Anatomy of the Cardiac Conduction System in the Rabbit

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ABSTRACT
Anatomy of the cardiac conduction system was studied in 15 rabbits with serial histologic sectioning of 4. The rabbit's sinus node is a simple and distinct structure located at the junction of the crista terminalis with the sinus intercavum nearly midway between the two cavae; it contains an unusually large percentage of P cells but is not organized about a large central artery. The AV node and His bundle are relatively small and are displaced anteriorly by the large coronary sinus normally present in the rabbit because of its persisting left superior vena cava. The AV node is organized with input system and bypass tracts similar to those of man and the dog. Both the AV node and His bundle contain many conspicuously large nerve trunks. The blood supply of the sinus node is from terminal small branches of both the right and left coronary arteries and that to the AV node and His bundle is from similar terminal branches of the septal artery only. The possible functional significance of some of these anatomic features is discussed.

ADDITIONAL KEY WORDS sinus node AV node internodal pathways His bundle rabbit coronary arteries left superior vena cava

Rabbits are frequently utilized in experiments on cardiac electrophysiology, and many of the most important recent observations with intracellular microelectrode recordings have been in this animal. There have been several previous studies of the morphology of the lapine cardiac conduction system (1-7), but these have generally concentrated on single areas such as the His bundle, were incidental to physiologic experiments, or were concerned principally with the ultrastructure. The purpose of the present study was a systematic examination of the anatomy of the rabbit's sinus node, internodal pathways, AV (atrioventricular) node, His bundle and proximal bundle branches. In addition, a corollary examination was made of the blood supply to these areas. Finally, these observations were compared to previous personal studies of the cardiac conduction system in human (8-12), canine (12-14) and bovine (15) hearts.

Methods
Fifteen fresh hearts from adult rabbits weighing 2 to 4 kg were studied in the following manner. All were grossly dissected to examine the topography and blood supply of the cardiac conduction system. In 5 of these a cannula was placed in the root of the aorta and a barium gelatin mass injected to fill the coronary arteries. The surface distribution of the arteries was immediately apparent but was further facilitated by dehydrating the entire specimens in a graduated series of increasing concentration of ethyl alcohol and then immersion in clear methyl salicylate. This standard anatomic technique permits examination of the coronary distribution in the deeper layers of ventricular myocardium, and renders relatively thin-walled chambers such as the atria entirely transparent. Four of the remaining hearts were prepared for serial sectioning as follows. Each specimen was fixed in 10% neutral formalin. The lower half of the ventricular chambers was removed, with the plane of this cut being such that sections cut perpendicular to it would pass transversely through the long axis of both the sinus node and AV node. The general orientation of this initial cut to remove much of both ventricles was...
parallel to the junction of interatrial and interventricular septa, and perpendicular to the plane of the diaphragmatic surface of the heart. A second orienting cut was made perpendicular to the first one and passing through the anterior margin of the main pulmonary artery and the crista supraventricularis. The principal purpose of the second cut was to orient the specimen for the start of serial sectioning. In all specimens this orienting cut proved to be anterior to any recognizable bundle branches. This block of tissue, comprising more than half of the heart, was then embedded in paraffin and cut serially at 6-μ intervals. Of these sections 2 successive ones of every 20 (nos. 1, 2; 20, 21) were mounted. The stain routinely employed was the Goldner modification of the Masson trichrome, but in selected specimens intervening sections were stained for elastic tissue or other special structures.

Results

General Topography of the Conduction System.—The sinus node of the rabbit is located nearly midway between the ostia of the right superior vena cava and the inferior vena cava, just beneath the epicardium of the junction of crista terminalis and sinus intercalvarum (Fig. 1). Since the rabbit normally has a left superior vena cava (16, 17), the ostium of the coronary sinus (embryologically derived from the terminal portion of the left superior vena cava in most mammals) is unusually large. This effectively displaces the AV node and His bundle anteriorly toward the root of the aorta. The large ostium of the coronary sinus also alters the size and distribution of the internodal tracts, as discussed later.

