

The Sequence of Normal Recovery of Excitability in the Dog Heart

By J. A. ABILDSKOV, M.D.

SUMMARY

The sequence with which 18 to 70 ventricular sites recovered excitability after normal excitation was determined in 15 dogs. At the epicardial level the recovery sequence was similar to that of normal activation. The sequence of excitation and recovery differed at the endocardium with some basal areas recovering excitability earlier than the apex despite later activation. Evidence of a normal epicardial to endocardial recovery sequence was also obtained. The findings are compatible with and provide a tentative explanation of some features of T waves in human body surface electrocardiograms.

THE SEQUENCE OF NORMAL VENTRICULAR EXCITATION has been defined in considerable detail and is the principal basis for interpretation of the QRS complex in the electrocardiogram.¹⁻¹¹ Comparable data for ventricular recovery would furnish a similar foundation for interpretation of the ST-T deflection. Although their significance is comparable, definition of the recovery sequence presents different problems than determination of activation order. Activation time in local cardiac areas can be identified by the rapid deflection in electrograms from closely spaced bipolar electrodes. These deflections have their origin in the rapidity with which cells pass from the resting to excited state. Recovery with its considerably slower time course is not evidenced by equivalent features in extracellular electrograms. One means of evaluating recovery sequence in the intact heart is determination of the time at which excitability to a particular stimulus is regained. In the study reported here, return of excitability was used to investigate the recovery sequence of the canine ventricles following normal excitation. This defines the sequence with which a particular stage of recovery related to excitability is reached but does not define the total time course of repolarization at any one site or in relation to other sites.

Materials and Methods

Experiments were carried out on 15 dogs anesthetized with pentobarbital, 30 mg/kg. The chest was opened in the

midline during artificial respiration. In five experiments needle-mounted electrodes were inserted into the ventricular myocardium through the pericardium. In these experiments a bipolar stimulating electrode was attached to the right atrium through a small pericardial incision. After determination of activation and recovery times with the needle-mounted electrodes, the pericardium was opened widely and the heart suspended in a pericardial cradle. Additional electrodes were then placed in the ventricular myocardium as in the other ten experiments.

In all experiments the heart was driven by atrial stimulation at a rate exceeding that of the spontaneous rhythm. The sinus node was crushed after the pericardium had been widely opened and the heart driven with a cycle length of 400 msec. Observations prior to wide pericardial incision were made while driving the heart with a cycle length of 300 msec.

Multiple electrodes were placed at various ventricular sites for determination of activation and recovery times. Needle-mounted electrodes were placed on an endocardial-epicardial axis and 2- to 10 sequential placements were made in various experiments. The needle electrode assembly consisted of 14 electrodes mounted at 1 mm intervals on a 20 gauge needle. Alternate electrodes were used to determine recovery times at seven locations on the endocardial-epicardial axis with each needle placement. Sequential pairs of electrodes were used to record seven bipolar electrograms for the determination of activation times. Wire electrodes at eight to 36 sites were also placed in various experiments. Each consisted of two helically wound strands of insulated silver wire as described in a previous publication.¹² Wire electrodes were sutured into superficial ventricular muscle or on the right ventricular endocardial surface. The wire electrodes were used in the bipolar mode for determination of activation time and one of the electrodes from each pair was used to measure recovery time. In two experiments, only subepicardial wire electrodes, and in four experiments, only needle-mounted electrodes, were used. In the other nine experiments both wire and needle-mounted electrodes were used. The number of electrode pairs used in individual experiments varied from 18 to 70.

Recovery times were determined using one electrode from each bipolar pair to deliver 2 msec duration, cathodal square wave stimuli from a constant voltage source, with the anodal electrode subcutaneously in the thoracic wall. Threshold voltage was determined for each electrode site and the time of recovery of excitability to twice threshold voltage stimuli was measured. Test stimuli were delivered

From the Cardiovascular Research and Training Institute and Cardiology Division, Department of Internal Medicine, University of Utah, College of Medicine, Salt Lake City, Utah.

Supported in part by Program Project Grant #HL 13480, Contract #NHLI 72-2988 from the National Institutes of Health, and the Richard A. and Nora Eccles Harrison Fund for Electrocardiographic Research.

Address for reprints: J. A. Abildskov, M.D., Cardiovascular Research and Training Institute, Building 100, University of Utah, Salt Lake City, Utah 84132.

