The Differences in Atrioventricular Conduction of Premature Beats in Young and Adult Goats

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ABSTRACT

Atrioventricular (AV) conduction was studied in anesthetized, open-chest, 1-35-day-old goats. Atrial, bundle of His, and ventricular bipolar electrograms were recorded, and the functional refractory periods of the AV conduction system and the ventricles were determined. Supraventricular premature excitation invaded the ventricles during their vulnerable period. This AV conduction property is different from that of the adult goat heart; thus, the existence of a lateral accessory bypass tract was investigated. Electrocardiographic leads I, aVF, and V10 revealed no delta waves indicative of ventricular preexcitation. Bundle of His electrograms showed that: (1) bundle of His excitation always preceded the onset of ventricular depolarization, (2) no shortening occurred in the bundle of His to ventricular activation time following early atrial premature beats, and (3) the functional refractory period of the AV node was less than that of the ventricle. The ventricular epicardial excitation sequence indicated no involvement of a lateral bypass tract in the AV conduction of basic or premature beats. Interruption of the bundle of His caused complete AV block. Therefore, no functional lateral accessory bypass tracts are present in the young goat heart, and the AV node and the ventricular specialized conduction system of the young goat are capable of conducting premature atrial excitation to the ventricles within ±10 msec of the expiration of the ventricular functional refractory period.

Methods

Thirty-seven young goats were studied; they ranged in age from 1 to 35 days and weighed up to 10 kg. Six adult goats over 1 year of age and weighing between 37 and 62 kg were also studied. The goats were anesthetized with sodium pentobarbital (30 mg/kg) injected into the jugular vein. Other drugs and solutions administered via this same route were: atropine sulfate, propranolol HCl, saline, 5% dextrose in saline, and dextran (Rheomacrodex 10% m/v). Atropine (0.5 mg/kg) was used to block cholinergic effects, and propranolol (1.0 mg/kg) was used to establish beta-adrenergic blockade. A heart treated with both of these agents was considered functionally denervated.

The goats were ventilated with a model 607 Harvard
respiration pump through a tracheal cannula with room air or 100% O₂. They were slightly hyperventilated (according to a nomogram [9]) to prevent hypoxia and hypercapnia and to partially compensate for the metabolic acidosis that often occurs following surgery. All goats were maintained at 39 ± 2°C.

The thorax was opened either midsternally or at the right fifth intercostal space. Ribs 3 and 4 of the right side were removed from adult goats. The pericardium was incised, the sinoatrial node was crushed, and its inactivation was maintained.

Bipolar stainless steel, Teflon-coated electrodes (10) were inserted at specific sites on the atria and ventricles for either stimulating or recording. Bundle of His bipolar electrograms were recorded from electrodes inserted through the right atrial free wall into the region of the bundle of His. The epicardial mapping electrode contained two Teflon-coated silver wires (0.01 inches in diameter) separated by 1 mm.

Vectorcardiographic leads I, aVF, and V₆₄ (spine of the seventh thoracic vertebra) and local activation times were measured using an Electronics-for-Medicine differential amplifier (band-pass frequencies: 12-2,000 Hz for myocardium, 40-2,000 Hz for bundle of His). All signals were displayed on a Tektronix 565 oscilloscope, photographed on 35-mm film at a film speed of 50 mm/sec, and analyzed at an enlargement of 14.5 times. Interpretation of electrograms followed the technique of Boineau and Moore (11): the peaks of monophasic potentials (maximums or minimums) or the intrinsic deflections of bипhasic potentials were identified as the local activation time.

Cardiac stimulation was programed using a digital timing unit. Ten basic stimuli, delivered at a basic cycle length, were followed by one or more premature stimuli and then were repeated. The digital timing unit drove Tektronix 161 pulse generators, and each stimulating pulse was 3-4 msec in duration and of at least twice diastolic threshold strength.

For determination of the ventricular functional refractory period, the premature stimulus was at least five times threshold. No variation in the ventricular functional refractory period resulted when the stimulating strength was increased to fifty times threshold.

DEFINITIONS

The following terms are used to describe the refractory properties of cardiac tissues. The functional refractory period of the ventricular myocardium is the minimum response interval between conducted basic, Vₛ, and conducted premature, Vₚ, responses elicited from direct stimulation of ventricular tissue (12). The functional refractory period of the AV node is the minimum response interval between conducted basic, Hₛ, and conducted premature, Hₚ, bundle of His responses propagated from the atrium (13). The functional refractory period of the AV conduction system is the minimum response interval between conducted basic, Vₛ, and conducted premature, Vₚ, ventricular responses propagated from the atrium (14).