The Sinus Node.—This loosely organized structure occupies the entire thickness between endocardium and epicardium at the junction of the midportion of sinus intercalvarum and crista terminalis, and is oblong with its long axis parallel to the crista terminalis (Fig. 2). Its total length varied from 500 to 800 μ. There is relatively little collagen in the rabbit's sinus node. The cells are organized into interweaving fibers and are easily differentiated from ordinary atrial myocardium by their smaller size and paler staining as well as by the difference in organization (Fig. 3). The proportion of P cells (12) to transitional or ordinary working myocardial cells in the rabbit's sinus node is exceptionally high. These cells are round or oval, occur in chains or clusters, contain relatively few myofibrils (which are randomly oriented instead of parallel to each other), and are thought to be the site of pacemaking within the node (6, 7, 12). The two other cell types are scattered, ordinary working myocardium, which is distributed mainly (but not exclusively) at the margins of the node, and a group of transitional cells with internal features intermediate between the simple pale P cells and the dark staining working myocardium. The distribution of P cells was rather homogeneous for the length of the node. The margins of the rabbit's sinus node are unusually distinct and this is attributable to the large percentage of P cells, making the contrast with ordinary atrial myocardium more apparent. The sinus node of the rabbit is not organized about a central artery but contains only small arterial branches of a size appropriate for a nutrient function alone.

The course of the left superior vena cava over the left atrium was carefully examined for nodal tissue, since it is both an anatomic and an embryologic counterpart to the right atrio caval junction. Myocardium in the wall of the left superior vena cava is inseparable from that of the left atrium and no collagen nor any other plane of cleavage was observed. At variable locations there were small clusters of pale cells, but under higher magnification (light microscope) these were not the same as P cells of the sinus node, resembling more the transitional cells. On an anatomic basis, no centers (nodes) similar to those with known spontaneous pacemaking activity could be identified along the junction of the left superior vena cava with the left atrium. The same was true of junctions between pulmonary veins and the left atrium.

The AV Node.—The AV node lies just beneath the right atrial endocardium anterior to the ostium of the capacious coronary sinus and above the septal insertion of the tricuspid valve (Fig. 4). Because the ostium of the coronary sinus is so large in the rabbit, the
FIGURE 1

FIGURE 2

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node is displaced anteriorly and the entire region occupied by it and the His bundle is foreshortened. The dimension of the AV node parallel to the septal base of the tricuspid valve is from 300 to 500 μ. Its maximal thickness in the direction from right atrium to left atrium is 150 to 250 μ, and its depth in the direction from interatrial to interventricular septum is 800 to 1000 μ. One can generally visualize the rabbit's AV node as tilted so its longest dimension is more nearly parallel to the long axis of the heart and at only a small acute angle from a line perpendicular to the junction of interatrial and interventricular septa. At its anterior and inferior margin the AV node veers into the central fibrous body and becomes separated from atrial tissue by a thin plane of collagen; anatomically, this is considered the junction of the AV node and the His bundle.

Cells of the AV node resemble those of the sinus node in being organized into fibers of smaller dimension and paler than those of ordinary atrial myocardium. However, the percentage of P cells is less in the AV node. Nerve trunks are impressively large and easily identified in the AV node of the rabbit, from which they course into the His bundle. The anatomic input system of the AV node from the atrial septum may be divided into two general regions, that of the superior and posterior crests of the node and that along its right atrial surface. Atrial septal cells forming these two input regions arrange into fibers which intermingle at the nodal margins.

Fig. 1.—Rabbit heart fixed in formalin with blood remaining in the chambers, thereby preserving its normal shape. A is a view over the right atrium (RA). The crista terminalis is seen as a pale band lying between the free wall of atrium and superior vena cava (SVC). The approximate location of the sinus node is indicated by the arrow. B is a view of the posterior surface of the same heart to demonstrate the normal large left superior vena cava which terminates as the coronary sinus (CS). Left and right ventricles are labeled LV and RV.

Fig. 2.—Low-power photomicrographs of the sinus node from two rabbits. The 1-mm reference bar indicates the same magnification for both A and B. The sinus node extends throughout the thickness of the section in the area between the two open arrows, which are placed on the epicardial surface. In each section the free wall of right atrium extends to the left and the wall of the sinus intercavarum extends to the right. The large mass of myocardium in each is a cross section of crista terminalis.
A, sections through the AV node and B, the commencement of the His bundle. These are from the same heart and the distance between the two sections is approximately 1.8 mm, B being anterior to A. In each, the interventricular septum is below and to the right, with atrial septum above; the right atrial cavity is to the left in the photographs; the 0.5-mm reference bar indicates the same magnification in both. In A the AV node is seen in cross section at approximately its maximal size, lying between the two arrows. Larger fibers of the bypass tract lie between the node and right atrial cavity, coursing beneath the endocardium and connecting with the AV nodal fibers along the right atrial surface of the node; the central fibrous body is along the right upper margin of the picture. In B the His bundle (arrows) is shown separated from the atrial septum above by collagen, as it courses to its ultimate position at the crest of the ventricular septum.

scribed in other species (9, 14, 15). The minimum thickness of the bypass tracts measured perpendicular to atrial endocardium (and the corresponding surface of the AV node) is 50 to 150 μ. The cells in the bypass tract in the rabbit are larger than those of the AV node but stain paler than those of ordinary atrial myocardium. The only arteries in the AV node are small branches of a size suitable for nutrient supply.

