Reaffirmation of the Auriculoventricular Conduction System in Man

The Introduction of a Unique Technic for Its Serial Motion Picture Reconstruction

By JOHN L. READ, M.D., ERLING S. HEGRE, PH.D., and SIMON RUSSI, M.D.

Gross and microscopic studies of the auriculoventricular conduction system were performed in 60 human hearts. A unique technic is introduced which will produce a photographic record of undistorted serial sections through a block containing the auriculoventricular node, auriculoventricular bundle and branches. By projecting the completed film as a motion picture, the course and changing relationships of component structures can be followed from level to level in uninterrupted sequence. The neurogenic versus the myogenic concept of cardiac conduction is reviewed at length.

The current or myogenic concept of cardiac conduction postulates that the impulse to contraction in the human heart and that of various ungulates originates in the sinoauricular node located at the junction of the superior vena cava and the right auricle. Thence it spreads radially over the walls of the auricles to reach the ventricles via a single muscular auriculoventricular bundle of His situated in the lower part of the interauricular septum. The latter stems from a distinct auriculoventricular node (node of Tawara). This node has a number of connections with myocardial fibers of the right auricle. The auriculoventricular bundle divides into right and left branches which are distributed to the corresponding sides of the interventricular septum. This concept has been established by various investigators and is lent collateral support from findings in other mammals. Each bundle forms a widespread subendocardial network in man.

The myogenic versus the neurogenic theory of conduction has long posed a controversial question in cardiac physiology. Prior to 1893 there was no known muscular connection between the auricles and the ventricles of the mammalian heart. Because nerve elements passed over the auriculoventricular groove, it was assumed that the impulse to contraction was transmitted by way of the neurogenic route. In 1893 His published his classic description of the auriculoventricular bundle. Shortly before this, Kent described muscular bridges connecting the auricles with the ventricles. He also dissected out the auriculoventricular bundle but failed initially to recognize its significance. This was followed in 1906 by Tawara's description of the auriculoventricular node. Their findings were endorsed by the investigations of Keith and Flack, Cohn, Kent, King and others. In 1907 Erlanger and Blackman, observing nerve trunks of the bundle and thereby produced complete experimental heart block. The block persisted during the remaining life span of the dogs (320 to 340 days). In 1935 Kountz and his associates sectioned the left bundle branch in human hearts which had been revived after death by perfusion of the heart and lungs in situ. Standard lead electrocardiograms revealed the pattern of bundle branch block. In the same year they produced bundle branch block in living monkeys. Similar results in monkeys were achieved by Storm in 1936. In conjunction with their work on revived human hearts, Kountz and associates attempted to explain the difference between...
the human electrocardiographic pattern of bundle branch block and the so-called classic interpretation derived from studies on canine hearts. This difference had been recognized by Barker, Macleod and Alexander,14 Oppenheimer and Pardee,15 Farr,16 and others. Kountz found that with the dog assuming its usual posture, the heart lay anteriorly and electrocardiograms so obtained were similar to those of man. In the experimental positions, however, with the chest open and the dog on its back, the heart falls posteriorly a considerable distance in the mediastinum and rotates clockwise. The human chest does not allow for such marked changes in heart position. The beating dog’s heart was next placed within the pericardial cavity of a human cadaver and electrocardiograms obtained were again similar to those from the human heart.

Thus, it was established that the auriculoventricular bundle represents the sole pathway by which the cardiac impulse is conveyed from auricle to ventricle; further, that the A-V bundle does not regenerate. In 1925, using electrocardiographic methods, Lewis17 demonstrated a difference in the rate of conduction in various cardiac fibers. He found the speed of conduction to be proportional to the glycogen content and fiber size but inversely proportional to the rhythmicity and refractory period. Conduction time varied from 0.2 meters per second in the small nodal fibers to 4.0 meters per second in the Purkinje fibers.

The myogenic theory remained firmly established until 1940 when Glomset and associates,18-21 in a series of papers, challenged the myogenic in favor of the neurogenic concept. They agree with the existence of a myogenic system in sheep, cattle and swine, but not in man, dog, and the horse where they feel that the system is vestigial and does not mediate conduction. They conclude as follows: (1) There is no distinct A-V node; (2) the bundle of His is structurally identical with other muscle fasciculi; it has no left branch and therefore does not bifurcate; (3) the ridge fasciculus (bundle of His) has no special vascular supply; (4) there is no muscular connection between the fibers of the ridge fasciculus and the right auricle; (5) in dog and man, all elements identified as Purkinje fibers are ordinary muscle fibers which have been altered slightly by their environment in regions where the bundle and its branches are supposed to exist; (6) the amount of glycogen revealed by staining with iodine and Best carmine does not constitute a distinguishing feature of the Purkinje fiber; (7) the vesicular, hollow or vacuolated appearance of the Purkinje fiber represents an artifact; nowhere did they find evidence of transition from Purkinje fiber to ordinary cardiac muscle fiber; (8) there is no anatomic evidence to support the myogenic theory of cardiac conduction.

