Studies on Left Atrial Automaticity in Dogs

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ABSTRACT
The site of origin and the sequence of atrial activation were studied in 21 open-chested dogs anesthetized with sodium pentobarbital. Bipolar plunge electrodes were used to record atrial electrograms simultaneously with surface lead II and His bundle electrogram. In sinus rhythm the sinus node was activated first, followed sequentially by Bachmann's bundle, right atrial appendix, left atrial appendix, posterior left atrium, and the proximal portion of the coronary sinus. In 15 dogs left atrial beats and rhythms of various rate were recorded, including instances of left atrial exit block and of rapid left atrial rhythm. In such beats one of the left atrial electrodes was activated first and was followed by Bachmann's bundle, sinus node, proximal portion of the coronary sinus, and by right atrial appendix. Left atrial beats were observed occurring (1) spontaneously; (2) as a result of vagal stimulation; (3) after destruction of the sinus node; (4) during ventricular pacing. Left atrial pacing through the electrode recording initial activity reproduced the sequence and configuration of atrial electrogram similar to that seen in the ectopic left atrial beats. These results demonstrate that in dogs ectopic activity frequently originates in the left atrium.

ADDITIONAL KEY WORDS
ectopic activity exit block left atrial rhythm vagal stimulation atrial pacing

The sinoatrial node is the normal pacemaker of the heart. However, under certain conditions the pacemaking function of the heart may be displaced to other areas such as the atrioventricular (A-V) junctional region and the Purkinje system of the ventricles. Recently, one of the authors (M. M.) has presented evidence, based on vectorial analysis of the surface P waves, suggesting that the left atrium may play an important role in the formation of ectopic impulses in man (1-5). Although the specificity of the electrocardiographic criteria, as suggested by this author, has been questioned by others (6-8), little recent information is available on the presence or absence of latent left atrial pacemakers.

Early reports on this subject have concluded that mammalian left atrial fibers act rarely, if ever, as pacemakers of the heart (10-13) and this view became generally accepted.

It was the purpose of this study to provide evidence that ectopic beats and rhythms may arise from the left atrium.

Methods
Studies were performed on 21 mongrel dogs (15 to 25 kg). The dogs were anesthetized with sodium pentobarbital, 30 mg/kg iv. Throughout the study, additional doses of 10 mg/kg were given as required. A tracheotomy was performed and the dogs were ventilated with room air using a Harvard respirator. The animals were placed on their left side, the chest was entered through the fourth right interspace and the pericardium incised.

Close bipolar electrodes were made by threading two teflon-coated steel wires (0.005 inches in diameter) into a 22-gauge needle. The wires were bent back over the point of the needle and cut 2 mm from the tip. This resulted in two small hooks which were insulated except at the very tip. When the needle was inserted into the myocardium and withdrawn, the two electrodes remained in the
tissues in close proximity to each other. Bipolar electrodes were placed at selected sites in both atria: in the sinus node, in the region of Bachmann's bundle, right atrial appendix, left atrial appendix, anterior portion of the left atrium, postero-inferior portion of the left atrium, and in the proximal portion of the coronary sinus. The proximal ends of each pair of electrode wires were led into the AC input of separate ECG preamplifiers. The filter frequencies of each preamplifier were set at 40 to 500 cps. Multiple bipolar electrograms, a standard lead II electrocardiogram, and usually a His bundle electrogram obtained by using the technique of Scherlag et al. (14) were simultaneously recorded on a multichannel oscilloscopic photographic recorder (Electronic for Medicine) at paper speeds of 100 or 200 mm/sec. The bipolar electrodes also served for pacing the heart using a battery powered pacemaker (model 5837, R wave-coupled pulse generator, Medtronic, Inc.).

The right cervical vagus nerve was isolated. Bipolar electrodes were placed on the peripheral cut end. Vagal stimulation was performed with a Grass stimulator (model S8) which delivered 6- to 10-v rectangular impulses of 2-msec duration at a frequency of 40/sec. In 16 experiments the sinus node was ablated by crushing, by injecting 40% formaldehyde into the sinus node with a 25-gauge needle, or by both.

