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Site of Origin of Halothane–Epinephrine Arrhythmia Determined by Direct and Echocardiographic Recordings

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A constantly coupled bigeminal arrhythmia was induced in dogs anesthetized with thiopental–halothane by infusion of epinephrine ($1\ \mu g \cdot kg^{-1} \cdot min^{-1}$). The site of origin of the abnormal beat was localized to the interventricular septum by bipolar recordings from the left and right ventricular epicardium and two sites in the septum. Simultaneous echocardiograms showed early movement of the septum with a pattern similar to that seen in left bundle branch block. Stimulation at the recording sites resulted in movement patterns which indicate that assessment of septal and posterior left ventricular motion can be helpful in localization of the origin of ventricular arrhythmias, although only with left ventricular arrhythmias is there potential for anatomic localization to a small area of muscle. (Key words: Anesthetics, volatile: halothane. Heart: arrhythmia, epinephrine; echocardiography.)

SMALL DOSES OF EPINEPHRINE injected into dogs anesthetized with a "sensitizing" hydrocarbon anesthetic cause a bigeminal arrhythmia with a constant coupling interval.[1,2] The coupling interval does not change when heart rate is changed, an observation which led to the original proposal that the mechanism of this arrhythmia is one of reentry rather than an increase in automaticity.[1] The arrhythmia is sensitive to changes in blood pressure, is partly dependent on heart rate, and can be converted to sinus rhythm on stimulation of the vagus nerve, whether or not the atrial rate is controlled.[2–4] Many of these characteristics have been described for both cyclopropane- and halothane-anesthetized dogs, in each case after induction with thiopental. An attempt to localize the site of origin of the abnormal beat was made only in cyclopropane-anesthetized animals; the conclusion, based on His-bundle and epicardial recordings, was that the site of reentry was most probably located in the interventricular septum.[5]

The present work had two major objectives: to confirm by direct recording that the septum was the first part of the heart activated by the abnormal beat, and to evaluate the possible usefulness of echocardiographic recordings generally in localizing the site of origin of a ventricular arrhythmia. It also served as a further indication of the similarity of arrhythmias induced in animals sensitized by halothane to those observed under cyclopropane anesthesia.

Methods

Dogs of either sex weighing 13–23 kg were anesthetized with thiopental sodium (30 mg/kg, iv), the trachea cannulated, and the vagus nerves cut. The animals were respired with 1.5 per cent halothane in oxygen during the 30–45 min required for the surgical procedure and were then equilibrated with 1 per cent halothane (1.2 MAC) for at least 20 min before experimentation. The chest was opened by midsternal splitting, and the heart suspended in a pericardial cradle. Small ring electrodes were sewn to the right and left ventricular free walls, with the former being placed approximately 2.5 cm from the apex and the latter between the two final diagonal branches of the anterior descending coronary artery. Two pairs of Teflon®-covered wires, bared at the tip, were inserted into the interventricular septum; one pair was positioned in the basal portion and the other in the apical region. They were held for insertion in 23-gauge needles which were pushed into the septum through the right ventricular free wall. Two clip electrodes were attached to the right atrium in some experiments to pace the heart during the arrhythmia. Blood pressure, recorded from a cannulated femoral artery with a Statham P23B® transducer, a lead II electrocardiogram (ECG), and the electrograms were all recorded on a Electronics for Medicine DR-8® recorder at 200 mm/s.

Echocardiographic recordings were obtained using a 3.75-MHz transducer with a -5 cm focal point and a commercially available ultrasonoscope (Smith Kline Instruments, 880 West Maude Avenue, Sunnyvale, California 94086). The transducer was held by a series of adjustable clamps and positioned on the right ventricular free wall so that the beam traversed the interventricular septum, left ventricular cavity, and the left ventricular posterior wall just caudad to the tip of the anterior mitral leaflet. This view is identical to that used clinically for assessment of left ventricular size and function. The echocardiogram and a lead II ECG were recorded at 200 mm/s with care taken to ensure simultaneous records for both electrical and echographic data.

Following preparation, $1\ \mu g \cdot kg^{-1} \cdot min^{-1}$ epinephrine

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($2\ \mu g \cdot kg^{-1} \cdot min^{-1}$ in one animal) was infused through a femoral vein to produce the bigeminal rhythm. In seven animals, multiple infusions were given to assess stability of the arrhythmia. In these, and an additional four dogs, the heart was paced successively from each of the pairs of electrodes with simultaneous recordings from the remaining electrodes and the echocardiogram. Since it seemed possible that movement delays might be a function of heart rate, the AV node was destroyed by local injection of 40 per cent formaldehyde for this part of the experiment, and the ventricles paced at 800-, 400-, and 300-ms intervals.

