Localization of Ventricular Irritability by Epicardial Mapping

Origin of Digitalis-Induced Unifocal Tachycardia from Left Ventricular Purkinje Tissue

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SUMMARY

Epicardial mapping technics were used to locate the origin of ventricular ectopic beats produced by pacing and by the administration of ouabain and acetylstrophanthidin in pentobarbital-anesthetized open-chest dogs. The sequence of epicardial depolarization was determined with close bipolar reference and roving electrodes. The wave of excitation spread in concentric manner from driven points with the origin having the earliest time. Nonparasystolic unifocal ventricular tachycardia (UVT) was then aroused in nine dogs with ouabain or acetylstrophanthidin. Plunge electrodes were inserted for recording and stimulating of bundle of His and Purkinje fibers. Earliest epicardial ventricular activation of the UVT beats always occurred at or near the apex of the left ventricle. Purkinje fiber (PF) spikes from the region of earliest epicardial depolarization appeared just prior to ventricular activation. Pacing at this point produced QRS configuration almost identical to that during UVT. His bundle pacing normalized QRS configuration and suppressed UVT. Isolated right ventricular and left ventricular PF were perfused in the same tissue bath for microelectrode impalement. Infusion of ouabain increased the rate of automatic discharge of left ventricular PF before those from the right ventricle in each of five preparations. These studies suggest that digitalis-induced unifocal ventricular tachycardia originates below the His bundle from Purkinje tissue supplying the left ventricle and demonstrate that automaticity of canine PF from the left ventricle is preferentially enhanced by ouabain.

Additional Indexing Words:

Ventricular aneurysm Accelerated idioventricular rhythm Fusion beats
Tyrode's solution

The point of origin of ventricular premature beats is of more than theoretical interest. Beats originating in the right ventricle, for example, appear more commonly in patients without obvious heart disease, whereas left ventricular premature beats are more frequently recorded from ischemic hearts. Logic suggests that such beating would arise close to the source of

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pathology. It is thus conceivable that foci of irritability could be excised as has been done successfully for many years by neurosurgeons in some cases of epilepsy. Recently patients have been reported who had dangerous repetitive ventricular tachycardia relieved by successful resection of ventricular aneurysms and even of acutely infarcted myocardium. Where do such arrhythmias arise: within or adjacent to the aneurysm or elsewhere, and unrelated to the injury itself?

In order to answer such questions, we investigated the possible applicability of the technic of epicardial isopotential mapping to localize the origin of ectopic irritability directly in the heart. Two models for these early studies were chosen: ventricular pacing and digitalis-induced unifocal ventricular tachycardia. First the accuracy of the method was investigated by pacing in open-chest dogs. Then ectopic arrhythmias were aroused with digitalis glycosides. The mapping technic suggested that the unifocal tachycardias produced by ouabain and acetylchlophenthibidin always originated in the left ventricle. Finally in vitro studies showed that ouabain preferentially increased the spontaneous discharge rate of left ventricular Purkinje tissue when compared in the same tissue bath with Purkinje fibers from the right ventricle.

Methods

In Vivo Studies

Healthy mongrel dogs weighing 25–35 lb were anesthetized with pentobarbital. Respiration with air was controlled by a Harvard pump through a tracheostomy or pharyngotraceal tube. The chest of each dog was opened through a medium sternotomy and the heart suspended in a pericardial sling. A catheter was inserted in the left femoral vein for administration of drugs. Standard electrocardiographic leads were attached to the extremities and to the area of the middorsal spine of the 7th thoracic vertebra (lead V10).

Mapping of Paced Beats

Close bipolar epicardial electrodes were sewn to the right and left ventricles for stimulation. A bipolar intramural electrode located at the base of the right ventricle was used to record a reference electrogram during mapping. The roving electrode was tripolar, and recordings were taken from two of the three leads. The atria were paced from the right atrial appendage through a bipolar intramural electrode.

A repetitive sequence of pacing was established with a digitally programmed stimulator. The atria were driven slightly faster than the sinus rate to suppress sinus activity. A sequence was cyclically repeated which consisted of four atrial beats (A) followed by two depolarizations of first the right ventricle (RV) and then the left ventricle (LV) (A-A-A-A-RV-RV-LV-LV). Mapping of ventricular activation during the three different modes of excitation (atrial, right ventricle, left ventricle) was conducted by methods described in detail elsewhere. Simultaneous recordings of the scalar electrocardiograms and of reference and roving ventricular electrograms were taken on an Electronics for Medicine recorder (DR-8) at paper speed of 200 mm/sec.