Received February 12, 1975; revision accepted for publication April 25, 1975.

sufficiently early that responses did not occur and then delayed in 1 msec increments until propagated ventricular excitation resulted. Delay of the test stimulus was referenced to the basic atrial driving stimulus.

Activation times were determined by recording from the electrode pairs with a recording paper speed of 400 mm per second. Recordings were made in banks of ten and the time of occurrence of the most rapid deflections measured with reference to the artifact of the basic atrial driving stimulus.

Results

With minor and inconsistent exceptions, the recovery sequence at the epicardial surface of both ventricles was similar to that of excitation. Earliest recovery occurred on the anterior right ventricular free wall near the right ventricular apex. Successively later recovery then occurred in roughly concentric areas surrounding that of earliest recovery. There was greater variability of the epicardial recovery sequence

of the posterior than of the anterior wall. In all experiments, however, earliest recovery on the posterior was later than that on the anterior wall and recovery near the apex was complete while some areas at the base had not yet recovered excitability. In some hearts there were areas of recovery near the base equally early to those near the apex on the posterior wall.

Figure 1 shows an example of the epicardial recovery sequence on anterior and posterior ventricular walls together with the excitation sequence determined from the same electrode sites. The example shown is representative of findings in other experiments with respect to major features of the orders of excitation and recovery and their relation to each other.

Endocardial and intramural recovery sequence in the left ventricle was investigated with needle-mounted electrodes and both needle-mounted and wire electrodes were used to define endocardial recovery of the right ventricle. The possibility that some endocardial measurements were of Purkinje fibers and others of myocardium could not be excluded, but a consistent pattern of recovery in several experiments was found. In both ventricles, endocardial recovery was earlier at some locations near the base than at the apex. There were also basal areas at which excitability was recovered later than apical areas and the areas of latest recovery were consistently those with the latest activation times. Examples of findings at the endocardium in the left ventricle are shown in figure 2. Recovery times at the left ventricular base include ones both earlier and later than those at the apex. The earlier basal recovery times occurred despite later activation than that at the apex, indicating briefer intrinsic recovery periods at the base. Basal sites with the latest activation times, however, recovered later than apical sites.

The relation between the right ventricular excitation and recovery sequence on the endocardial surface also differed from the relation between the excitation and recovery sequence at the epicardium. As in the left ventricle, earliest recovery occurred at the base. Other basal areas recovered equally late or later than apical areas. An example of right ventricular recovery sequence together with the recovery sequence at the epicardial surface of the same heart is shown in figure 3.

Although the relation of recovery sequence to activation order on endocardial and epicardial surfaces was consistent, the recovery times on endocardial as compared to epicardial surfaces varied in different experiments. Most of the preparations were, however, inappropriate for study of this item. In most experiments the hearts were exposed and subject to epicardial cooling with subsequent prolongation of recovery. In five experiments in which transmural