The records were assessed independently by the authors and correlated after interpretation. In the halothane–epinephrine experiments, the delay between the upstroke of the QRS complex of the lead II normal beat and the zero-crossing point of each bipolar electrogram from both the normal and the bigeminal beat were measured. The site of origin of the abnormal beat was taken to be nearest to the first recording site activated, and this was correlated by noting the sequence of activation of the electrodes. Similarly, the interval from the onset of lead II QRS to the initial movement of the septum and left ventricular posterior wall was measured from the echocardiogram for both the normal and bigeminal beat. For the pacing studies, the pacing artefact was used as the time reference for both electrical and movement measurements.

All data are presented as means ± standard deviations. Statistical comparisons are by Student's *t* test using paired data.

Results

Halothane–Epinephrine Bigeminy

Electrical Recordings. Figure 1 shows the electrical records from a typical experiment. The electrograms of the bigeminal beat have different morphology than the normal beat at some, but not all of the electrode sites. In addition, the sequence of activation is quite different between the normal and abnormal beat, and it is clear that the high septal electrode is the first one activated during the latter. Table 1 shows the results obtained in seven experiments with the earliest activation time in each experiment being underlined. The high septal electrode was the earliest site of activation in at least one of the recordings obtained in six of the seven animals. The left ventricular electrode, which had been placed close to the base of the papillary muscle, was the earliest site of activation in a single complex in one experiment; none of the other abnormal beats in this or the other animals showed early left ventricular activation. This unusual complex and the immediately adjacent pair of beats is shown in figure 2. Note the change in the lead II QRS complex and that activation of the left ventricle is early in the abnormal beat of the first pair, whereas the high septal electrode is early in the second.

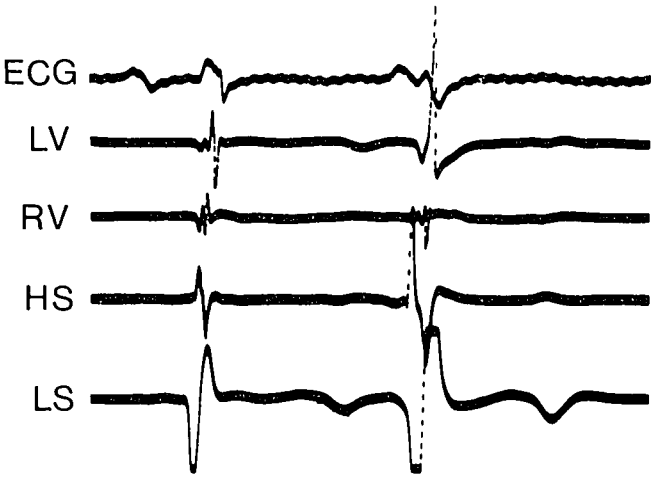

FIG. 1. Electrical recordings during typical bigeminal arrhythmia. EKG = Lead II; RV and LV are bipolar recordings from the right and left ventricular free walls; HS and LS are high and low septal locations of bipolar electrodes. Note early activation of HS electrode relative to other sites and small change in interval between RV and LV activation during abnormal beat.

Echocardiographic Recordings. Figure 3 shows the echocardiographic record from a typical experiment and table 2 contains the septal and posterior wall movement times obtained in the seven animals. Note that in the normal complex, the onset of septal movement precedes the anterior movement of the posterior wall. Similarly, following the ectopic complex, the septum moves first but the pattern of motion is distinctly different from that of the normal beat. Within 40 ms of the ectopic beat, there is an initial posterior movement of the septum, followed by anterior (paradoxical) movement throughout most of

TABLE 1. Activation Times during Halothane–Epinephrine Arrhythmia

Experiment	Q-RV (ms)	Q-HS (ms)	Q-LS (ms)	Q-LV (ms)
1	317	295	299	319
2	272	261	270	284
3	239	215	239	238
4	228	225	232	256
5	284	251	262	267
6	265	281	272	291
7*	285	270	295	310
MEAN	270	256.9	267.0	280.7
SD	29.9	28.9	25.4	29.1

Abbreviations: HS = high septum; LS = low septum; LV = left ventricle; RV = right ventricle. All measurements were made from onset of normal QRS.

