known. In one case in which we followed the changes in electrical activity during coronary occlusion for 12 hours, premature beats occurred which showed a constant form of the epicardial and intramural complexes. They were presumably caused by activity of a constant focus. Because these premature beats remained present for a few hours, a complete epicardial excitation pattern could be recorded. The excitatory wave from this focus had the earliest epicardial break-through at a region which appeared to lie on the boundary of the infarcted area. Therefore, the focus was situated in the area of transition between the ischemic and normal myocardial tissue.

Intramural excitation pattern. In all instances, S-T-segment elevation was present in all unipolar leads from intramural terminals situated in the ischemic area, but the degree of S-T shift varied (Fig. 7). The S-T shift was measured at the end of ventricular depolarization in the ischemic area. At many places, maximal S-T shift was present in the subepicardial layers (needle electrodes 2, 3, 4, 5), and at other places in the mid-mural layers (needle electrode 6). A few hours later, S-T shift at needle electrode 2 was maximal in the subendocardial layers.

In the intramural layers of the ventricular wall surrounding the ischemic area, we could never reach a negative side of the boundary responsible for the S-T shift. S-T depression, however, was always found in the left ventricular cavity at the opposite side of the heart. We think that a sharply defined boundary is not present, but that there is a very gradual transition between injured and noninjured fibers.

Bipolar intramural complexes. During occlusion, the bipolar complexes registered between successive intramural terminals changed profoundly, but the observed changes did not follow a constant pattern.

The diameter of the coronary vessel occluded varied in different dogs, and the role of the collateral circulation responsible for the maintenance of a reduced blood supply could not be ascertained. It is not possible, therefore, to give an adequate description of the changes of the excitatory process as a function of the changes in blood supply.

The bipolar complexes may change in different ways. In some cases, only broadening of the bipolar complex was found. In

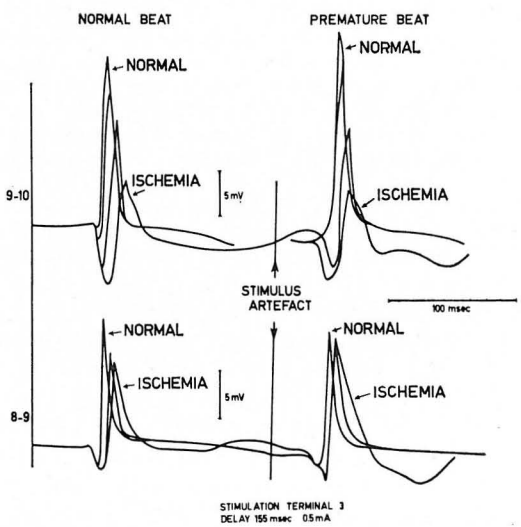

Fig. *9*. Bipolar complexes 8-9 and 9-10. The complexes labeled *ischemia* were recorded 5 minutes after beginning of coronary occlusion. A negative deflection precedes a small and broad positive deflection, falling late in the cardiac cycle. They retain their form during endocardial stimulation. The complexes labeled *normal* were recorded 22 seconds after release of coronary occlusion. The transition of the abnormal complexes to normal, intramural complexes can be clearly seen.