Results

AV CONDUCTION IN YOUNG GOATS

The functional refractory period of the AV conduction system in 26 of 37 young goats ranging in age from 1 to 35 days was within ±10 msec of the ventricular functional refractory period. Figure 1 presents the basic and premature right atrial (A₁ and A₂, respectively) and right ventricular (V₁ and V₂, respectively) electrograms and the lead I electrocardiogram (ECG) obtained from a young goat heart that was functionally denervated. The heart was paced at a basic cycle length of 500 msec. In Figure 1A, a premature atrial response interval (A₁-A₂ interval) of 200 msec evoked the minimum ventricular response interval (V₁-V₂ interval) of 249 msec. By definition, this Vₚ-V₂ interval is the functional refractory period of the entire AV conduction system. Figure 1B shows the determination of the ventricular functional refractory period at the same ventricular recording site as that considered in A. After ten basic cycle lengths at 500 msec, a premature stimulus evoked the earliest ventricular response 249 msec after the last basic beat; stimulation 5 msec earlier failed to evoke a ventricular response. Therefore, the ventricular functional refractory period was 249 msec. These data confirm the finding of Preston et al. (6) that the functional refractory period of the AV conduction system is within ±10 msec of the ventricular functional refractory period; Figure 1C schematically summarizes the data.

Figure 2 presents V₁-V₂ intervals determined from three different ventricular recording sites: the central right ventricle (cRV), the basal right ventricle (bRV), and the anterior left ventricle (LV). The V₁-V₂ interval (y axis) is plotted as a function of a series of driving A₁-A₂ intervals (x axis). If there were no prolonged conduction of premature atrial beats, the resulting plot would follow the broken line (line of identity). Displacement of a point above the line indicates that prolonged conduction of the premature beat occurred due to the relative refractoriness of the AV conduction system. At A₁-A₂ intervals of 240 msec or less, the V₁-V₂ intervals were slightly different at the three sites, but at longer intervals they were identical to the responses at cRV. Arrows point from the line of identity to the V₁-V₂ intervals equal to the functional refractory periods determined at each site. Despite prolonged conduction, premature atrial beats were able to excite all recording sites within 10 msec of their respective ventricular functional refractory period. This re-

1 Built by M. Bloom, 116 Elmwood Avenue, Narberth, Pennsylvania 19072.
Records of AV conduction in a young newborn goat heart. Bipolar electrograms were recorded from the right atrium (A) and the right ventricle (V) along with the lead I ECG. The time of stimulation is indicated in record S, and the time calibration, record T, indicates 100 msec between dashes. The heart was paced at a basic cycle length (S1-S2 interval) of 500 msec and prematurely stimulated (S1-S2 interval).

A: Right atrial pacing with a premature A1-A2 interval eliciting a minimum V1-V2 interval.

B: Right ventricular pacing showing the minimum elicited V1-V2 response (ventricular functional refractory period).

C: Lewis diagram summarizing the results presented in A and B. Shaded areas adjacent to ventricular responses represent the functional refractory period of the respective ventricular beat. The cervical vagi were cut; atropine and propranolol were administered.

The relationship of the functional refractory period of the AV conduction system to the ventricular functional refractory period was verified in 26 of 37 young goats. Of these 26 goats, 9 were not and 15 were treated with propranolol; 2 goats were examined before and after propranolol administration. The interrelationship of the functional refractory periods was the same in each state. Table 1 includes data for young goat hearts paced at a basic cycle length of 500 msec. There is no statistically significant difference among any of the listed functional refractory periods determined in the young goats. Therefore, the finding that the functional refractory period of the AV conduction system is within 10 msec of the ventricular functional refractory period is true regardless of whether the heart is functionally denervated. Within the age groups studied, neither age nor body weight appeared to be a functional factor.

The influence of basic cycle length was tested in seven experiments. At a basic cycle length of 500 msec or longer, the functional refractory period of the AV conduction system was within ±10 msec of the ventricular functional refractory period more often than it was at shorter basic cycle lengths.

AV CONDUCTION IN ADULT GOATS

In four adult goats with functionally denervated hearts, the average functional refractory period of the AV conduction system was 80 msec longer than the average ventricular functional refractory period (Table 1). Figure 3 presents data from one adult...
goat before and after propranolol administration. With the absence of only vagal tone, A_2 was blocked at A_1-A_2 intervals less than 130 msec, and the functional refractory period of the AV conduction system was 240 msec (AV conduction pattern indicated by solid circles). Propranolol produced a conduction pattern (crosses) in which A_2 was blocked at an interval of 240 msec, and the functional refractory period of the AV conduction system was increased to 312 msec. The ventricular functional refractory period remained unchanged. This phenomenon was observed in all of the adult goats studied. As a result of propranolol administration, the average AV conduction system functional refractory period changed from 256.9 ± 6.4 to 323.0 ± 18.2 msec (P < 0.05). This finding contrasts with the finding that propranolol produced no significant changes in functional refractoriness in young goats. In either state of autonomic innervation, the AV conduction system of adult goats functions like that of other adult mammalian hearts in protecting the ventricles from early supraventricular excitation.