The His Bundle.—Continuing from the anterior and inferior margin of the AV node, the His bundle descends through the central fibrous body to the crest of the ventricular septum, where it begins to divide into a sheet of left bundle branches and a slender, small right bundle branch. The impressively large and easily identified nerve trunks of the AV node continue through the His bundle (Fig. 5) and then become more difficult to identify in the bundle branches. Cells of the His bundle organize into more longitudinally oriented fibers which are generally of larger dimension than those of the two nodes, but this dimension is not consistent, some of the fibers being smaller. The region of membranous interventricular septum so conspicuous in many mammals is barely identifiable separate from the central fibrous body in the rabbit. The length of the His bundle through the central fibrous body before the bundle branches is less than 200 μ. Its shape on cross section is oblong, with the larger dimension (about 150 μ) being lateral. The total length of anatomically identifiable undivided His bundle in the rabbit is thus remarkably small. Beginning with left bundle branches, the length of the His bundle continues 100 to 200 μ, and in this course, at variable points of departure, the right bundle branch originates. The maximal dimension on cross section of the right bundle branch near its origin is about 40 μ. While

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Figure 5
A section still further anterior in the same heart as Figure 4 at low (A) and high (B) magnifications. This section is 1.0 mm anterior to that in Figure 4B and 2.8 mm anterior to that in 4A. Some obliquely sectioned right bundle branch is visible here. The larger left bundle branch courses down the side of the ventricular septum on the right in this picture. An arrow indicates one of three easily identified nerve trunks in B. The magnification reference bars represent 0.1 mm.

This is also about the maximal thickness of the left bundle branch system, the shape of the right bundle branch on cross section is approximately circular, while the left bundle branches from a sheet 40 μ thick but over 100 μ long.

The Internodal Pathways.—These are generally distributed in the same way as in other species studied (10, 14, 15), but there are certain significantly different points. The general distribution includes anterior, middle, and posterior internodal pathways (or tracts). The anterior internodal pathway leaves the anterior margin of the sinus node and enters the crista terminalis (the node being located normally an unusual distance back from the superior vena cava) to pass anterior to the right superior vena cava and enter the anterior interatrial myocardial band (Bachmann's bundle); there it divides into two nearly equal portions with one passing to the left atrium and the other curving back to descend through the anterior margin of the interatrial septum to the crest of the AV node. The middle internodal pathway passes from the superior margin of the sinus node across the sinus intercavum and along the right atrial side of the septum to the crest of the AV node. The posterior internodal pathway leaves the sinus node to enter the crista terminalis in the direction of the inferior vena cava, there dividing beneath it to send some fibers over the coronary sinus ostium and others beneath the ostium, both penetrating the posterior margin of the crest of the AV node but also supplying most of the fibers in the bypass tract (Fig. 4A). All three internodal pathways contain both ordinary myocardial cells as well as larger and paler ones resembling Purkinje cells. The percentage of these paler large cells seems greater in the rabbit internodal pathways than in man or the dog and in some regions comprises over half of the cells present.

Two factors influence the anatomy of the internodal pathways in the rabbit. One is the more posterior location of the sinus node in the crista terminalis, and the other is the more anterior location of the AV node because of the large ostium of coronary sinus. It is difficult to measure the lengths of the internodal pathways (which normally curve more than once) in the postmortem heart, but particularly in one as small as the rabbit's. From the appearance on gross dissection and of serial sections, however, there appears to be no obvious difference between lengths of the three pathways. But there is an impressive gross difference in their cross-sectional size. Both the middle and posterior internodal pathways contain relatively few fibers, and the fewest are in the posterior. Those fibers in the posterior internodal pathways which

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Coronary arteries of the rabbit heart. This and the photographs in Figures 7 and 8 are all of the same heart, which was prepared by injection of barium gelatin into the root of the aorta and then clearing of the specimen in oil of wintergreen. In A the typical course of left coronary artery is shown, with the major mural branch indicated by the short white arrow. Next to it toward the right ventricle (RV) is a branch coursing within the myocardium in the interventricular septal sulcus, and thus corresponding to the human anterior descending ramus; this branch is not large in the rabbit. The next two branches are both over the right ventricle but originate from the branch in the anterior interventricular sulcus; the one corresponding to the conus artery in man is indicated by the enclosed black arrow. A long thin branch of the main left coronary trunk (which corresponds to a diagonal left ventricular artery in man) is seen coursing between the left ventricle (LV) and the body of the left atrium (LA), corresponding roughly to the human left circumflex branch, although it courses below the AV sulcus. The final important branch in A is the left atrial artery indicated by the thin arrow as it leaves the left coronary to course beneath the left atrial appendage and enter Bachmann’s bundle.