Results

In all 21 dogs studied, initial records were made to map the sequence of activation during normal sinus rhythms. Sinus rhythm was considered to be present when initial electrical activity of the atria was recorded by the sinus node electrode, followed next by the Bachmann's bundle electrogram. The sequence of atrial activation during sinus rhythm was as follows: sinus node, Bachmann's bundle, right atrial appendix, left atrial appendix, anterior portion of the left atrium, postero-inferior portion of the left atrium, and in the proximal portion of the coronary sinus (the electrograms of the anterior portion of the left atrium were only rarely recorded). Occasionally, minor variations of the above sequence were noted and felt to reflect either physiological variations of intra-atrial conduction or minor variations in the exact positioning of the electrodes from one experiment to the other. However, in each dog the sequence of activation of normal sinus beats was constant. In all cases, sinus beats exhibited upright P waves in surface lead II.

In 15 out of the 21 dogs studied, beats originating in the left atrium were recorded. The criteria for an ectopic beat arising in the left atrium were as follows: (1) Initial electrical activity was recorded by one of the left atrial electrodes; (2) the sequence of activation had differed from that seen in normal sinus rhythm with Bachmann's bundle being activated before the sinus node.

In the majority of cases, the electrogram of the postero-inferior portion of the left atrium was the first to record initial electrical activity and was followed sequentially by left atrial appendix or Bachmann's bundle, proximal portion of coronary sinus, sinus node and right atrial appendix. The sequence of activation in left atrial beats was, however, less stereotyped than in the sinus beats and variations from the above pattern were frequent. Not infrequently, the left atrial appendix electrode was the earliest activated.

Left atrial beats were observed in the following situations:

1. Spontaneously.—Spontaneous left atrial beats were not common. When they occurred, it was usually toward the end of a study in which the chest had been opened for several hours. These beats usually occurred singly or in pairs (Figs. 1 and 2).

2. During Vagal Stimulation.—Very commonly, left atrial ectopic beats were elicited by vagal stimulation. These were usually escape beats, occurring either singly or in short salvos (Figs. 3-5). Not infrequently, they were blocked proximal to the His bundle, presumably at the level of the A-V node, and in a few cases the block occurred at the level of the ectopic pacemaker (Fig. 4). Occasionally, vagal stimulation gave rise to multifocal left atrial activity (Fig. 5).

3. Destruction of the Sinus Node.—This was accomplished by crushing, by injecting, or both, the sinus node, resulting in elimination of sinus electrical activity. The ectopic rhythm that then controlled the atria frequently arose from the left atrium. An example of a sustained rapid left atrial rhythm is shown in Figure 6. Even when the sinus node was destroyed and the pacemaker was located in...
Spontaneous left atrial beat. The first beat is a normal sinus beat. The second beat originates in the left atrium. The LAA electrogram records the earliest electrical activity, and is followed sequentially by BB, LAP, SN, CS, and RAA. Time interval between the vertical lines is 1000 msec. Abbreviations used in this and in the following figures: II = lead II of the surface electrocardiogram; SN = sinus node; BB = Bachmann’s bundle; RAA = right atrial appendix; LAP = postero-inferior portion of the left atrium; LAA = left atrial appendix; CS = inferior portion of the left atrium corresponding to the proximal end of the coronary sinus; SB = sinus beat; LAB = left atrial beat. A represents atrial depolarization; H represents His bundle potentials; V represents ventricular depolarization as reflected in the His bundle electrogram (HBE).

Figure 1:

Figure 2:

a: Control recording showing sinus rhythm. b: Spontaneous left atrial rhythm. The LAA electrogram shows the earliest electrical activity, sequentially followed by BB, SN, and RAA. c: Stimulation through the recording LAA electrode. Note the similarities in the sequence of activation and in the configuration of the atrial electrograms as compared with b. SA = stimulus artifact. Other abbreviations same as for Figure 1.
Left atrial beats elicited during vagal stimulation. The first three beats are blocked sinus beats followed by a functional escape beat. The last two beats originate in the left atrium, the LAP electrogram recording the earliest electrical activity, followed sequentially by LAA, BB, CS, SN, and RAA. All these beats are nonconducted to the ventricles. The time interval between the vertical lines is 1000 msec. Abbreviations as in Figure 1.