### EVIDENCE OF A LATERAL ACCESSORY BYPASS TRACT IN YOUNG HEARTS

**Electrocardiography.**—In young goats demonstrating AV conduction patterns like those shown in Figure 1, Wilson, x, y, and z scalar leads I, aVF, and V_10 showed no delta waves. The P-R intervals in hearts paced at a basic cycle length of 500 msec depended on beta-adrenergic innervation. With beta-adrenergic innervation intact, the P-R interval (measured from lead I) was 55.3 ± 2.46 msec; after administration of propranolol, the P-R interval was significantly prolonged to 71.4 ± 2.40 msec (P < 0.005).

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**Figure 2**

A_1-A_2 interval vs. V_1-V_2 interval from three different ventricular sites in a young goat heart. The A_1-A_2 interval on the x axis represents different driving premature atrial intervals, and the y axis represents the ventricular response intervals. Solid circles = central right ventricular response pattern (cRV,V_2), open circles = basal right ventricular response pattern (bRV,V_2), and crosses = basal left ventricular response pattern (LV,V_2). The broken line is the line of identity; it has a slope of one and an intercept of zero. The arrows pointing from this line indicate the V_1,V_2 intervals equal to the functional refractory period (FRP) determined at each recording site. The heart was paced at a basic cycle length of 500 msec; the vagi were cut cervically, and atropine and propranolol were administered.
Table 1

Functional Refractory Periods at a Basic Cycle Length of 500 msec

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Adult</th>
<th>Young</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Propranolol Absent</td>
<td>Propranolol Present</td>
</tr>
<tr>
<td>AVCS</td>
<td>256.9 ± 6.4 (9)</td>
<td>269.4 ± 13.7 (8)</td>
</tr>
<tr>
<td>V</td>
<td>233.1 ± 8.7 (9)</td>
<td>265.2 ± 12.7* (8)</td>
</tr>
</tbody>
</table>

All values are means ± se; the number of data points averaged is given in parentheses. AVCS = AV conduction system, and V = ventricle.

*Significantly different (0.05 < P < 0.1) from the corresponding value in the adult heart.

†Significantly different (P < 0.05) from the corresponding value in the adult heart in the absence of propranolol.

‡Significantly different (P < 0.05) from the corresponding value in the adult heart.

Bundle of His Electrograms.—The minimum H1-H2 interval elicited from premature atrial excitation was less than the functional refractory period at a ventricular recording site in all five goats in which bundle of His electrograms were recorded. Figure 4 presents electrograms recorded from the right atrium, right ventricle, and bundle of His of a young goat heart having a functional refractory period of 255 msec. In each record, the bundle of His electrogram precedes ventricular activation, indicating that conduction from the AV node excites the bundle of His. In Figure 4A, a premature atrial beat (A2) was prolonged only 4 msec in its conduction through the AV node. However, there was a substantial delay in the conduction of A2 when the A1-A2 interval was shortened to 250 msec (Fig. 4B). The H1-H2 and V1-V2 intervals were each 270 msec, indicating that the prolongation of AV conduction time was imposed by the AV node. At an A1-A2 interval of 150 msec (Fig. 4C), intra-atrial conduction was prolonged by 47 msec. The H1-H2 interval was 250 msec (less than the ventricular functional refractory period) and the V1-V2 interval was 260 msec. The tissues causing delay below the bundle of His could be either ventricular specialized conducting tissue, ventricular muscle, or both. Records of His bundle activity in all five goats showed prolongation of H-V intervals, but the prolongation was never more than 11 msec.

Atrial fibrillation has been shown to provoke ventricular fibrillation in animals with the Wolff-Parkinson-White syndrome due to simultaneous conduction through the normal AV conduction system and over the accessory bypass tract (11). Atrial fibrillation was experimentally initiated in several young goats, and bundle of His electrograms were recorded; every ventricular response was preceded by a bundle of His electrogram.

Conduction of premature beats through the AV node of the adult goat was also studied using bundle of His electrograms. In the two functionally denervated adult goat hearts studied, the functional refractory period of the AV node was at least 100 msec greater than the ventricular functional refractory period. This relationship of AV nodal functional refractory period to ventricular functional refractory period is similar to that measured in other adult mammalian hearts but different from what has been shown to exist in the young goat heart.

