Activation Studies following Experimental Hemiblock in the Dog
By John J. Gallagher, Andres R. Ticzon, Andrew G. Wallace, and Jackie Kasell

ABSTRACT
Electrocardiograms (ECG), McFee vectorcardiograms (VCG), and ventricular activation data were collected from 25 anesthetized dogs before, immediately after, and 4 weeks after surgically induced discrete left anterior divisional block. Left anterior divisional block resulted in minor ECG changes: small S waves developed in leads II, III, and aVF and the QRS complex was prolonged 5-15 msec (mean 9 ± 2.7 [sd] msec). Prominent VCG changes also occurred: maximal and terminal forces were shifted posteriorly, superiorly, and slightly leftward, the duration of the loop was increased 5-15 msec (mean 9.8 ± 2.8 msec), and the terminal portions of the loop were slurred. Epicardial surface mapping revealed a consistent area of 5-20-msec delay (mean 12 ± 5.1 msec) confined to the lateral-basal surface of the left ventricle. Transmural activation studies in this area invariably revealed 6-20-msec (mean 12.8 ± 4.8 msec) delays in Purkinje and 3-25-msec (mean 12.4 ± 5.6 msec) delays in endocardial activation. The wave front propagated across the wall with normal velocity. Q waves developed due to a "window effect" in the area of delay. Combining division of the septal fibers with left anterior divisional block resulted in surface delays of greater magnitude with marked axis shifts toward the left. Despite the extensive interconnections of the left ventricular conduction system, discrete proximal left anterior divisional block resulted in a significant alteration in the sequence of ventricular activation, confirming the fascicular nature of the left ventricular conduction system. The septal division appears to be an integral part of this system. The methodology described in this paper can be used to readily differentiate between epicardial delay due to conduction delay and that due to intramural myocardial delay.

KEY WORDS  epicardial mapping  left anterior hemiblock  vectors  myocardial conduction delay  Purkinje activation  myocardial infarction

- Experimental injury to subdivisions of the left bundle branch was first reported in 1910 (1). Subsequent studies over the ensuing 60 years have gradually led to the concept of two functionally distinct subdivisions of the left bundle, i.e., the anterior and posterior divisions (2-24). More recently, in vitro studies by Myerburg et al. (25, 26) have suggested that widespread interconnections between the anterior and posterior Purkinje networks of the left ventricle make it unlikely that isolated lesions in proximal subdivisions of the left bundle branch would result in significant changes in ventricular activation. Furthermore, histological examinations of the human conduction system in patients who exhibited electrocardiographic evidence of left anterior divisional block have demonstrated extensive pathological changes in the left ventricular conduction system that are not confined to the anterior division (27-30).

The present investigation was undertaken to determine the effects of discrete superficial left septal lesions on the vectorcardiogram (VCG), the electrocardiogram (ECG), and the sequence of ventricular activation in the intact dog. An attempt was also made to develop a method to differentiate conduction disturbances associated with endocardial activation delays from those secondary to intramural factors.

Methods
Epicardial, intramural, and endocardial studies were carried out in 25 adult mongrel dogs of both sexes weighing 15-20 kg. Each dog was anesthetized with sodium pentobarbital (25 mg/kg, iv), intubated, and placed on a respirator in the supine position.

Standard ECGs were obtained as well as VCGs using the McFee orthogonal system (31); care was taken to use identical foreleg positioning (32). The surface landmarks for the vector leads were marked with permanent sutures in the chest wall. The heart was exposed through a sternotomy and positioned in a pericardial cradle. A reference electrode was sewn on the anterior right ventricle. A purse-string suture was placed in the subepicardial
layers of the left ventricular apex to facilitate positioning of the heart during mapping and for purposes of hemostasis during subsequent introduction of a probe.

The epicardial recording system consisted of an electrode with two terminals located 1 mm apart. Unipolar and bipolar inputs from these terminals together with the reference electrogram and the ECG were connected by field-effect amplifiers to a system with an input impedance of $10^{11}$ ohms and an overall frequency response of 0.1 Hz to 1.2 kHz. All data were recorded on a magnetic tape recorder (Honeywell) at a speed of 7.5 inches/sec and reproduced subsequently at paper speeds of 400 mm/sec.