Left atrial ectopic activity elicited during vagal stimulation. The first beat is a blocked sinus beat, followed by a ventricular escape beat. The ventricular beat is followed by a left atrial beat, the LAA electrogram recording the earliest electrical activity (solid arrow). This beat, too, is not conducted to the ventricles. The third atrial impulse (open arrow) also originates in the left atrium, not far from the LAA electrode which records a corresponding electrogram. This impulse, however, is blocked at the level of the ectopic pacemaker, without any evidence of electrical activity in the remaining atrial electrograms. The possibility that the second atrial beat is retrogradely conducted is unlikely since the sequence of atrial activity does not follow the pattern repeatedly observed during retrograde atrial conduction in other studies from this laboratory (A. N. Damato, unpublished observation. ALA = anterior portion of left atrium. Other abbreviations same as in Figure 1.)
LEFT ATRIAL AUTOMATICITY

FIGURE 5
Multifocal left atrial elicited by vagal stimulation. The first atrial beat is a sinus beat. The second beat is a left atrial beat, the LAA electrogram recording initial electrical activity (see arrow). The third beat is also a left atrial beat but arising from a different focus, the LAP electrogram being the first to record the earliest activity (see arrow). Note the differences in sequence and configuration of the electrograms in the three various beats. The time interval between the vertical lines is 1000 msec. Abbreviations same as in Figure 1.

FIGURE 6
Left (C): control recording showing sinus rhythm; Right (LAR): sustained rapid left atrial rhythm after destruction of the sinus node. The LAP electrogram records the initial electrical activity, sequentially followed by LAA, BB, CS, and RAA. C = control recording; LAR = left atrial rhythm. Other abbreviations same as in Figure 1.

Another focus (i.e., in the His bundle), ectopic left atrial beats were easily induced by vagal stimulation or seen to occur spontaneously (Fig. 7).

4. Ventricular Pacing.—Left atrial beats were occasionally observed during right or left ventricular pacing. An example of this type of phenomenon is shown in Figure 8, in which sinus and left atrial beats compete for the control of the atria during A-V dissociation.
FIGURE 7

Left: control tracing showing normal sinus beat. Middle: left atrial beat recorded after destruction of the sinus node. The order in which atrial electrograms are recorded is as follows: LAP, BB, LAA, CS, and BAA. Right: left atrial stimulation through the LAP electrode. Note the similarities in the sequence of atrial activation and in the configuration of the electrograms between the spontaneous and paced left atrial beats. LA = left atrial; SA = stimulus artifact. Other abbreviations same as in Figure 1.

FIGURE 8

Comparison between left atrial and sinus beats during A-V dissociation elicited by ventricular pacing. C: control recording showing normal sinus beat. Right (VP): recordings during ventricular pacing. Atrial beats numbered 1 and 3 are of left atrial origin, with LAA electrogram showing the earliest electrical activity. Beats numbered 2 and 5 are of sinus origin, similar to that present in the control tracing. Beat number 4 may represent a retrogradely conducted impulse with a reentry. The time interval between the vertical lines represent 1000 msec. Hr represents His bundle potentials recorded retrogradely. VP = ventricular pacing; SA = stimulus artifact. Other abbreviations same as in Figure 1.

5. Left Atrial Stimulation.—In several experiments, left atrial pacing was performed through the left atrial electrode which recorded the earliest electrical activity. The beats produced by this type of stimulation always exhibited a sequence of activation...
which closely resembled that present in the unpaced left atrial beats. The configuration of the resulting electrograms was also similar to that seen in the unpaced left atrial beats (Figs. 2 and 7).

The configurations of the P waves in the surface electrocardiogram were not analyzed because of the well-known variability of P waves in open-chested dogs.

Discussion

The approach on which the present study is based deals with electrical activity of the atria in toto. At this level of organization, it is possible to study normal and ectopic activity by electrodes directly implanted into the atrial wall. Simultaneous recordings from several such electrodes strategically located within the atria yield information about the site of initial activation, the sequence in which the various parts of the atria pass into the active state and, to a lesser extent, about the direction followed by the activation process. It seems reasonable to assume that the electrode recording the earliest electrical activity is located not far from the impulse-forming center. This can be confirmed when stimulation from the site where initial electrical activity was recorded reproduces the sequence of activation seen in the spontaneous beats. Further confirmation of the above assumption can be obtained if the electrograms of the paced beats exhibit a configuration similar to that present in the nonpaced beats.