Sequence of Epicardial Activation.—The epicardium of the right ventricle was mapped during basic and premature beats in eight young goats in which the interval of premature ventricular response was within ±10 msec of the ventricular functional refractory period. In three of these experiments, the epicardium of both ventricles was mapped. A reference ventricular electrogram was recorded using a fixed plunge electrode or a plaque electrode sewn securely on the epicardium; a mapping electrogram registered the local depolarization under a hand-held, roving, bipolar electrode. An ECG lead was recorded simultaneously. Figure 5 illustrates the results from one of the hearts studied. The map was constructed from 24 different epicardial points. Five to seven beats were measured for each epicardial site; the time of local excitation plotted on the ventricular activation map is the mean time of these multiple measurements. Isochronic lines surround the areas of the epicardium which excited within 5 msec of one another. In Figure 5A the sequence of epicardial excitation following basic atrial beats is presented, and in Figure 5B the pattern of ventricular excitation following early premature atrial beats is shown. Measurements were made from records taken during the tenth beat of a ten-beat train and during the premature beat that immediately followed this tenth basic beat. Consequently, any variations due to the movement of the roving mapping electrode were minimized by measuring sequential beats. During the basic beat, the earliest area of excitation was in the anterolateral mid-left ventricle. Excitation spread laterally, the posterior left and right ventricles being the last.
Records of AV conduction in the young goat heart. Bipolar electrograms were recorded from the right atrium (RA), the right ventricle (RV), and the bundle of His (BH). The lower right atrial septum electrogram (LRA), the bundle of His electrogram (H), and the upper interventricular septum electrogram (SV) are individually designated in the BH electrogram in A. Also included are a stimulus marker (S) and a time calibration (T) (distance between dots is 10 msec and between dashes is 100 msec). A: A₁, A₂ = 346 msec, H₁, H₂ = 350 msec, and V₁, V₂ = 350 msec. B: A₁, A₂ = 250 msec, H₁, H₂ = 270 msec, and V₁, V₂ = 270 msec. C: A₁, A₂ = 150 msec, H₁, H₂ = 250 msec, and V₁, V₂ = 260 msec. The heart was paced at a basic cycle length of 500 msec and propranolol was administered. The cervical vagi were not sectioned and atropine was not given.
Records of AV conduction in the young goat heart. Bipolar electrograms were recorded from the right atrium (RA), the right ventricle (RV), and the bundle of His (BH). The lower right atrial septum electrogram (LRA), the bundle of His electrogram (H), and the upper interventricular septum electrogram (SV) are individually designated in the BH electrogram in A. Also included are a stimulus marker (S) and a time calibration (T) (distance between dots is 10 msec and between dashes is 100 msec). A: \( A_1-A_2 = 346 \) msec, \( H_1-H_2 = 350 \) msec, and \( V_1-V_2 = 350 \) msec. B: \( A_1-A_2 = 250 \) msec, \( H_1-H_2 = 270 \) msec, and \( V_1-V_2 = 270 \) msec. C: \( A_1-A_2 = 150 \) msec, \( H_1-H_2 = 250 \) msec, and \( V_1-V_2 = 260 \) msec. The heart was paced at a basic cycle length of 500 msec and propranolol was administered. The cervical vagi were not sectioned and atropine was not given.
Sequence of ventricular epicardial excitation in a young goat heart. Anterior, left lateral, and posterior views of the heart are shown from a goat in which the vagi were cut and atropine and propranolol were given. Each number is placed over a site where the mapping electrode was placed and is the mean time of excitation (from at least five determinations) of the area under the number with reference to the earliest measured time of ventricular epicardial excitation. The shaded areas correspond to areas exciting within approximately 5 msec of one another as indicated by the sequence key. A: Pattern of ventricular epicardial excitation following basic atrial beats. B: Pattern of epicardial excitation following early premature atrial beats.
A: Atrial fibrillation evoking ventricular fibrillation during a spontaneous sinus rhythm having a basic cycle length of 750 msec. Following the last sinus beat pictured (arrow) rapid atrial pacing at a basic cycle length of 100 msec was begun; this pacing precipitated atrial fibrillation. After five electrocardiographically synchronous ventricular responses, ventricular fibrillation occurred. The stimulus artifacts indicate the rate of atrial stimulation and are particularly clear in the RV and lead I records just prior to ventricular fibrillation.