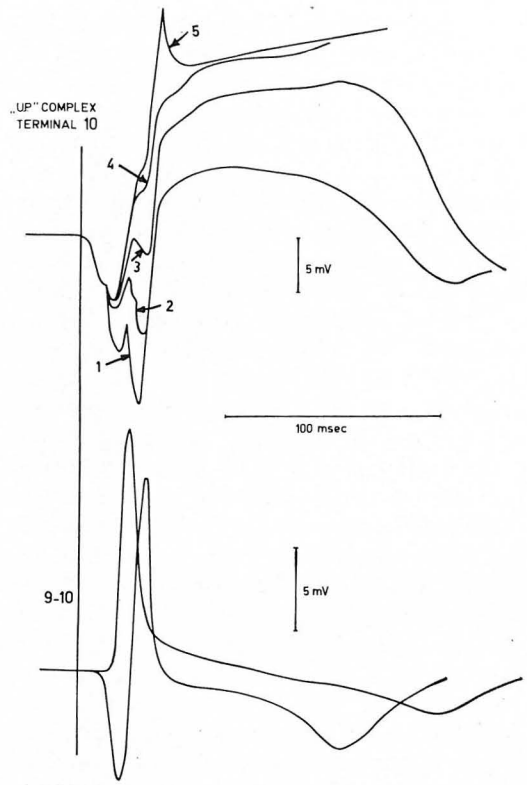

Fig. *10*. Changes in complexes during progressive coronary ischemia. Complex *1* was recorded 15 seconds after beginning of coronary occlusion; complex *2*, 60 seconds; complex *3*, 100 seconds; complex *4*, 120 seconds; complex *5*, 225 seconds after beginning of coronary occlusion. The arrows indicate the location of the intrinsic deflection. Bipolar complex 1 was registered synchronously with unipolar complex 1, complex 2 synchronously with unipolar complex 5. The downstroke of the "R" in unipolar complex 5 occurs synchronously with the downstroke in 9-10, and is caused by excitation of muscle layers in contact with terminal 10.

other cases, there was a loss of voltage in the bipolar complexes, but this change was always associated with broadening of the bipolar complexes. Fig. 8 is a typical illustration. The complexes are broad and show loss of voltage, notching, and S-T shift. The broadening of these complexes is caused by a diminished conduction velocity of the excitatory process in the ischemic area—sometimes 10 cm. per second or less. The loss of voltage can possibly be related to a reduction of the membrane action potential. The notching may be caused by the fact that the muscle fibers in the ischemic area are not changed to a similar degree by anoxia, and do not conduct the excitatory process at the same rate.

Sometimes, and most frequently after the occlusion of a major branch or after prolonged occlusion of the coronary vessel, complexes of a perplexing form are found (Fig. 9, complex labeled *ischemia*). These bipolar complexes show a large reduction in voltage of the R, and a large negative wave precedes the "R." Sometimes this R wave may disappear and the complex is completely negative.

Bipolar complexes of this type may even be present in successive layers of the ventricular wall. The changes which occur after restoration of blood supply may shed some light on the genesis of these complexes (Fig. 9). It can be seen that the depth and duration of the negative wave diminish. Simultaneously the positive deflection increases in voltage and also falls progressively earlier in the cardiac cycle. After 20 to 30 seconds it is very high again and only a small negative wave precedes the positive deflection: the complex has regained its preocclusion form. It is an astonishing fact that the disappearance of the ischemic complexes occurs very rapidly, mostly within one-half to one minute, after the coronary circulation has been re-established. During that period, multiple ventricular premature beats frequently occur. Many experiments terminated in ventricular fibrillation during that period.

It is possible that these bipolar complexes are caused by an increase in distance between sources and sinks of the polarized surface which represents the electrical effects of excitation.

Changes in unipolar epicardial and intramural complexes. During acute occlusion the form of the QRS complex, of the unipolar epicardial complexes, [6,16,17] and, as we could prove, also of the intramural complexes, changes in the following manner: (1) decrease in voltage of S, sometimes even disappearance of the S; (2) a gradual delay in the onset of the intrinsic deflection; (3) decrease of the voltage and duration of the intrinsic deflection; and (4) perhaps complete disappearance of the intrinsic deflection.

Fig. 10 depicts the changes in the form of the unipolar intramural complex during coronary occlusion. The intrinsic deflection demonstrates the changes just described.

In the complex 4 the intrinsic deflection has disappeared; only a small notch is present on the ascending limb of the monophasically deformed complex. One might be led to conclude that the excitation wave does not reach this terminal anymore.

However, because the bipolar complex 9-10 shows a downstroke caused by excitation of 10, this conclusion is wrong. Therefore the disappearance of the intrinsic deflection does not necessarily mean that no excitation of the ventricular muscle in contact with the exploring terminal occurs. With prolonged ischemia the upstroke increases and upright deflection of short duration appears (complex 5, Fig. 10), followed by a slow downstroke coinciding with the last portion of the descending limb of the bipolar complex 9-10. This deflection in the unipolar complex, therefore, is caused by local excitation at terminal 10.