Our results demonstrate the existence of important left atrial ectopic activity in dogs. The analysis of the sequence of atrial depolarization in the control and in the ectopic beats proves that in the former the sinus node is the site of origin of the impulse, while in the latter it is the left atrium. The possibility that the ectopic atrial impulses might be caused by the plunge wires themselves used in this study should be considered, but seems unlikely for the following reasons: (1) The insertion of the wires was never sufficiently traumatic to elicit premature atrial beats or other arrhythmias, (2) in spite of the multiple atrial impalement, stable sinus rhythm was always present in the early stages of the experiment.

Although the role of the wires in enhancing ectopic activity cannot be absolutely excluded, such a situation may well simulate the clinical conditions when abnormal impulses arise in an irritable atrial focus. The exact determination of the site of the ectopic pacemaker is limited by the small number of electrodes inserted into the left atrial wall. This aspect of our study may be improved in the future if technical handicaps can be overcome. In the majority of cases, the electrode located in the postero-inferior portion of the left atrium recorded the earliest ectopic activity, suggesting this region as the most frequent pacemaker site. Such a localization is in agreement with previous studies (1-3, 5) and was also predicted by Hoffman and Cranefield (9) who suspected that "... if there are areas in the left atrium which do contain specialized pacemaker tissue, they are probably to be found posteriorly in the tissue surrounding the entry of the pulmonary veins and adjacent to the interatrial septum." In some instances, however, the electrogram of the left atrial appendix preceded that of the postero-inferior portion of the left atrium in recording the initial activity. The possibility that several pacemaking centers exist in the left atrium thus seems very likely, and is supported by observations of more than one type of left atrial beat not only in various experiments but also in the same animal (Fig. 5).

Another aspect of the present study is to expose the quantitative and qualitative characteristics of left atrial ectopic activity. It is worth reemphasizing that this activity was easy to elicit. In the total group, the vast majority (more than 70%) of the dogs exhibited one or more types of left atrial beats and rhythms. It seems likely that by prolonging the duration of the experiments or by enhancing even more the inherent automaticity of the ectopic foci by conventional physical or pharmacological means, this percent could be increased. This would indicate that left atrial automaticity is not a rare phenomenon but represents a basic physio-
pathological mechanism, the practical importance of which has yet to be appreciated.

The wide range of left atrial arrhythmias recorded during this study also deserves special comment. At one end of the spectrum of these arrhythmias were rapid left atrial rhythms. Their firing rate ranged between 240 (Fig. 6) and 600 beats/min (under our experimental conditions, the normal heart rate in dogs is approximately 150 to 180 beats/min). Some of these rhythms may represent the canine counterpart of human atrial flutter and will be the subject of a separate communication.

On the other end of the spectrum of rhythm disturbances originating in the left atrium were single ectopic beats, either conducted or nonconducted to the ventricles. Most frequently, these were escape beats elicited during vagal stimulation. On a few occasions, it was possible to record a single left atrial beat which was not propagated to other portions of the atria, as demonstrated by the absence of electrical activity in the remaining electrograms as well as in the surface lead (Fig. 4). This phenomenon represents an example of an exit block in the area of the ectopic pacemaker and is the counterpart of what occasionally happens to a sinus node discharge and is known in clinical electrocardiography as sinoatrial exit block. As far as ectopic atrial activity is concerned, there are only a few clinical communications reporting this kind of phenomenon (15-17) and no experimental demonstration of it. The present report thus fills this gap.

Our results are also consonant with recent human studies from this laboratory using the technique for recording His bundle activity with a catheter (18). These studies have suggested that in the so-called lower and middle nodal rhythms the impulse originates in the His bundle rather than in the A-V node; also, that in the “upper nodal” variety the impulse originates either in the coronary sinus or inferiorly in the left atrium.

The present study, in conjunction with previous clinical observations (1-5), indicates that left atrial ectopic activity may play an important role in the genesis of certain types of clinical arrhythmias. Additional work is needed to further elucidate the means of recognizing this activity in the surface electrocardiogram in man.

References
LEFT ATRIAL AUTOMATICITY

Studies on Left Atrial Automaticity in Dogs
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