B: Atrial premature beats precipitating ventricular fibrillation. Following a basic cycle length of 500 msec, two premature stimuli were delivered to the right atrium; ventricular fibrillation ensued in this young goat heart. Bipolar electrograms: atrium (RA), right ventricle (RV), and left ventricle (LV). ECG leads: aVF. The time of stimulation is indicated in record S and the time calibration (T) indicates 100-msec intervals.

Discussion

The present study defined the nature of AV conduction in the young goat heart: the functional refractory period of the AV conduction system and that of the ventricles are within 10 msec of one another when the heart is functionally denervated. These results clearly indicate that this AV conduction property is intrinsic to the heart itself and it is not dependent on extrinsic neural influences.

In contrast, the relationship between the AV conduction system and the ventricular functional refractory period in the adult goat is similar to that in other adult mammalian hearts: the functional refractory period of the AV conduction system is considerably (32–115 msec) longer than that of the ventricles when the heart is functionally denervated.

Preston et al. (6), who reported that premature atrial beats could excite the ventricles during the ventricular vulnerable period, recorded only cardiac surface electrograms and used the interval between excitation at the atrial and ventricular recording sites as an indication of AV conduction time. In the present study, ECG leads were recorded during each experiment. No delta waves were observed in any goat. This fact strongly suggests that preexcitation was not the basis for rapid conduction of atrial premature beats in these young goat hearts.

Figures 1A and 6 show that the QRS complex is
different during the premature beat than it is during the basic beat, thus indicating that the sequence of ventricular activation is different. Such an inversion or prolongation of the lead I QRS complex occurred frequently in young goat hearts following the shortest $A_1-A_2$ intervals. Because experiments ruled out the existence of lateral accessory bypass tracts, the aberration of the QRS complex during the premature beat is interpreted as a manifestation of conduction delays and blocks within the ventricular specialized conduction system and the ventricular muscle.

Bundle of His electrograms showed that the functional refractory period of the AV node was less than that of the ventricles in the young goat heart. Thus, the AV node is capable of sustaining AV conduction of very early premature beats. If atrial premature beats were conducted via both the AV node and a bundle of Kent, with the bundle of Kent conducting premature beats more rapidly than the AV node, then the interval between bundle of His excitation ($H_2$) and ventricular excitation ($V_2$) would shorten for progressively shorter premature intervals ($A_1-A_2$). This phenomenon was not found to occur.

Mahaim or paraseptal fibers, musclelike fibers arising from the distal AV node or the upper bundle of His and terminating in the muscular ventricular septum (16), could be a route by which ventricular muscle is activated by excitation coming from the AV node and bypassing the ventricular specialized conduction system. However, the bundle of His electrograms of Figure 4 argue against this possibility. During a basic or premature beat, a paraseptal fiber should activate the upper interventricular septum immediately after the bundle of His. The earliest that an electrode placed near the bundle of His registered an electrogram from the upper interventricular septum was 55 msec (Fig. 4), which would be an extraordinarily long time for conduction by a Mahaim bundle. In addition, the electrogram recorded from the right ventricular free wall preceded the ventricular septal electrogram, indicating that the ventricular free wall activation occurred before interventricular septal activation.

James fibers, septal atrial fibers which circumvent the body or all of the AV node (17), would shorten the apparent AV nodal conduction time (lower interatrial septum activation to bundle of His activation time). However, in Figure 4, the LRA-H interval is 55 msec, too long for conduction to have bypassed the AV node. Therefore, the involvement of Mahaim or James fibers as the basic mechanism for rapid conduction of atrial premature beats in young goats is most unlikely.

The epicardial mapping studies in young goats do not support the presence of lateral accessory AV pathways, because (1) no sites were excited until after the initiation of the QRS complex, (2) the QRS complex was not preceded by a delta wave, and (3) all of the hearts mapped did not show ventricular epicardial excitation beginning along the ventricular base. Interruption of the bundle of His resulted in complete AV dissociation. It is therefore concluded that AV conduction in young goats occurred only via the normal AV conduction system.

The present study indicates that ventricular fibrillation occurs infrequently in a goat whose heart has an AV conduction system functional refractory period less than or within 10 msec of the ventricular functional refractory period. Theoretically, such a relationship between these two tissues should allow atrial premature beats to evoke ventricular fibrillation. However, it may be that the fast conducting Purkinje system that extensively penetrates the ventricular walls of the goat heart is able to excite the ventricles quickly enough during premature beats that the inhomogeneity necessary for the subsequent development of ventricular fibrillation cannot be established.

In summary, this study has shown that the AV conduction system of the young goat heart has the intrinsic property of conducting an atrial premature beat which will excite the ventricles during the vulnerable period. The AV node has the functional properties to support this conduction, and all evidence strongly suggests that no lateral bypass tracts are operative during such conduction.

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