More than 40 predetermined locations on the right and left ventricles were recorded to construct ventricular epicardial activation maps. The point in time where the epicardial spike moved most rapidly was taken to represent the instant when the electrical force passed between the bipolar reference or roving electrode. The intervals between rapidly moving points from the two electrodes were measured to the nearest 1 msec. Isochronic maps were then constructed.

Mapping of Beats Produced by Infusions of Ouabain and Acetylchlophenthibidin

In another group of dogs, ouabain and/or acetylchlophenthibidin* were administered by repeated intravenous bolus injections. When ouabain was used 0.5 mg was given as a loading dose in all cases and then 0.125-mg increments were added at approximately 15-min intervals. With acetylchlophenthibidin, 0.5-mg loading doses were administered and 0.25-mg incremental boluses were injected at 5–10-min intervals.

Ventricular automaticity revealed itself with the development of the nonparasystolic unifocal tachycardia (accelerated idioventricular rhythm) which competed with the sinus supraventricular rhythm. Fusion beats were commonly observed. Measurements for mapping were only made from beats which were clearly ventricular in origin, without contribution from the sinus and which produced consistent patterns on the three simultaneously recorded external electrocardiographic leads (I, AVF, V10). In some dogs the sinus node was crushed and the ventricular rhythms which appeared at slower rates under these circumstances were mapped.

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Unifocal ventricular tachycardias (UVT) first appeared after administration of from 0.625 to 1.0 mg of ouabain. The stable unifocal tachycardias persisted for different periods of time, usually from 30 min to 1 hour, whereupon irritability from other sources appeared and further mapping could not be conducted. In all but two studies sufficient time was available (about 30 min) to record more than 30 points during the presence of the stable unifocal rhythm. However after beats from other locations began to appear, the UVT was disrupted and no longer dominated the rhythm of the heart.

Use of acetylstrophanthidin proved more convenient than ouabain and was utilized in the later studies. UVT appeared when 1.00-2.00 mg of acetylstrophanthidin had been administered. Arrhythias persisted for 15-30 min, whereupon sinus rhythm dominated. The UVT could be reestablished for another similar period by administering additional amounts, usually 0.25 mg.

**Confirmation of Origin of Ectopic Beats**

To establish that the UVT was originating in the ventricles, His bundle electrograms were recorded and His bundle pacing was performed from bipolar electrodes inserted into the atrioventricular junctional region as described by Scherlag et al. Depolarization of Purkinje fibers were also recorded through Scher-type 10-lead intramural electrodes plunged into ventricular muscle. These signals were identified as small high-frequency spikes that appeared just before the larger and wider spikes of nearby myocardial depolarization. When a Purkinje fiber potential was recorded from near the source of an idioventricular beat, the Purkinje spike appeared just before the QRS deflection of the three simultaneously recorded external electrocardiographic leads.

**In Vitro Studies**

The heart was rapidly removed from anesthetized dogs through a left lateral thoracotomy. In some cases animals who had apparently totally recovered from the effects of intravenously administered acetylstrophanthidin were used for the in vitro studies. The excised heart was then immediately immersed in Tyrode's solution. The right and left ventricles were opened. Purkinje networks coursing between the free walls and the septum were excised from each ventricle. These tissues were pinned without stretch to a paraffin block in a single muscle chamber perfused with oxygenated Tyrode's solution maintained at a temperature of 37°C. Electrograms and intracellular records were taken simultaneously from the right and left Purkinje fibers after the tissues appeared stable in terms of rate of spontaneous discharge. Ouabain was then introduced into the chamber at a concentration of 0.5 mg/liter of Tyrode's solution. Records were taken at frequent intervals until both tissues were no longer excitable by maximal stimulation.

**Results**

**In Vivo Studies**

**Mapping of Paced Ventricular Beats**

Paced beats from each ventricle were mapped in two dogs. In each case the point of earliest epicardial depolarization coincided with the location of the pacing electrodes in the myocardium. The excitation front then spread in an essentially concentric fashion from the point of origin.

An isochronic map from one of two dogs paced from the right ventricle is shown in figure 1. Points depolarized within particular time periods are indicated by dots of similar size. A total of 48 points was mapped on the ventricles in the study shown in figure 1, and 54 in the other. The electrodes had been inserted in the right ventricle at the point marked with a cross (+). The latest points mapped in the two studies were depolarized 72 and 80 msec after the point of origin and were located in each case on the posterolateral wall of the left ventricle (not pictured).