In B the heart has been rotated so the main left coronary trunk (short white arrow) courses along the right margin of the heart, and the conus artery over the pulmonary conus is indicated by the short enclosed black arrow. The main right coronary artery (long arrow) is seen coursing over free wall of the right ventricle (RV) below the AV sulcus, with only a small branch lying in the sulcus between the ventricle and the right atrium (RA); this small branch corresponds to the usual location of the main right coronary artery in man. The rule in Figures 6–8 = 1 cm.

The Coronary Arteries.—With the method employed in this study, the distribution of the coronary arteries in the rabbit was found to be similar to that described by Day and Johnson (18) from studies utilizing injection and corrosion. The rabbit has a right and left coronary artery, but most of the heart is supplied by the left coronary and its branches (Figs. 6, 7). In addition to those branches which supply the free wall of left ventricle, the left coronary artery consistently provided a large septal branch similar to that of the dog (19). Unlike the pattern in the dog, however, a major left ventricular branch does not course to the crux of the heart in the rabbit, nor is there a posterior descending artery. Other important distinctive features of the
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FIGURE 7
The lateral and posterior surfaces of the right ventricle and atrium are shown in A, including the distal distribution of the right coronary artery, the only major vessel visible; there are two small atrial branches. The asterisk indicates the poorly vascularized region of the crux. In B the heart is viewed directly from above, demonstrating the origin of the right (R) and left (L) coronary trunks from the root of the aorta (Ao). The undivided proximal portion of the left coronary artery is obscured here but well shown in Figure 6A. The left atrial artery is indicated by the arrow.

rabbit's coronary arteries are a predominantly intramyocardial course of even the main trunks, and an early divergence of both the main right and left coronary arteries from the AV sulcus. Unlike those in the dog and man (19), the major trunks of these two vessels early descend obliquely over the free walls of their respective ventricles and terminate by dividing almost randomly over this surface. Day and Johnson correctly stress that this distribution leaves the region of the crux in the rabbit peculiarly vulnerable to the effects of coronary occlusion, since there is little anatomic opportunity for anastomosis in this area (Fig. 7A). Of even more importance for the present observations, the crux and its blood supply are of critical importance to the arterial distribution to the AV node and the His bundle. Since the principal purpose of the arterial observations were to determine the supply to the rabbit's conduction system, the remaining observations are to that end.

For the AV node and the His bundle, the only arterial circulation available in the rabbit is that from the septal artery. At their

FIGURE 8
The free wall of the right ventricle has been cut away from the region of the interventricular septum (IVS) and retracted upward to expose the septum, in which the septal branch of the left coronary artery is well shown. The branch supplying the region of AV node and the His bundle is indicated by the arrow.

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origin, branches from the septal artery are perpendicular to its long axis and ascend across the right ventricular septal endocardium to reach the His bundle and then the AV node (Fig. 8). This sequence of arterial penetration is opposite to that in man, in whom the blood supply of this region enters from the posterior margin of the AV node after originating at the crux (9, 19). In the dog, the blood supply of this same region is dual from the posterior and anterior margins (14, 19), and thus resembles that of both man and the rabbit. To understand this particular void in arterial distribution to the region of the crux of the heart of the rabbit, it should be kept in mind that a left superior vena cava is normally present, the coronary sinus consequently very large, and most atrial septal structures (including the AV node) displaced anteriorly away from the epicardium of the crux.

Day and Johnson described only one constant atrial artery in the rabbit, arising from the left circumflex branch (Figs. 7B, 8A), with no large or constant atrial branches of the right coronary artery. In the present study the presence of the left atrial artery was confirmed, as was the absence of any sizable right atrial arteries. The left atrial artery coursed beneath the atrial appendage to enter Bachmann’s bundle, but by that point it had already divided into at least two smaller branches. In no specimen did this artery continue as a large trunk to the region of the sinus node, although its terminal branches appeared to supply that region. Other smaller atrial arteries ascended toward the crista terminalis from the proximal right coronary artery, but the distal right coronary was too far from the AV sulcus to provide any significant atrial branches. In no specimen studied was there a grossly visible atrial artery in the region of the sinus node, although small ones could be identified in the histologic sections.