Local activation times measured with respect to the reference were determined on 50-70 surface points and plotted on Polaroid photographs of the heart. On-line determinations of these intervals were made using a special digital timing device triggered by the bipolar derivative of the right ventricular reference. All activation times were subsequently corrected to time relative to onset of cavity potential.

Intramural activation was determined by multipolar electrodes containing 15-30 points assembled 1 mm apart along the shaft of a beveled 23-gauge needle. Unipolar and bipolar data were recorded in five-channel segments with the epicardial reference, using the same system described earlier in the present paper. By convention, a downward polarity of the bipolar recording indicated spread from endocardium to epicardium. Six to nine insertions were placed across the ventricular wall in each experiment and recorded.

Following control activation studies, a curved knife with a retractable blade was used to produce a lesion of the left anterior division. The knife was introduced into the left ventricular apex (20 dogs) or the aortic root (5 dogs) and positioned against the left septal surface. With the tip directed toward surface landmarks on the anterior wall, the blade was exposed and drawn 0.5-1 cm along the anterior interventricular septum.

One hour after a lesion had been produced, the activation study was repeated; the chest was then closed, and the dog was allowed to recover. The VCG, the ECG, and the activation study were repeated 3-6 weeks later; the heart was then removed and examined using Lugol's stain.

In an additional group of five dogs, similar activation studies were performed before and after infarction induced by the Harris technique (33), and the mechanism of epicardial delay was compared with that in the dogs with hemiblock.

**Results**

**HEMIBLOCK STUDIES**

In 15 dogs, a discrete lesion that transected only the left anterior division was achieved. In 5 dogs, a lesion was created which involved septal branches of the left bundle branch in addition to the anterior division. Two sham experiments in which the conduction system was not injured were performed. Three of the 25 dogs did not survive the postoperative period because of infection.

An example of a lesion 4 weeks after its creation is shown in Figure 1: the heart has been stained with Lugol's solution. Note the discrete raised lesion transecting the anterior division of the left bundle branch and the intact state of the septal branches and the posterior division.

**FIGURE 1**

Canine left ventricular endocardium stained with Lugol's solution. Note the discrete raised lesion transecting the anterior division of the left bundle branch and the intact state of the septal branches and the posterior division.
with Lugol's solution to highlight the glycogen-rich conduction system. This lesion was confined to the anterior division; the septal branches and the posterior division remained intact. The lesions were generally 0.5–1 cm in length and 1–2 mm in depth. Figure 2 is a photomicrograph of a histological section through the lesion shown in Figure 1; the lesion’s superficial nature is evident.

**Electrocardiogram.**—Left anterior divisional block resulted in minor electrocardiographic changes. Small S waves developed in leads II, III, and aVF and the QRS complex was prolonged 5–15 msec (mean 9 ± 2.7 [sp] msec). A representative tracing is shown in Figure 3. In this example, the QRS complex was prolonged from 45 msec to 55 msec, the R-wave amplitude was increased in leads II, III, and aVF, and the S waves were enhanced in these same leads. The mean QRS axis was essentially unchanged. Generally, the electrocardiographic alterations were small, and only minimal axis shifts were observed in the frontal plane.

**Epicardial Mapping.**—Local activation times were plotted on silhouettes of the heart, and isochronous lines were drawn at 5-msec intervals. The onset of left ventricular cavity potential was taken as the zero time reference for all data. A surface map depicting epicardial activation before and after the lesion shown in Figures 1 and 2 is presented in Figure 4. In the control state, early breakthrough occurred in the area trabecularis and the apex with a spread of activity toward the outflow tract and the posterobasal portions of the ventricles. Following left anterior divisional block, an area of delay appeared on the high basal portion of the left ventricle beneath the left atrial appendage. Very little delay was noted in the frontal projection, and the posterior projection remained unchanged.

Figure 5 demonstrates the change in activation time at 13 representative surface points (A–M) in the 15 dogs in which discrete left anterior divisional
block was successfully produced. Significant delays of 4–25 msec (mean 12 ± 5.1 msec) were reproducibly noted (P < 0.001) at sites E, F, and H located on the high anterolateral wall.