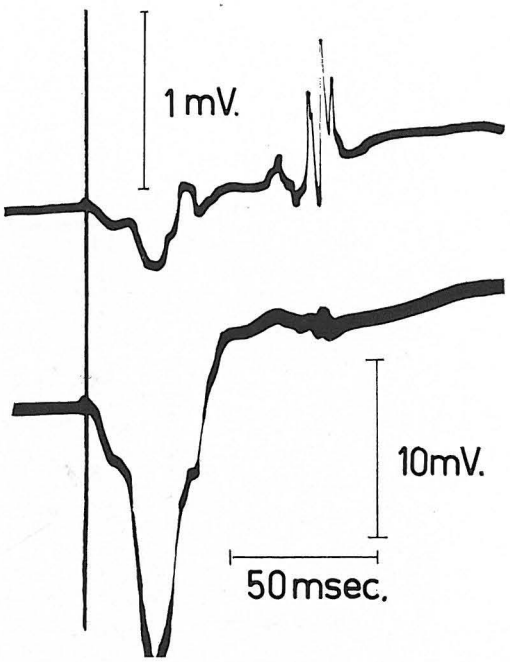

Fig. *11.* Differential complex (*upper record*) synchronous with unipolar complex (*lower record*) from one of the terminals of the differential electrode placed on the epicardial surface of a transmural infarction. The small deflections which occur 75 milliseconds after the beginning of QRS are caused by excitation of tissue in contact with the differential electrode.

Chronic myocardial infarction

In 1934, an important paper by Wilson, Johnston and Hill[18] was published which forms the basis of much of our knowledge about the electrocardiographic changes in myocardial infarction.

Since the excitatory process spreads from the endocardial surface to the outer layers, it is difficult to see how it can reach the outer layers when the inner layers are dead or replaced by scar tissue. The aforementioned authors were unable to understand how the excitatory process can cross the infarcted tissue unless they supposed that this tissue is penetrated by living Purkinje fibers or by surviving strands of ordinary muscle.

With the methods outlined at the beginning of this lecture, this important problem was tackled. Epicardial and intramural excitation patterns were investigated.

Epicardial excitation. The epicardial excitation pattern in myocardial infarction was changed profoundly. The unipolar complexes showed definite abnormalities, even if the infarction was situated in the subendocardial layers. Up until now we have not encountered a situation in which an infarction of the subendocardial region did not result in an abnormal epicardial complex. The major change in the QRS complex was the occurrence of abnormal

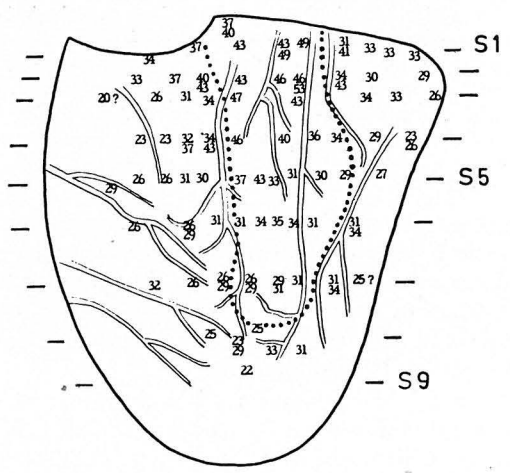

Fig. *12.* Activation time (msec.) of epicardial surface in myocardial infarction. The epicardial surface above the subendocardial infarction, indicated by the dotted line, is activated late in the cardiac cycle. In the region bordering the A-V groove an area is activated with only slight delay (*30*, 41 msec.) and is lying close to an area activated much later (*49*, 53 msec.). Between those two areas, fibrous tissue strands reach the epicardial surface, acting as a boundary for the crossing of the excitatory wave.