* With another infusion, the RV activation time was earliest.

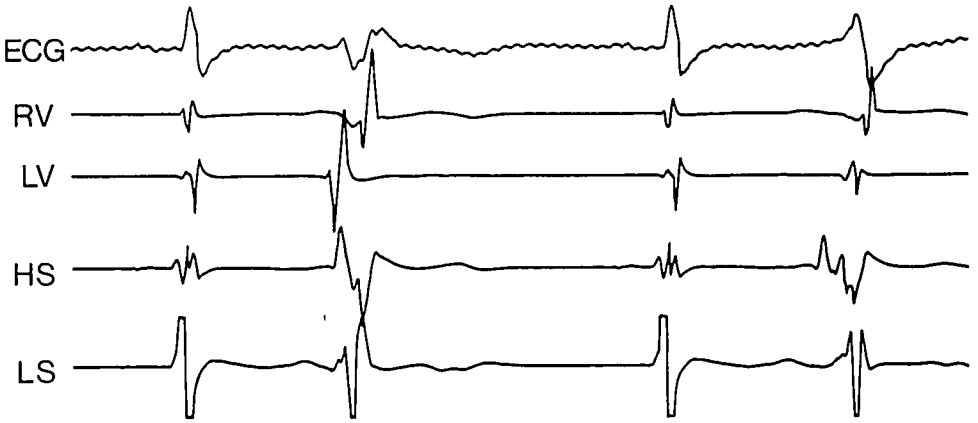

FIG. 2. Electrical recordings corresponding to single bigeminal beat of left ventricular origin as discussed in text. The immediately following coupled beat is also shown. Records are labeled as in figure 1. (Retouched for reproduction.)

systole. This is followed by a second posteriorly directed movement late in systole. This septal movement pattern which is typical of that observed in left bundle branch block[6-8] was the dominant pattern in each experiment, although in two experiments other motion patterns were observed in some complexes. One of these was the unusual complex for which the electrical recordings are shown in figure 2. With this complex, the QRS to septal movement time was increased and motion was directed posteriorly throughout systole.

The anterior movement of the posterior wall of the bigeminal beat always interrupted the relaxation phase from the normal beat. In four of seven dogs the onset of posterior wall movement clearly occurred after septal movement. In the remaining three experiments there was very little difference between QRS to septal and QRS to posterior wall movement times. Considering that the septum normally moves prior to the posterior wall [mean 30 ± 6 (SD) ms in these seven animals] this observation implies that mechanical activity of the posterior wall occurs relatively early with the epinephrine-induced arrhythmia.

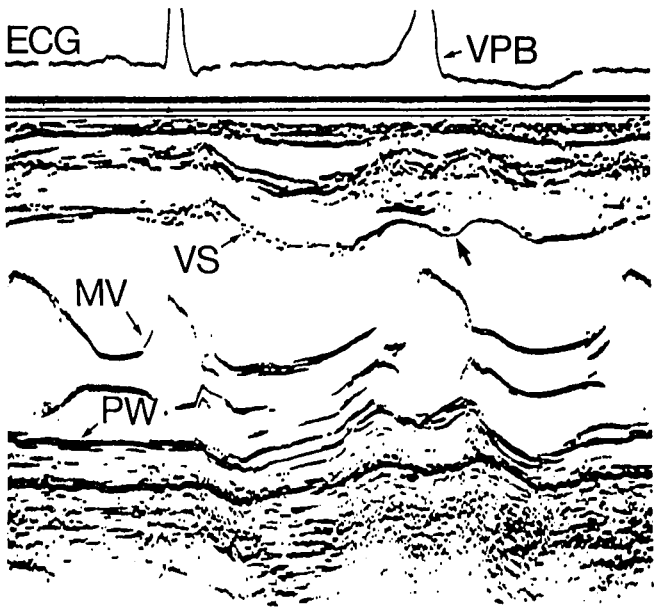

FIG. 3. Echocardiographic features of a typical bigeminal beat. With the onset of the bigeminal beat (VPB), there is early (indicated by arrow) initial posterior movement of the ventricular septum (VS). This is followed by slight anterior movement and a late and more sustained second posterior movement. MV = mitral valve; PW = posterior left ventricular wall.