Discussion

In the rabbit heart the conduction system is organized in a pattern generally similar to that of the steer, dog, and man, but there are certain important anatomic differences. There are a sinus node, intermodal pathways, AV node, His bundle and bundle branches in the rabbit. The differences from the other species concern their internal organization, topographical location in the heart, relative sizes, and the origin and distribution of their arterial blood supply.

The sinus node of the rabbit is relatively long, considering total heart size, and it is unusually far posterior on the line from superior to inferior vena cava, but the two most impressive anatomic features concern its internal structure. It contains an inordinately large percentage of P cells, and it is distinctly not organized about a central artery. The percentage of P cells is probably comparable to that of the steer, but considerably greater than that of either dog or man. What this signifies concerning pacemaking potential in the rabbit heart is uncertain, but it should be simpler to locate pacemaking cells with an exploring microelectrode in the rabbit than in the dog. In attempting to predict the precise location of pacemaking, it would be helpful anatomically if a larger concentration of P cells were present at the anterior or posterior margin of the rabbit’s sinus node, but this is not the case. Functionally, of course, any portion of the node may predominate for pacing, despite the anatomic homogeneity.

In man and the dog the sinus node is distinctly organized about a conspicuously large centrally located artery, but not in the rabbit (or the steer). There is some physiologic evidence that pulsations of the sinus node artery may influence the rate of pacemaking by the cells of the sinus node in the dog (20-23), acting as a stabilizing feedback signal or servomechanism. If this is true, then the sinus node of the rabbit may function as a less stable pacemaker. The possibility is supported by the well-known instability of sinus pacemaking in the intact rabbit, particularly when unanesthetized.

Both the AV node and the His bundle as anatomically defined are relatively small in the rabbit. This may be in part due to the
foreshortening of the entire area produced by the presence of the large ostium of the coronary sinus, which drains not only the cardiac veins but the normally present left superior vena cava. Despite its small size, the AV node of the rabbit is organized like that of man, dog, and the steer. There is no os cordis of the type found adjacent to the AV node and the His bundle in the bovine heart (15). The similarity of AV nodal organization includes the input system at the nodal crest and the presence of anatomic bypass tracts. For considerations of function of the AV node and His bundle, one may question the "maturity" of this region in the rabbit because of the normal presence of the left superior vena cava. Patten (24) has suggested that the embryologic origin of the AV node is from the junction of the left superior cardinal vein with the sinus venosus, in a position identical to that of the sinus node at the junction of the right superior cardinal vein and the sinus venosus. As the sinus venosus is normally absorbed into the atri in most mammals, the left superior vena cava is incorporated in the formation of the coronary sinus, and the only recognizable residual in the adult heart becomes the oblique vein of Marshall (16). In this process, the embryologic AV node migrates into the atrial septum with the dorsal endocardial cushion, remaining near the primitive junction, which ultimately becomes the ostium of the coronary sinus. If this concept of the origin of the AV node is correct, then one may predict on an anatomic basis that the region of the AV node in the rabbit is relatively less mature, since the left superior vena cava was not resorbed. The physiologic significance of such a possibility is uncertain, but may be considerable and thus should not be ignored.

On an anatomic basis, one must predict that the major internodal conduction route in the rabbit should be through the anterior internodal pathway, and the interatrial conduction route through Bachmann's bundle. This is based on the much larger size of fiber bundles in these regions compared to the middle and posterior internodal pathways. However, the possibility exists of better conduction through smaller anatomic paths. Present physiologic evidence indicates there is more rapid conduction through the lapine anterior and posterior internodal pathways (25) than in ordinary myocardium, although not as rapid as that in the His bundle. This would be predictable on the basis of a smaller percentage of cells with Purkinje or specialized characteristics in the internodal pathways than in the His bundle. However, one may anticipate that the speed of conduction in the internodal pathways would be slightly greater in the rabbit than in man or the dog, since the proportion of specialized cells in the rabbit seems greater. In all three species, the speed should still be greater in internodal paths than in ordinary myocardium. Rapid conduction has been demonstrated in one region of the posterior internodal pathway of the rabbit (5) which is at least partially diverted beneath the coronary sinus instead of over it as in the dog or man. This minor anatomic difference may be attributable to the size of the rabbit's coronary sinus.

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