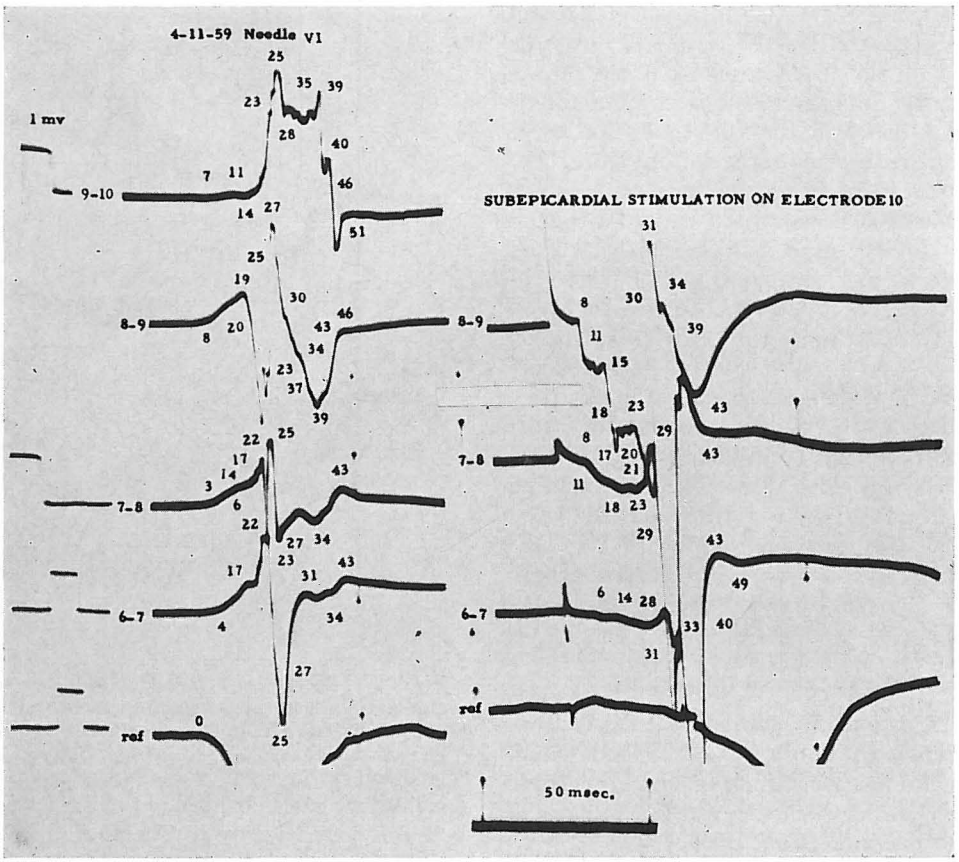

Fig. *13.* Bipolar complexes from terminals lying in the infarcted area. The voltage of the complexes is greatly reduced, multiple notches are present, and the complexes are very broad. The numbers indicate the time of occurrence of the notches and deflections after beginning of left ventricular cavitary potential. Many small excitation waves are present in this area. During subepicardial stimulation the polarity of the bipolar complexes reverses, and the complexes are grossly deformed and notched.

Q waves. Under the conditions of our experiments the normal Q wave was never deeper than 2.2 mV., and the duration from beginning to nadir did not exceed 8 milliseconds. The total duration of the Q never exceeded 12 milliseconds.

In all of the hearts with chronic myocardial infarction it appeared that the area which showed abnormal Q waves coincided rather closely with the infarcted area. The anatomic infarction, as detected by very careful microscopic examination, was only slightly smaller than the area showing changes in electrical activity.

In all cases of subendocardial infarction the beginning of the epicardial Q was synchronous with the beginning of negativity of the left ventricular cavity, suggesting the correctness of Wilson's "window theory."

The intrinsic deflection in the unipolar complexes of the area overlying the infarction was changed and sometimes difficult to recognize. In Fig. 11 the unipolar complex recorded from the epicardial surface of a nearly complete transmural infarction is shown. In the complex, small pips which occur from 75 to 80 milliseconds after the beginning of the QRS complex are seen. The duration of the main QRS complex is 50 milliseconds.