A map of pacing from the left ventricle is shown in figure 2. Again all points were depolarized later than the point of origin. The spread of depolarization was essentially concentric within the limitations of observation imposed by the number of points which were mapped. The latest points studied with LV pacing were depolarized 50 and 60 msec after the origin and were located opposite the pacing electrodes on the lateral wall of the LV in one case and near the outflow tract of the right ventricle in the other (not pictured).

**Mapping of Unifocal Ventricular Tachycardia Aroused by Ouabain and Acetylstrophanthidin**

In nine dogs the ventricular epicardial depolarization sequence was mapped after the arousal of UVT by either ouabain or acetylstrophanthidin. In each case the arrhythmia originated near the apex of the left ventricle. In figure 3 an isochronic map is shown...
UNIFOCAL VENTRICULAR TACHYCARDIA

Epicardial depolarization map from pacing of the right ventricle as developed on the anterior surface of the dog heart. The wavefront spreads out concentrically from the point of insertion of the electrodes (+). RV = right ventricle; LV = left ventricle; IVC = inferior vena cava; SVC = superior vena cava; RA = right atrium. Numbers in milliseconds.

Figure 1

illustrating the depolarization sequence for such an arrhythmia induced by ouabain. The latest point observed in the study was activated 35 msec after the point of origin which is marked with a cross (+). The activation sequence did not spread entirely concentrically. An area higher on the left ventricle was activated earlier than regions closer to the zero point, although later than the point of origin itself.

A map of UVT developed by acetylstrophanthidin in one dog is shown in figure 4. Again the region of earliest activity appeared in the left ventricle. The latest time recorded after the zero point was 47 msec which was near the junction of the right ventricle with the right atrium. In this case nonconcentric breakthroughs were observed on the posterior left ventricle.

The external electrocardiogram recorded from leads I, AVF, and V10 showed that the forces generated from UVT aroused by ouabain and acetylstrophanthidin were directed superiorly, to the right, and somewhat dorsally. An example is shown in figure 5. In A the UVT drives the ventricles. In B the ventricles were paced at a slightly faster rate from an electrode inserted where the origin of the tachycardia had appeared by epicardial mapping. The basic form of QRS is very similar in appearance although slightly wider.

Confirmation of Origin of Ectopic Beats

To establish further that the UVTs were ventricular in origin, His bundle pacing was carried out as shown in figure 6. After four ectopic beats, His bundle pacing was instituted (at the arrow). The QRS assumed its supraventricular form and the tachycardia was suppressed because the His bundle was driven at a rate which was slightly faster than the ectopic foci.

Recordings from the bundle of His and from two Purkinje fibers were made during sinus rhythm (fig. 7A) and during ventricular tachycardia (fig. 7B). During supraventricular rhythm the His spike appeared before ventricular depolarization. The Purkinje spike from the left ventricular apex followed a spike from the base of the LV. However, during the tachycardia the Purkinje spike from the apparent origin of the tachycardia at the apex preceded any ventricular depolarization as noted on the external electrocardiogram. The ventricular base was now activated later. A depolarization complex was recorded from the
bundle of His early in ventricular activation but no longer in advance of QRS.

**In Vitro Studies**

Right and left Purkinje tissues were evaluated simultaneously in the same tissue bath from each of five dogs. Extracellular electrograms were recorded in each experiment, and intracellular potentials were recorded in three studies. After a variable period of stabilization, spontaneous depolarization appeared in both left and right Purkinje fibers (PF). Epinephrine was sometimes given to induce diastolic depolarization. In four of five preparations the left PF discharged more rapidly than the right PF before digitalis was applied; in the other the right PF were slightly faster (figure 8). After addition of ouabain to the baths, the left PF always increased their rate before the right PF (fig. 9). Furthermore, the fibers from the left PF ceased their rapid discharge and failed to be excitable before the right PF, and in most cases before the right PF had increased their rates from the resting rate. Possible reversibility of the effects of ouabain on the PF was not evaluated in these studies.

**Discussion**

The arousal of digitalis-induced unifocal ventricular tachycardia (UVT) from the same area of the canine heart was an unexpected
UNIFOCAL VENTRICULAR TACHYCARDIA

Epicardial depolarization map of unifocal ventricular tachycardia produced by acetylstrophanthidin on the anterior-left lateral surface of the dog heart. As with tachycardia produced by ouabain the point of earliest epicardial depolarization is in the left ventricle. Abbreviations as in figure 1.