Intramural Activation.—Intramural activation was examined in areas of surface delay and compared with that in areas without delay. Figure 6 is an example taken from the same experiment considered in Figure 4. On the left is a surface map viewed in the left sagittal projection before (top) and after (bottom) section of the left anterior division. On the right are unipolar and bipolar complexes recorded from the five innermost electrode points on a needle inserted into an area of epicardial delay (arrow). In the control state, a rapid Purkinje deflection appeared 4 msec before the onset of cavity potential (−4 msec) followed by endocardial activation 7 msec after the onset of cavity potential (+7 msec). Following left anterior divisional block, a Purkinje deflection was recorded at +10 msec (a delay of 14 msec), and muscle activation followed at +23 msec (a delay of 16 msec). Multipolar needles placed across the ventricular wall in areas of surface delay invariably demonstrated delays of 6–20 msec (mean 12.8 ± 4.8 msec) in the onset of Purkinje potentials and 3–25 msec (mean 12.4 ± 5.6 msec) in the onset of endocardial muscle activation following left anterior divisional block. Figure 7 illustrates the change in transmural activation recorded from a multipolar electrode inserted close to the electrode shown in Figure 6. Endocardial activation was delayed from +5 msec in the control state to +15 msec after left anterior divisional block; surface activation was delayed from +29 msec to +40 msec. The sequence of activation across the wall, shown by the polarity and the timing of the 15 potentials, was similar to the control sequence but was displaced in time after the block.

Activation data obtained using multiple simultaneously recorded electrodes revealed that the sequence of activation and the propagation velocity across the wall were generally maintained. Purkinje-muscle intervals demonstrated a variable behavior; they became slightly shorter or longer following left anterior divisional block. Evidence of intramural penetration of Purkinje fibers was observed on occasion. In three experiments, septal
activation was also studied. These studies revealed a delay in activation of the anterior-superior interventricular septum after left anterior divisional block. Collisions were observed at the periphery of delayed areas with tangential spread from neighboring normally activated areas.

Unipolar epicardial activation data following left anterior divisional block demonstrated delayed intrinsocid deflections over the high lateral left ventricular wall and increased R-S ratios that probably resulted from lack of cancellation due to the relatively unopposed forces in the delayed area of activation. Surface Q waves frequently developed in areas of surface delay. This phenomenon is demonstrated in Figure 8 which shows data recorded from a typical delayed area. The first unipolar tracing in each column records a cavity potential (electrode no. 1). Following left anterior divisional block, the endocardium (electrode no. 2) was delayed from +13 msec to +24 msec. Following this initial delay in input, activation proceeded across the wall without further retardation. A Q wave proportional to the magnitude of activation delay developed on all intramural leads and was reflected on the epicardial tracing (electrode no. 10) presumably due to a Wilson type of “window effect.” The development of a larger R-S ratio was seen on the epicardial tracing.

No significant difference existed between activation studies obtained 1 hour after production of the lesion and those obtained 3-5 weeks after the surgical intervention.

**Vectorcardiographic Changes.**—Figure 9 is the VCG recorded during the control state and 4 weeks after section of the left anterior division in the same dog considered in Figure 4. To the left are the X, Y, and Z leads and to the right are the frontal, horizontal, and left sagittal derivations. The loops were interrupted at 1-msec intervals. In the center is a schematic presentation of the area of delay viewed in the frontal and left sagittal projections. In the control state, the loop moves counterclockwise in all three planes; such movement is characteristic of canine vectorcardiograms recorded by the McFee system (31, 34). The frontal plane loop showed no marked axis change after left anterior divisional block; however, the terminal forces were shifted superiorly and delayed. The initial forces were unchanged. The horizontal plane loop demonstrated a shift in the maximal vector posteriorly, and the terminal forces were shifted to the left and delayed. The left sagittal loop showed a shift in the maximal vector posteriorly. The terminal forces were shifted superiorly and delayed.

In most instances, no significant axis shift was observed in the frontal plane derivations. Loop duration increased 5-15 msec (mean 9.8 ± 2.8 msec). The area of delay demonstrated by activation data was posterior to the electrical center of the heart, which explains why significant changes in activation were not observed in the frontal plane derivations. Similar reasoning explains the failure of standard limb leads to adequately reflect changes in activation.