A differential electrode was placed on that area (Fig. 11). The arrival of the excitatory wave at the muscle fibers in contact with this differential electrode is signaled by the occurrence of small, fast

deflections. Therefore, the deflections in the unipolar complex are caused by local excitation of the subepicardial muscle layers. This excitation occurs late in the cardiac cycle (75 to 80 milliseconds), at the moment at which depolarization of the remainder of the heart is completed and even repolarization in a large part of the ventricles is taking place. The pathway of excitation in this area of a few square millimeters is very bizarre, but, nevertheless, the pathway is constant from beat to beat. No variations, however small, are allowed: the pathway of excitation is strictly determined.

The form of the differential complexes shows that, even in that small area, large desynchronization of excitation occurs; the excitatory wave is highly fragmented.

Time relations of the epicardial surface. Analysis of the time relations of epicardial break-through above a subendocardial infarction reveals some interesting facts. In most of the cases it occurs late in the cardiac cycle (Fig. 12).

An accurate analysis of epicardial excitation reveals that areas lying very close together may show great differences in times of arrival of the excitatory wave. In this case an offshoot of fibrous tissue from the subendocardial infarction reached the epicardial surface and acted as a barrier for the crossing of the excitatory process from the region activated early toward the neighboring region activated late in the cardiac cycle.

Bipolar intramural complexes (Fig. 13). The form of the bipolar complexes in the intramural leads was changed: (1) The voltage was reduced; sometimes a large reduction of voltage was present. (2) The complexes showed broadening and multiple notching.

They may become polyphasic. Small, fast deflections are nearly always present. In our opinion, these small deflections are caused by successive excitation of strands of muscle fibers in contact with the exploring terminals. During subepicardial stimulation the polarity of the bipolar complexes points to the presence of a highly fragmented excitatory wave, progressing in an endocardial direction.

Intramural time relations. A gradual "mopping up" process of the intrainfarction muscle fibers takes place. It takes a long time before all of the intrainfarction muscle fibers are depolarized. The excitatory waves take devious routes, but they are constant from beat to beat.

Wilson, in the paper already cited, wrote that it was the hope of himself and his colleagues that studies of the refractory period in the infarcted region would yield important information in regard to the ability of the affected muscle to respond to the excitatory process.

We measured the excitability of intrainfarction muscle fibers (Fig. 14). There appeared to be no large change for cathodal and anodal excitability, compared to normal ventricular muscles. Sometimes the diastolic threshold was somewhat higher than in normal muscle, perhaps due to short-circuiting by nonexcitable tissue.

How does the excitatory wave reach the muscle fibers in the infarcted area? We looked for evidence of Purkinje activity in the subendocardial tissue, but could only demonstrate it in a few cases. In most of these cases, Purkinje activation occurred at a normal time, at the beginning of the left ventricular cavitary potential. No delay in activation of the subendocardial Purkinje fibers could be demonstrated. In

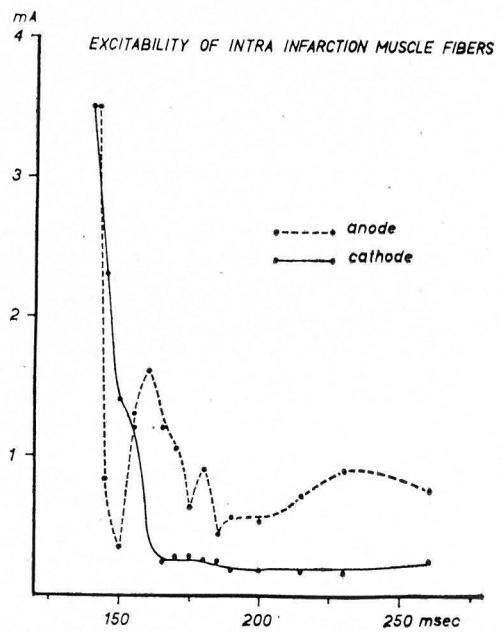

Fig. *14.* Excitability of viable muscle fibers lying in a 6-week-old infarction. The excitability of the surviving muscle fibers is nearly normal.

only one case were subendocardial Purkinje fibers activated relatively late in the cardiac cycle.

Because of the tangential excitation which may take place in the outer layers above the infarcted area, the Q/R relation does not necessarily give evidence about the degree of intramural extension of a subendocardial infarction.