The increased slope of phase-4 diastolic depolarization accounts for the more rapid discharge of Purkinje fibers when stimulated by digitalis glycoside. This arrhythmia can be observed first to compete with the sinus pacemaker and then as its rate increases the UVT dominates the rhythmicity of the heart.

Such ectopic pacemakers are assumed to arise in Purkinje rather than myocardial cells. With administration of ouabain in tissue baths myocardium does not acquire spontaneous diastolic depolarization whereas this development is characteristic of the drug's effect on Purkinje preparations. This greater sensitivity of Purkinje fibers than ventricular muscle fibers to the effects of ouabain is probably related to different degrees of active ion (potassium) transport between the two types of tissues.

Origin of Irritability, His Bundle Studies, External Electrocardiograms

Exactly where in the Purkinje network ventricular arrhythmias arise has been in the past primarily a matter for speculation, although recently more direct search for such points has been undertaken. In 1960 the origin of certain ventricular arrhythmias was assumed to be in the "terminal twigs of the Purkinje system," but no direct proof for this supposition was available at that time. Very recently, ventricular tachycardia aroused by ouabain was investigated with intracardiac recording catheters by Damato, Lau, and Bobb. Their studies revealed that the left bundle was depolarized before the His and

**Figure 4**

Similarity of the electrocardiogram between unifocal ventricular tachycardia and pacing from approximate site of origin of unifocal ventricular tachycardia. (A) Acetylstrophanthidin-induced unifocal ventricular tachycardia. (B) Beats driven from the left ventricular apical region at a slightly faster rate.
Figure 6

Change in morphology of external electrocardiogram between unifocal ventricular tachycardia induced by ouabain (first four beats) and His bundle pacing (after arrow) at a slightly faster rate. RV = right ventricle; II = external ECG lead II; time markers = 100 msec.

Figure 7

Depolarization of His and Purkinje fibers with normal conduction (A) and unifocal ventricular tachycardia (B). BH = bundle of His; LPF₁ = left ventricular electrocardiogram recorded through Scher multiple-lead electrode in apex of left ventricle; LPF₂ = same as LPF₁ at base of left ventricle; p = Purkinje spikes; time markers = 10 msec.
right bundles in 10 of 15 dogs, which suggested that the rhythm had originated somewhere within the left bundle. In five of the 15 dogs the Hs and both bundle branches were depolarized after onset of QRS, and these workers suggested that this implied that the tachycardia had started in the Purkinje tissues themselves and not in the left bundle.

With the catheter recording technic electrical activity can be observed in the closed-chest animal. It allows comparisons to be made between time of discharge of a few specific parts of the conducting system relative to the external electrocardiogram and to each other. Sometimes, however, the nearby muscle electrogram “drowns out” the smaller spike from the specialized conducting system. Because of such limitations, it seemed advisable to use a technic which would permit records to be taken from more locations and thus, hopefully, localize the site of origin more precisely.

Such direct measurements would best be made together with observations of the external electrocardiogram which can be used to localize indirectly the approximate origin of ectopic beats. By pacing various points on the heart, predictable ECG patterns are produced, and clues about the origin of irritability can be drawn from examination of the QRS in different planes.

Specific localization of the origin of ventricular premature beats has been inferred from the morphology of the external QRS by Rosenbaum (table 1). However, experimental correlation for some of these suppositions is not available to our knowledge. Rosenbaum’s conclusions are based on the logical assumption that depolarization spreads away from the origin of such ectopic centers. Points which are...
Further effects of ouabain on automatic function of Purkinje fibers from canine left (LPF) and right ventricles (RPF). (C) Shortly later (after B in fig. 8) automatic function from the LPF stopped as the resting potential approached 0 mv. At the arrow, the microelectrode was withdrawn from the cell. By now the right ventricular Purkinje fiber was responding to ouabain with an increase in rate to 150/min (interval of 0.40 sec) and rise in resting potential. In D the RPF also stopped discharge, 13 min after similar failure of the LPF. Same time lines and voltage as in figure 8.