**LEFT ANTERIOR DIVISIONAL BLOCK PLUS DIVISION OF THE SEPTAL FIBERS**

The effects of combining laceration of the septal fibers with a discrete lesion in the left anterior division were observed in five dogs. In each of these dogs, surface delays were of greater magnitude (7-35 msec at comparable sites E, F, and H; mean 19.3 ± 8.8 msec) and area (areas G, J, and K in addition to E, F, and H) than they were after left anterior divisional block alone (Fig. 10). Following production of the lesion, delay was evident on the
Intramural activation following left anterior divisional block. **Left:** Epicardial map of the left sagittal surface of the heart before (top) and after (bottom) section of the left anterior division (LAD). **Right:** Recordings of electrocardiographic lead II (II), right ventricular bipolar reference (REF), and unipolar and bipolar complexes from the five innermost electrode points (1-5) on a needle inserted into an area of delay (arrow). To the right of the bipolar recordings are the activation times (msec) and calibration marks (CAL). All activation times are corrected to the onset of cavity potential which is indicated by the broken vertical line. This convention is also followed in subsequent illustrations. Time marks are recorded at 10-msec intervals beneath each tracing.

Mechanisms of epicardial delay

The methodology presented in this paper could be used during open heart surgery to investigate the mechanism of surface delays associated with electrocardiographic evidence of “conduction disturbances.” To demonstrate the feasibility of this approach, we compared the intramural activation underlying areas of epicardial delay due to myocardial infarction with that induced by injury to the specialized conducting tissues.

In Figure 12, two hearts are viewed in the left sagittal plane. On the left is an area of surface delay that appeared on the anterolateral left ventricle following myocardial infarction; on the right is an area of delay that appeared on the lateral free wall following interruption of the anterior and septal divisions of the left bundle branch. Transmural needles were inserted at the border of these delayed areas at the sites indicated by the arrows.
Transmural activation changes following section of the left anterior division (L.A.D.). Cavity potential is recorded on electrode points 1-3, endocardium on lead 4, and epicardium on lead 15. See Figure 6 for abbreviations.

The unipolar and bipolar recordings obtained from the infarction experiment are shown in Figure 13. In the control recording, Purkinje potentials were recorded at +1 msec after the onset of cavity potential, followed by endocardial activation at +5 msec. Epicardial activation followed at +30 msec. After infarction, Purkinje and endocardial activation occurred on time. Intramural propagation was, however, severely retarded and manifest by delay, fragmentation, and diminished voltage of the recorded potentials.

Multipolar needle recordings from the heart with the conduction system disturbance (Fig. 14) sharply contrasted with those from the infarcted heart. In the control state, Purkinje activation occurred at +1 msec, followed by endocardial activation at +10 msec. Epicardial activation was recorded at +25 msec. After division of the septal and the left anterior divisions of the left bundle branch, Purkinje activation was recorded at +27 msec (a delay of 26 msec) and endocardial activation was recorded at +36 msec (a delay of 26 msec). Epicardial activation followed at +43 msec. Q waves developed as a result of the window effect. Activation generally proceeded across the ventricular wall so that the transmural activation data obtained from a multipolar insertion in an area of epicardial delay faithfully reflected the mechanism of the surface delay.

**Discussion**

It has long been recognized that lesions of the specialized conduction system in the ventricles can produce shifts in the QRS axis and increase the duration of the QRS complex. Early studies of this phenomenon were concerned with the criteria for various forms of bundle branch block and the derivations of the dextro-and levo-cardiograms (1-7, 9).

In 1954, Smith and his associates (8) reported their findings using epicardial mapping before and after "incomplete and complete bundle branch block." They concluded that certain segments of the myocardium appeared to be supplied by fixed portions of the conduction system without cross connections. Incomplete bundle branch block was accompanied by relatively slight alterations in the limb lead electrocardiogram.

The clinical implications of delay in activation of the left ventricular free wall resulting from a
Conduction disturbance in the anterior division of the left bundle were recognized by Grant in 1953 (35). Further experimental confirmation came from the studies of Van Bogaert et al. (10, 36) and those of Pruitt and Watt and their associates (12-16, 22). The work of Pruitt and Watt is perhaps the best known. They demonstrated by epicardial recording that activation delay could result from experimental lesions in the anterior radiations of the left bundle branch in dogs. Similar experiments in baboons resulted in a significant leftward shift of the QRS axis. However, the lesions produced in their studies involved extensive areas of septal muscle and specialized fibers of the septal network in addition to the left anterior division.