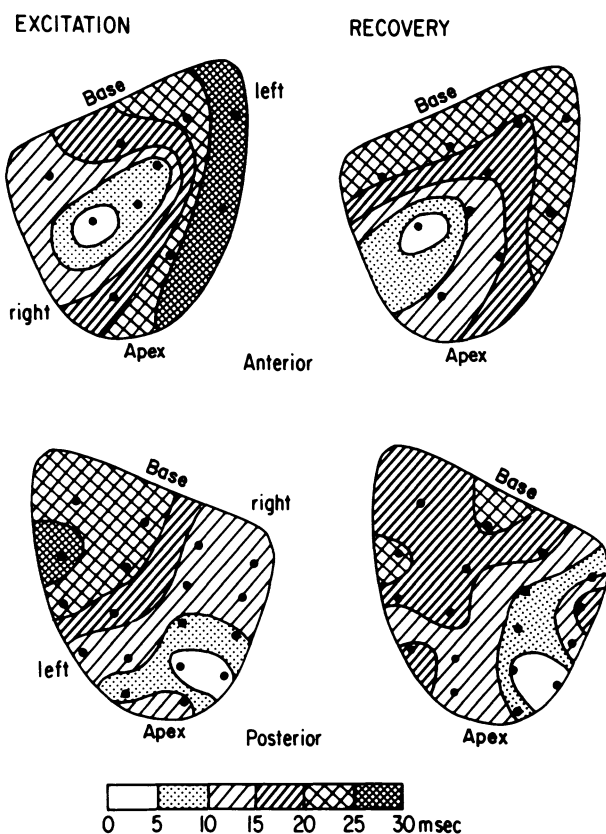


Figure 1

Epicardial excitation and recovery sequences on anterior and posterior walls in a representative experiment. The patterns illustrated are based on measurements at the 28 sites indicated by dots. Excitation times at each site were determined from the most rapid spike in electrograms recorded from the sites. Recovery times were based on the earliest propagated response to a cathodal stimulus of twice threshold intensity. Excitation and recovery patterns are shown at 5 msec intervals and earliest excitation and earliest recovery detected on the epicardial surface are each illustrated as zero.

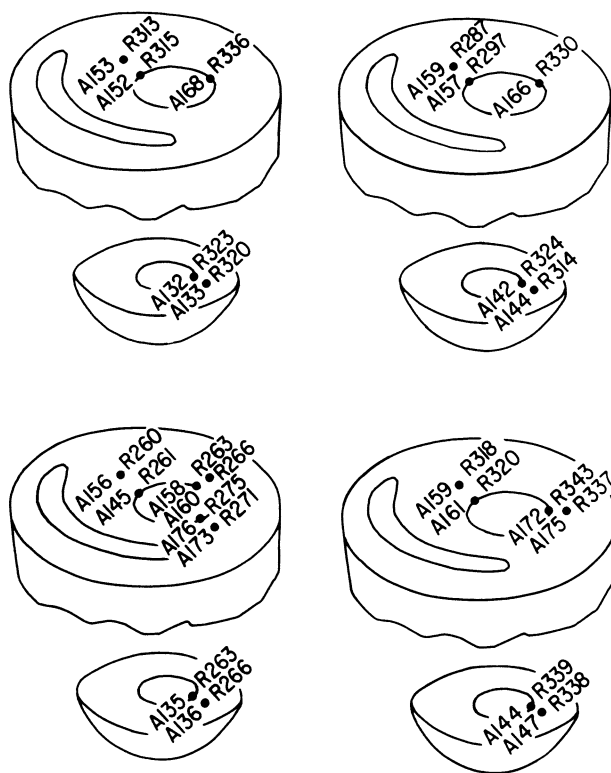


Figure 2

Activation and recovery sequence data from the left ventricular endocardial wall. Activation times are indicated by A and recovery times by R. Data are shown for apical and basal sites from four dog hearts. The numbers shown are in milliseconds following atrial stimulation. The position of electrodes is shown by dots. In each case where pairs of sites are shown in the same cardiac region with one indicated to be endocardial, the other one shown as intramural is not illustrated to scale. The sites represent locations of electrodes with 1 mm separation of the two bipolar electrodes nearest the endocardium. Activation times near the apex were earlier than those near the base but recovery times at the base included ones both earlier and later than apical recovery. Activation and recovery times in the upper right diagram are such that the maximal disparity of refractory periods is 54 msec. This is considerably larger than maximal refractory period disparity in the other diagrams or in the experiments not illustrated. It is possible that the apical site with an activation time of 142 and recovery time of 324 adjacent to a site activated 2 msec later but recovery 10 msec earlier represents measurement of a Purkinje fiber.

recovery times were measured immediately after thoracotomy using needle-mounted electrodes inserted through the pericardium, recovery times were always later at the endocardial than the epicardial level. An example of the transmural recovery pattern from one of these experiments is shown in figure 4. Activation times showed the well established endocardial-to-epicardial propagation of normal excitation. Refractory periods were longer at the endocardium than the epicardium as previously documented. Recovery times were also later at the endocardium than at the epicardium, reflecting a

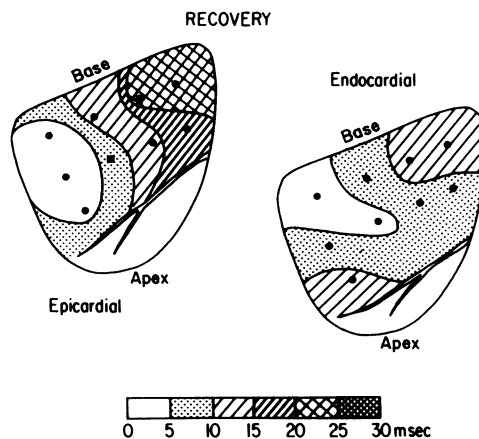


Figure 3

Recovery sequence on the epicardium and endocardium of the right ventricle in the same dog heart. Epicardial recovery sequence has the general features characteristic of epicardial excitation. Endocardial recovery includes areas near the base with earlier recovery than apical areas in which recovery is as late as that near the right ventricular apex. Earliest recovery detected at each surface is illustrated as zero.

recovery sequence opposite to that of excitation on that axis.