Table 1

Localization of the Origin of Ventricular Ectopic Beats from Examination of the External Electrocardiogram

<table>
<thead>
<tr>
<th>Appearance of QRS</th>
<th>Origin of ventricular beat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left bundle-branch block (chest leads)</td>
<td>Right ventricle</td>
</tr>
<tr>
<td>With left axis</td>
<td>Apex</td>
</tr>
<tr>
<td>With normal axis</td>
<td>Near tricuspid valve</td>
</tr>
<tr>
<td>With right axis</td>
<td>Outflow tract</td>
</tr>
<tr>
<td>Right bundle-branch block (chest leads)</td>
<td>Left ventricle</td>
</tr>
<tr>
<td>With left axis</td>
<td>Posterior wall</td>
</tr>
<tr>
<td>With right axis</td>
<td>Anterior wall</td>
</tr>
<tr>
<td>Predominant R wave (all chest leads)</td>
<td>Left ventricular base</td>
</tr>
<tr>
<td>With left axis</td>
<td>Posterior</td>
</tr>
<tr>
<td>With right axis</td>
<td>Anterior</td>
</tr>
<tr>
<td>Predominant Q or S waves (leads V₂–V₆)</td>
<td>Left ventricular apex</td>
</tr>
<tr>
<td>With left axis</td>
<td>Posterior</td>
</tr>
<tr>
<td>With right axis</td>
<td>Anterior</td>
</tr>
</tbody>
</table>

Further away are depolarized late, thus giving the appearance of bundle-branch blocks and particular axis deviations. Watanabe, furthermore, has devised a scheme for localizing the
origin of parasystolic beats by analyzing the morphology of both ectopic beats and conducted beats.27 Again, however, direct experimental proof of each of these assumptions has not been published to our knowledge.

**Relation of Epicardial to Endocardial Depolarization**

Epicardial mapping appeared to be a convenient technic for finding by more direct means the origin of such arrhythmias. Validity of such an approach is based on the assumption that the point of earliest ventricular epicardial depolarization overlies the actual Purkinje focus adjacent to the endocardium. A close relationship between the epicardial excitation pattern and the intramural excitation wave has been observed by Durrer and his colleagues in revived perfused human hearts.26 Endocardial activation occurred before epicardial breakthrough in these hearts, but by 30 msec after the start of the left ventricular cavity potential “excitation has already reached the epicardial surface of those sites overlying the areas of earliest endocardial activation.” Furthermore, close correlation between epicardial depolarization and underlying conduction has been established in patients with preexcitation.29 Resection of the anomalous pathway has normalized the preexcited QRS and eliminated the abnormal points of early activation of the ventricles. It seems likely that the same relationships would hold true for ectopic foci as for normal conduction and preexcitation. Despite these observations, however, the objection can be raised that ventricular ectopic beats may be rapidly conducted away from their point of origin along the Purkinje network and first “erupt” onto the epicardial surface at a distance from the inciting focus. We have not disproven this contention. Simultaneous epicardial mapping, and transmural and endocardial (Purkinje) records will be required in this regard, and efforts to obtain such proof are now in progress.

Sometimes nonconcentric epicardial breakthrough was observed (fig. 3). This phenomenon occurs during the normal activation sequence in the dog heart and should not be taken to imply the presence of two foci of automatic activity. It is thought to represent nonuniformity of the wavefront approaching the epicardial surface.

**Origin of UVT below the Junctional Tissues**

To establish that the ectopic activity clearly originated below the A-V junction, His bundle records were taken. During UVT the His potential appeared after the onset of external QRS, the Purkinje spike, and the electrogram taken from the point of earliest depolarization. The digitalis-induced beats could not, therefore, have originated in the His bundle and have been conducted aberrantly to the ventricles. Vassalle and co-workers have used a similar approach to authenticate the ventricular origin of ectopic beating from digitalis.12 Production of supraventricular QRS by rapid His pacing as performed in our study or by atrial pacing further substantiates this point.17

The similarity in QRS morphology of leads I, AVF, and V10 from both UVT and beats paced from the earliest epicardial point also helps to confirm the infra-His onset of the digitalis-induced beats (fig. 5). Great precision in localization cannot be attached to this comparison, however, since similar electrocardiographic configurations may be obtained for several paced sites within this general area.

**Characteristics of Digitalis-Aroused Unifocal Ventricular Tachycardia**

The unifocal ventricular tachycardias whose point of origin was localized in these studies are essentially accelerated idioventricular rhythms. They are seen relatively late in the course of digitalis toxicity after the sinus rate has decreased and following the at least temporary suppression of nonaccelerated ventricular automaticity.12, 30, 31 Suppression before acceleration of ventricular automaticity can be revealed by carotid sinus stimulation and in heart block.31, 32 This biphasic effect of digitalis upon ventricular pacemakers is incompletely understood.