EFFECTS OF VENTRICULAR PACING

Table 3 shows the times from pacing artefact to electrical activation (at each recording site) and to septal and posterior wall movement. Only the data obtained during pacing at the 400-ms interval are shown, as those from the other pacing rates were not appreciably different. Activation times were similar to all electrodes regardless of stimulating site. However, conduction times between the low septal and right ventricular electrodes were significantly shorter than between low septal and left ventricular electrodes, suggesting that activation of the left ventricle might have occurred by direct trans-septal conduction.

The stimulation to movement times reveal several interesting features. First, the septal movement time occurred within 60 ms of the pacing artefact following stimulation of right ventricle in all animals. This reflected the early posterior movement of the septum characteristic of left bundle branch block conduction.[6-8] Pacing stimulus to septum movement times were also brief with high septal (mean 58.1 ms) and low septal (mean 58.4 ms) stimulation. However, in one animal septal movement was delayed after high septal stimulation with a subsequent normal posterior movement of the septum. A similar pattern was observed in two animals with low septal stimulation. These findings suggest that the respective electrodes in these animals were causing initial stimulation of the left ventricular myocardium. This conclusion is supported by the observation that the septal

TABLE 2. Septal and Posterior Wall Movement Times during Halothane-Epinephrine Arrhythmia

	Q-VS (ms)		Q-PW (ms)		VS-PW (ms)	
Experiment	Normal	Ectopic	Normal	Ectopic	Normal	Ectopic
1	49	318	80	333	31	15
2	37	286	71	288	34	2
3	50	247	75	276	25	29
4	43	284	79	292	36	8
5	33	302	66	366	33	64
6	28	255	61	248	33	−7
7	36	212	57	255	21	43
MEAN	39.4	272.0	69.9	294	30.4	22.0
SD	8.2	36.2	8.9	42.2	5.4	25.0

Abbreviations: PW = posterior (left ventricular) wall; VS = ventricular septum. All measurements were made from the initial deflection of the normal QRS.

movement times were prolonged (mean 99.1 ms) following left ventricular stimulation ($P < 0.001$) compared to septal movement times after right ventricular stimulation (mean 57.3 ms).

The second observation of interest is the posterior wall movement times. The mean values were not different for all stimulation sites indicating that the movement time is not strictly a function of activation times. However, in three experiments the left ventricular posterior wall moved early (60–82 ms) with both low septum and left ventricular stimulation. An example of this phenomenon is illustrated in figure 4. Soon after the pacing artefact and frequently before septal movement, there was an abbreviated anterior movement of the posterior wall. This was followed by a more sustained (and normal) anterior movement of the wall in each instance.

Discussion

The results of this study are in agreement with previous data obtained from cyclopropane-anesthetized animals[5] which suggested that the epinephrine-induced bigeminy arises in the interventricular septum. This is supported by the bipolar recordings from the septum which showed that the high septum was the earliest site of activation in six of seven experiments. In the remaining animal, the right ventricular electrode was activated earliest. However, the arrhythmia tends to be variable in its initial stages, and different QRS configurations and activation sequences may then be observed. Following this initial phase, however, the arrhythmia is usually a stable bigeminy, with a constant QRS morphology, a fixed coupling interval, and as demonstrated in this study, earliest activation occurring in the septum.

The site of origin of the abnormal beat cannot be determined from echocardiographic data alone. However, the septal movement pattern provides strong evidence that the site of origin of the abnormal beat is either in the interventricular septum or within the right ventricular free wall. This is suggested by the early posteriorly directed septal movement followed by paradoxical or anteriorly directed movement during much of systole before a terminal small posterior motion. This pattern was apparent in six of the seven animals in all complexes, and in some of the complexes from the remaining experiment. This pattern is typical of that observed in left bundle branch block[6–8] and suggests that the site of origin of the arrhythmia, if in the high septum as indicated by the electrical readings, probably arises near the right ventricular surface. In the only complex in which left ventricular activation occurred earliest, the septal motion was distinctly different. Initial movement was delayed

TABLE 3. Electrical and Echocardiographic Data from Paced Beats

		Site of Stimulation			
		RV	LV	HS	LS
Activation times (ms)	RV	——	56.1 ± 11.3	56.6 ± 12.9	32.8 ± 15.2*
	LV	57.5 ± 9.3	——	55.2 ± 19.2	52.4 ± 11.8
	HS	53.0 ± 11.8	57.9 ± 15.9	——	43.4 ± 9.7
	LS	34.4 ± 14.6	57.1 ± 8.4	39.7 ± 10.7	——
Movement times (ms)	VS	57.3 ± 10.2	99.1 ± 22.4	58.1 ± 32.6	58.4 ± 28.7
	PW	134.6 ± 24.3	133.8 ± 38.1†	156.9 ± 26.8	121.4 ± 40.1†

N = 11 except where noted. Abbreviations: HS = high septum; LS = low septum; LV = left ventricle; PW = posterior (left ventricular) wall; RV = right ventricle; VS = ventricular septum.