Discussion

Findings in this study showed a systematic relation of ventricular recovery to normal excitation in the dog heart. Recovery occurred in the same sequence as excitation at the epicardial surface and with a partially opposite sequence at the endocardium. The observations of intramural recovery suggest a gradual transition between the epicardial and endocardial recovery orders. These findings are compatible with established features of normal ventricular excitation and ventricular recovery properties. Intrinsic ven-

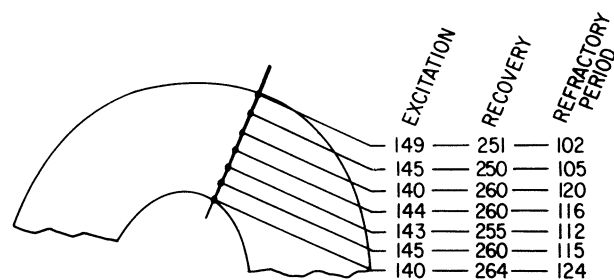


Figure 4

Excitation times, recovery times and refractory periods on the endocardial-epicardial axis in the posterolateral left ventricular wall. The times shown are in milliseconds after atrial stimulation. Findings are representative of five experiments in which comparable measurements were made shortly after thoracotomy and without pericardial incision over the ventricles. Excitation was earliest at the endocardium and endocardial refractory periods were longer than those near the epicardium, as has been previously established.

tricular recovery properties evaluated by measurement of refractory periods have been reported to have an inverse relation to the order of normal ventricular excitation.¹² Endocardial refractory periods exceeded those at epicardial sites. Apical refractory periods were longer than those at the ventricular base and the left side of the interventricular septum had longer refractory periods than those of the right side. In each of these instances, the area normally activated earliest had the longer refractory period. A similar organization of recovery properties was suggested by the refractory periods measured in this study. A recent study by Autenrieth, Surawicz, and Kuo also furnished evidence of an inverse relation of normal ventricular excitation and intrinsic ventricular recovery properties based on epicardial monophasic action potential durations.¹³ This organization of intrinsic recovery properties together with established features of the normal activation sequence appears to account for the recovery sequence demonstrated in this study.

Activation of a large portion of the endocardium is completed during a briefer interval than excitation of epicardial muscle. This does not exclude late excitation of some portions of the basal endocardium as evidenced by findings in this study of the dog heart and by the most detailed studies of human heart excitation.¹¹ The shorter time required for a portion of endocardial excitation means activation sequence at that location has relatively little influence on recovery time. The organization of intrinsic recovery properties therefore becomes the major determinant of recovery sequence. At the epicardial level, the time required for excitation exceeds the difference in intrinsic recovery times and the sequence of excitation determines the order of recovery of excitability.

Results of this study extend previous ones of ventricular recovery sequence by measurements at a larger number of sites and by relating recovery sequence to that of activation in individual experiments. Variations of normal excitation sequence in individual hearts of the same species have been noted by many investigators. These have limited the degree to which refractory period measurements could be applied to describe normal ventricular recovery. The determination of activation sequence in the present study was considerably less detailed than have been carried out to define that process alone. Measurements of recovery of excitability were made at a larger number of sites than in previous related studies and were the same sites from which activation order was determined. The number of sites studied and consideration of recovery of excitability following normal activation permitted description of the normal recovery sequence as similar to excitation at the epicardium and different at the endocardium.