In 1964, Uhley and Rivkin (11) examined the effects on the ECG and VCG of selected cuts in the left ventricular conduction system created during cardiopulmonary bypass. Following section of the left anterior division, they noted the appearance of terminal forces oriented superiorly, posteriorly, and to the right without significant delay in these forces.

Medrano et al. (18, 19) also studied the VCG changes associated with left anterior divisional block and found 20-30-msec increases in the duration of the loop with delayed terminal forces directed leftward, superiorly, and posteriorly (cube system). They also documented delays of 20-30 msec in the upper one-third of the septum and on the high anterolateral wall of the left ventricle.

Myerburg et al. (25, 26) have recently reported a series of experiments performed in isolated canine tissues in which patterns of endocardial activation were studied after one of the main divisions of the left bundle branch had been incised. Using micro-

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**Figure 8**

Genesis of surface Q waves following section of the left anterior division (LAD). Unipolar records are from a transmural needle inserted into an area of delay. Cavity appears on electrode no. 1, endocardium on electrode no. 2, and epicardium on electrode no. 10. See Figure 6 for abbreviations.
Vectorcardiograms recorded before and 4 weeks after section of the left anterior division (LAD). Left: X, Y, and Z leads. Right: Frontal, horizontal, and left sagittal derivations. Loops are interrupted at 1-msec intervals. In the center is a schematic presentation of the area of delay (cross-hatched) in the frontal and left sagittal projections.

Vectorcardiograms before and after section of the left anterior division (LAD) and septal fibers of the left ventricular conduction system. (same experiment as that shown in Fig. 10).

Epicardial activation before and after injury of the left anterior division (LAD) and septal fibers of the left ventricular conduction system.

Epicardial activation following myocardial infarction (left) and injury of the conduction system (right). LAD = left anterior division.

In the present study, we demonstrated that in the canine heart abnormalities of activation can be ascribed to discrete pathological lesions in the proximal specialized conduction system. Our data agree with those of Myerburg et al. (25, 26) in that comparable delays (6-20 msec relative to control) were noted in Purkinje activation of the left ventricular wall. We also demonstrated that these changes had profound effects on the sequence of
FIGURE 13
Transmural activation before (left) and after (right) infarction. Time marks were recorded 10 msec apart.

FIGURE 14
Transmural activation before (left) and after (right) injury to the left ventricular conduction system.

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ventricular activation. The studies of Spach et al. (37) have amply demonstrated the complexity of the Purkinje network; the functional interconnections of the conduction system act as a safety factor; they permit activation of tissues distal to lesions. However, the changes in the resulting sequence of ventricular activation can only be appreciated by studying transmural activation.

Recent controversy has arisen regarding the existence of an additional subdivision of the left bundle branch—the septal division (38-41). The existence of such a branch was noted by earlier workers in several mammalian species (2, 42). Subsequent studies of the conduction system with saturated Lugol’s solution have confirmed this finding in dogs and man (43, 44). In a study of the excitation of the isolated human heart, Durrer et al. (45) have demonstrated three areas of early endocardial activation: an area near the base of the left anterior free wall just below the attachment of the mitral valve, an area in the lower one-third of the posterior paraseptal region, and a central area on the left side of the septum. In activation studies of revived human fetal hearts, similar findings have been documented by Brusca and Rosettani (46). In the present study, combining septal division block with left anterior divisional block resulted in surface delays of greater area and magnitude, suggesting the functional importance of this division. Similar observations were made in the in vitro studies of Myerburg et al. (25, 26).

Despite extensive studies to date regarding the association of conduction system disorders with axis deviation, few studies have attempted to determine the role of intramural and myocardial factors (47-53). One must question whether all variations of the QRS axis in man can be explained on the basis of conduction disturbances. Such conditions as intramural fibrosis, hypertrophy (54), or congenital variation in the distribution of the Purkinje system (55) could alter the course of ventricular activation—the most important determinant of QRS configuration—and the role which such factors might play has not been unequivocally established.

One approach is to study intramural activation in areas underlying epicardial delay. An opportunity to explore this phenomenon exists during open heart surgery, and the present study provides the rationale for such an approach. Indeed, van Dam et al. (56) have recently reported their observations on septal and free wall activation in patients with idiopathic hypertrophic subaortic stenosis. Their investigation, which combined epicardial and plunge electrode techniques, indicated apparent incomplete degrees of left anterior divisional block in these patients and demonstrated the safety of these techniques in the clinical setting.

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