* N = 8.

† Premature anterior movement of the PW in three of 11 animals. See text.

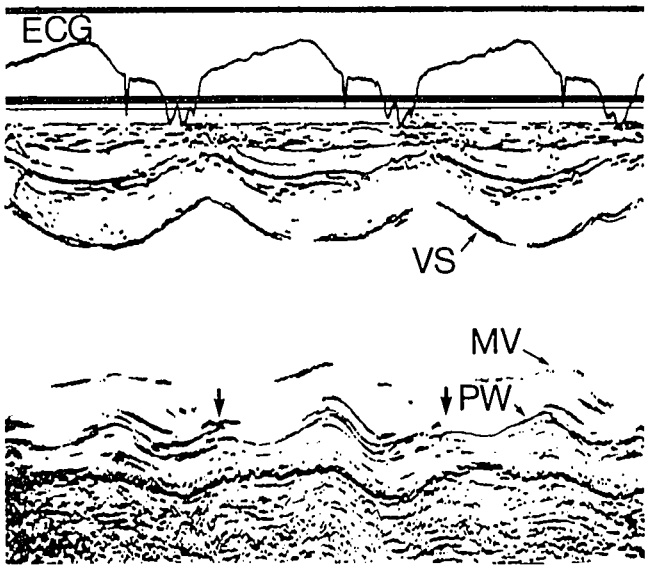

FIG. 4. Echocardiogram of left ventricular paced rhythm. Note the early (indicated by arrows) and non-sustained anterior movement of the posterior left ventricular wall (PW). Conversely, the septal (VS) movement is delayed compared to PW but the septum moves normally. (Abbreviations as in fig. 3.)

beyond that of the posterior wall but was subsequently normal with a sustained systolic posterior movement.

The reason for the unusual septal movement pattern in left bundle branch block is unknown.[6-8] Indeed, in some cases of LBBB septal motion appears normal,[8] suggesting that the phenomenon is localized and therefore might only be apparent in a small area and not always viewed by the echocardiographic beam. Since it is apparent both with spontaneously occurring LBBB and that resulting from right ventricular pacing,[8] it is generally assumed that the motion pattern is the result of the conduction abnormality. It is not clear whether this occurs because of localized septal contraction[6] or because of early onset of right ventricular pressure development; if the latter occurred, one might expect the septum to move leftward at this time secondary to reversal of the trans-septal pressure gradient.

The pacing studies indicate why echocardiography can be helpful, but only in a general way, in identifying the origin of ventricular ectopic rhythms. The stimulation-to-septal movement times were significantly shorter following right ventricular and septal stimulation than with left ventricular stimulation. The shorter movement time combined with the abnormal (LBBB) motion pattern makes identification of a right-sided (or septal) origin quite easy. Conversely, the prolonged stimulation-to-septal movement time plus the subsequent normal septal motion pattern makes a left ventricular origin obvious.

In three animals, the left ventricular posterior wall moved early (60–82 ms) after stimulation. As indicated in figure 4, however, this initial movement was incomplete and was followed by the normally sustained anteriorly directed motion. A similar phenomenon has been observed in some patients with type A WPW syndrome.[9,10] It is believed that this represents localized contraction of a small segment of left ventricular myocardium in the region of entry of the bypass tract. De Maria and co-workers have demonstrated this same pattern with pacing of the posterior left ventricular wall,[11] and Strasberg *et al.*[12] have reported a case with ventricular tachycardia with premature posterior wall movement. We did not attempt to place the stimulating electrodes in the same region as that being examined by the ultrasound beam so that it is perhaps surprising that we detected premature movement in three of 11 experiments. This implies that the premature movement may be less localized than previously suspected.

In summary, the results of this study provide electrical and supportive echocardiographic data that the site of origin of halothane–epinephrine ventricular bigeminy is in the basal portion of the ventricular septum, most likely close to the right ventricular surface. The study further documents that assessment of septal and posterior left ventricular wall motion can be helpful in localization of the origin of ventricular dysrhythmias, although only with left ventricular arrhythmias is there a potential for anatomic localization to a small area of muscle.

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