The UVT which arose after sufficient amounts of ouabain or acetylstrophanthidin had been administered were relatively stable in our studies. If the sinus had not been
crushed, then the first sign of their presence was a slight distortion of QRS by fusion with the supraventricular beat. Appearance in this manner is characteristic of an accelerated escape rhythm. The rate of the lower pacemaker, having become equal to or slightly faster than the previously dominant rhythm, discharged before the primary beat arrived at the ectopic focus. Previously the ventricular focus had been predischarged before its own threshold was reached. As the accelerated idioventricular rhythm sped, it dominated the heart's rhythmicity. For long periods only this regular ectopic rhythm with unvarying QRS morphology and vector totally drove the ventricles. No supraventricular beats appeared because of: (1) some degree of A-V block, (2) ventriculoatrial conduction without reciprocation, and (3) retrograde penetration of the junctional tissues making antegrade conduction more difficult. It was also clear that these unifocal ventricular tachycardias were not parasystolic, since during competition between conducted and ectopic beats the ventricular focus was "reset" by the supraventricular beats. Thus "protection" of ectopic ventricular centers was not produced by digitalis intoxication. The rarity of parasystole in clinical digitalis toxicity is well established despite the frequent appearance of ventricular beats.33

Because of the time required to complete the mapping procedure it was fortunate that the tachycardias remained present and stable. Earlier in this series we observed that with use of ouabain multifocal ventricular rhythms always appeared after a variable period of time to compete with the UVT despite addition of no further ouabain.32 Mapping could not be continued when these signs of further toxicity developed. With acetylstrophanthidin, however, a dose could be established which produced the UVT alone. After about 15-20 min the accelerated ventricular rhythm slowed and sinus rhythm was reestablished without the stage of multifocal tachycardia having been entered. Acetylstrophanthidin also appeared to arouse the same UVT focus repeatedly in the same animal, thus lending further support to the likelihood that particular parts of the peripheral Purkinje tissue are selectively more sensitive to the automaticity-enhancing effects of digitalis.

We do not mean to imply from these studies that ouabain and acetylstrophanthidin have uniquely different effects on the left ventricular Purkinje system. Most likely, the drugs act quite similarly to arouse UVT, and differ principally in their onset and duration of action.

The more basic problem raised by these studies relates to the nature of ventricular automaticity. It is assumed that coupled reentrant extrasystoles are caused primarily by localized abnormalities in conduction and repolarization. Strictly competitive arrhythmias, however, such as those aroused by digitalis, can originate theoretically in any cell which has or can acquire phase-4 depolarization at a rate faster than the primary pacemaker. In human digitalis intoxication such accelerated pacemakers usually appear to be localized in the A-V junctional tissues or at least above the bifurcation of the bundle since QRS is usually "supraventricular" in form.34 Idioventricular rhythms are seen occasionally, but they appear less often. A species-related difference may be present since the rate of nodal escape rhythms in dogs is decreased by ouabain before the onset of ventricular tachycardia.31

Origin of Ventricular Irritability

Why these digitalis-induced unifocal ventricular tachycardias should always originate in left ventricular Purkinje tissues is not known. As a rule, right ventricular fibers are usually selected for certain investigations because they are said to be more likely automatic than left. However, we are unaware of studies of other possible differences in electrophysiologic characteristics such as functional refractory periods, resting or threshold potentials, and action potential durations between Purkinje fibers from the two ventricles. Some physical differences, however, are obvious to the naked eye. The right-sided Purkinje tissue is concentrated in relatively thick bands, whereas the network on the left
side is thin and more diffusely distributed. Cell size may also be different with left Purkinje fibers having larger diameter than right Purkinje fibers. Left fibers also appear to be better differentiated than right fibers (Truex R: Personal communication). The relationship of these characteristics to the data reported here is unknown.

Digitalis is not the only drug or irritant which causes the development of ventricular tachycardia. Catecholamines, hypoxia, and hypoperfusion, among others, must be investigated for their possible specific effects on localized ventricular automaticity. Also of interest is the location of nonaccelerated ventricular escape foci which drive the heart in infranodal atrioventricular block. Finally, we would like to understand the anatomic relationship of ventricular irritability to infarction, ischemia, and aneurysm. Whether the mapping technic used in the pacing and digitalis-induced UVT models will be applicable to the study of these conditions remains to be seen.

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