The Q in subendocardial myocardial infarction is caused mainly by the reduction in voltage generated during activation of these regions. In only one case could we find evidence of a delay in transmission of the excitatory process from the Purkinje fibers to the muscle fibers.

Closing remarks

Mr. Chairman, looking back to what has been achieved with the methods given to the world by the man whose birthday we commemorate today, we are deeply impressed by the great amount of work that has been done. But looking forward, we feel humble because there is still so much to do. One point is very important. The bridge separating electrocardiography as a part of physiology from electrocardiography as a part of clinical medicine has been bridged by workers in both fields: physiologists working in one direction, clinicians, in the other one. They can at last understand what the other party is doing, because more or less they have learned to speak a common language.

REFERENCES

1. L. Zbyszewski: Beobachtungen über das Ekg. des isolierten Herzens, Aus d. physiol. Institut der Universität Lemberg.
2. Boden, E., and Neukirch, P.: Elektrokardiographische Studien am isolierten Säugetier- und Menschenherzen bei direkter und indirekter Ableitung, Pflüger's Arch. **171**:147, 1918.
3. Durrer, D., and Van der Tweel, L. H.: Excitation of the left ventricular wall of the dog and goat, Ann. New York Acad. Sc. **65**:779, 1957.
4. Durrer, D., and Van der Tweel, L. H.: Spread of activation in the left ventricular wall of the dog. II, Am. Heart J. **47**:192, 1954.
5. Scher, A. M., and Young, A. C.: Ventricular depolarization and the genesis of QRS, Ann. New York Acad. Sc. **65**:768, 1957.
6. Sodi-Pallares, D., and Calder, R. M.: New bases of electrocardiography, St. Louis, 1956, The C. V. Mosby Company.
7. Pruitt, R. D., Essex, H. E., and Burchell, H. B.: Studies on the spread of excitation through the ventricular myocardium, Circulation **3**:418, 1951.
8. Meyling, H. A., and Ter Borg, H.: The conducting system of the heart in hoofed animals, Cornell Veterinarian **47**:419, 1957.
9. Ter Borg, H.: The atrioventricular conduction system of the big domestic animals, and more especially on the terminal arborization of the Purkinje fibers and the so-called interventricular connections, Acta neerl. morphol. **4**:97, 1941.
10. Scher, A. M., Young, A. C., Malmgren, A. C., and Erickson, R. V.: Activation of the interventricular septum, Circulation Res. **3**:56, 1955.
11. Burchell, H. B., Essex, H. E., and Pruitt, R. D.: Studies on the spread of excitation through the ventricular myocardium. II. The ventricular septum, Circulation **6**:161, 1952.
12. Medrano, G. A., Bisteni, A., Brancato, R. W., Pileggi, F., and Sodi-Pallares, D.: The activation of the interventricular septum in the dog's heart under normal conditions and in bundle-branch block, Ann. New York Acad. Sc. **65**:804, 1957.
13. Van Dam, R. Th.: Over het prikkelbaarheidsverloop van de hartspier, Thesis, Amsterdam, 1960.
14. Durrer, D., Büller, H., Graaff, P., Lo, G. I., and Meyler, F. L.: The excitation of the isolated, revived human fetal heart, Circulation Res. (To be published.)
15. Lewis, Th.: The mechanism and graphic registration of the heartbeat, London, 1925, Shaw and Sons, Ltd., p. 115.
16. Wilson, F. N., Johnston, F. D., and Hill, I. G. W.: The interpretation of the galvanometric curves obtained when one electrode is distant from the heart and the other near or in contact with the ventricular surface. Part II. Observations on the mammalian heart, Am. Heart J. **10**:176, 1934.
17. Johnston, F. D., Hill, I. G. W., and Wilson, F. N.: The form of the electrocardiogram in experimental myocardial infarction. II. The early effects produced by ligation of the anterior descending branch of the left coronary artery, Am. Heart J. **10**:889, 1935.
18. Wilson, F. N., Johnston, F. D., and Hill, I. G. W.: The form of the electrocardiogram in experimental myocardial infarction. IV. Additional observations on the later effects produced by ligation of the anterior descending branch of the left coronary artery, Am. Heart J. **10**:1025, 1935.