The significance of these findings to human physiology and medicine is unproven, but there are several reasons to expect that normal recovery of the human heart is similar to that found in the canine heart. It is widely recognized that the polarity of normal T waves in the human electrocardiogram requires differences in the sequence of excitation and recovery.¹³⁻¹⁵ Certain other electrocardiographic findings, however, suggest substantive similarities in orders of excitation and recovery. The usual normal inscription direction of the T loop is the same as that of the QRS in the same planar projection of the vectorcardiogram. This requires similar activation and recovery orders with respect to those features of the process reflected in loop inscription direction.^{16, 17} It has also been observed that body surface isopotential maps from extensive electrode arrays repeat major features of the QRS during ventricular repolarization.¹⁸ This suggests a similar sequential cardiac location of events during excitation and recovery. The recovery patterns demonstrated in this study are compatible with all the human electrocardiographic features of ventricular recovery just described. The difference of endocardial-epicardial recovery order in relation to that of excitation is compatible with the polarity of normal T waves. The similarity of recovery and activation orders at the epicardial level provides an explanation for the normal T loop inscription direction and the repetition of QRS isopotential patterns during ventricular recovery.

It should be noted that the time sequence of recovery of excitability and of repolarization sequence are not synonymous. Recovery of excitability defines a particular stage of a complex process with a local time course as well as a sequence with which various stages of the process are reached at different local areas. More detailed studies including direct observations on the human heart are desirable to establish the normal ventricular repolarization sequence. Until such data become available, results of the present study provide a tentative explanation of normal T waves in body surface electrocardiograms.

References

1. SCHER AM, YOUNG AC, MALMGREN AL, PATEN RR: Spread of electrical activity through the wall of the ventricle. *Circ Res* 1: 539, 1953
2. DURRER D, VAN DER TWEEL LH: Spread of activation in the left ventricular wall of the dog. I. *Am Heart J* 46: 683, 1953
3. DURRER D, VAN DER TWEEL LH: Spread of activation in the left ventricular wall of the dog. II. *Am Heart J* 47: 192, 1954
4. DURRER D, VAN DER TWEEL LH, BLEEKMAN JR: Spread of activation in the left ventricular wall of the dog. III. *Am Heart J* 48: 13, 1954
5. DURRER D, VAN DER TWEEL LH, BENEKLOUW S, VAN DER WEY LP: Spread of activation in the left ventricular wall of the dog. IV. *Am Heart J* 50: 860, 1955

6. SCHER AM, MALMGREN AL, ERICKSEN RV: Activation of the interventricular septum. *Circ Res* 3: 56, 1955
7. SODI-PALLARES D, BISTENI A, MEDRANO GA, CISNEROS F: The activation of the free left ventricular wall of the dog's heart. *Am Heart J* 49: 587, 1955
8. MURRUMI RA, GOLDMAN A, RAKITA L, KURAMOTO K, PRINZMETAL M: Studies on the mechanism of ventricular activity. *Am J Med* 19: 832, 1955
9. DURRER D, BÜLLER J, GRAAFF GIL, MEYLER FL: Epicardial excitation patterns as observed in the isolated revived and perfused fetal human heart. *Circ Res* 9: 29, 1961
10. SCHER AM: Newer data on myocardial excitation. *In* *Electrophysiology of the Heart*, edited by B TACCARDI, G MARCHETTI. New York, Pergamon Press, 1965, p 217
11. DURRER D, VAN DAM RT, FREUD GE, JANSE MJ, MEIJLER FL, ARZBAECHER RC: Total excitation of the isolated human heart. *Circulation* 41: 899, 1970
12. BURGESS MJ, GREEN LS, MILLAR K, WYATT R, ABILDSKOV JA: The sequence of normal ventricular recovery. *Am Heart J* 84: 660, 1972
13. AUTENRIETH G, SURAWICZ B, KUO CS: Sequence of repolarization on the ventricular surface in the dog. *Am Heart J* 89: 463, 1975
14. MACLEOD AG: The electrocardiogram of cardiac muscle, an analysis which explains the regression of T wave deflection. *Am Heart J* 15: 165, 1938
15. WILSON FN, MACLEOD AG, BARKER PS: The T deflection of the electrocardiogram. *Trans Assoc Am Physic* 46: 29, 1931
16. WILSON FN, JOHNSTON FD: The vectorcardiogram. *Am Heart J* 16: 14, 1938
17. ABILDSKOV JA, MILLAR K, BURGESS MJ, GREEN LS: Characteristics of ventricular recovery as defined by the vectorcardiographic T loop. *Am J Cardiol* 28: 670, 1971
18. PEARSON RB, VICARS J, SELVESTER RH: Local characteristics of T wave maps in infarct. *In* *Body Surface Mapping of Cardiac Fields — Advances in Cardiology*, edited by RUSH S, LEPESCHKIN E. Basel, S. Karger, 1974, vol 10, p 283