Finally, they state: “We therefore believe that the cardiac musculature is under a nervous control similar to that of other muscle tissue and consider it physiologically unsound to draw conclusions concerning cardiac conduction without taking cognizance of the rich intrinsic nerve system of the heart.”

Faced with these apparently heretical observations, the exponents of the myogenic thesis renewed their investigations. Since the work of Glomset and coworkers, a series of studies of human and mammalian embryos has tended to reaffirm the myogenic hypothesis.

Walls22 studied serial sections of human embryos in an attempt to determine whether the conducting tissue developed as other organs of the body or are simply remnants of junctional tissues found at the sinoauricular and auriculoventricular rings. He concluded that, “The bundle is a new formation which arises from that primitive nodal tissue by a process of active growth.” This view is also adhered to by Tandler,23 Retzer,24, 25 Shaner,26 and Davies.27

Structural differentiation of the human heart was found to commence at the 8 mm. stage, the auriculoventricular node and bundle of His being formed in advance of the sinoauricular node. The auriculoventricular node extends from a position behind the dorsal endocardial cushion to reach the crest of the interventricular septum where it bifurcates. The sinoauricular node appears at the 10 mm. stage and nerve elements at the 20 mm. stage. Function begins before the appearance of nerve elements. In studies on living rat embryos, Goss28 ob-
served the initial activity of contraction to occur at the two somite stage in the left heart just to the ventricular side of the A-V junction at a regular rate of 32 to 42 beats per minute. This was followed in a few hours by contractions from the corresponding area of the right side so that the ventricles contracted asynchronously. By the eight somite stage, however, the tardier sinoauricular node became the pacemaker, initiating contractions 0.1 to 0.2 second before the ventricles with a consequent increase in rate. Patten and Kramer29 (1933) had made similar observations in the living chick embryo. They point out that the change of pacemaker occurs before any neuroblasts approach the heart.

In 1948 Robb and Kaylor29 carried out a detailed study of the specialized tissue of the human fetal heart at various stages of development. Their observations on the distribution of the specialized cells of the A-V system were somewhat at variance with those of Tawara3 and Monckeberg31 who reported that specialized fibers to the septal and lateral walls arose from recurrent branches in the apical regions. The authors found that the specialized cells of the A-V system also occurred throughout the septum. They stress the importance of this finding on the present day interpretation of electrocardiograms. The constant appearance of more than one right branch is also emphasized and its possible relation to the Wolf-Parkinson-White32 syndrome is discussed. The authors hesitate in their acceptance of the myogenic concept on the grounds that complete knowledge is lacking concerning the exact pathways, terminations and function of sympathetic nerves which accompany the bundle and branches. The pathways of the parasympathetic nerves, however, have been superbly demonstrated by Nonidez.33 They mention the present day tendency to overlook this gap in our knowledge and state:

"We must realize that the exclusive allocation of the function of the specialized cells depends on one type of experiment. The method was to cut or crush the bundle and allow the animals to recover. The assumption was made that if the conducting tissue were nerve, regeneration would not occur and the block would be permanent. The comment may be made that scar tissue barriers may prevent peripheral regeneration of axones. Such barriers are present following cutting, crushing, ligation, or injection experiments at the base of the heart. Thus we may say the presumptive (but not the absolutely proven) opinion is that the specialized tissue is the ordinary conducting pathway from auricle to ventricle. At times this pathway probably yields to one consisting of ordinary muscle fibers."

Davies and Francis34 approached the problem from the ontogenic viewpoint in poikilo- and homothermic vertebrates and concluded that nodal and Purkinje fibers represent morphic developments in the hearts of mammals and birds, whereas in poikilothermic vertebrates, there is no specialization of cardiac muscle fibers. They postulate a differential distribution in the various chambers of certain chemicals known to affect muscular contraction to be responsible for the ordered function of the poikilothermic heart.

It has been shown that the foundation for the myogenic concept rests upon a number of conclusive anatomic and physiologic investigations. Most important has been the observation that the conduction system is composed of modified muscle or Purkinje35 tissue. In 1947 Truex and Copenhaver36 reviewed the literature and made a detailed study of Purkinje fibers from the hearts of man and various mammals. They successfully resolved many of the controversial problems pertaining to the structure and identification of these fibers in man. They describe Purkinje fibers as containing fewer myofibrillae but more interfibrillae and interfibrillar sarcoplasm, which accounts for their clearer, less compact appearance. The center of the fiber is devoid of myofibrillae and is filled with a granular sarcoplasm in which the nuclei are seen usually in groups of two or more. Purkinje fibers were identified most easily by the Azan and Masson technic in sheep, pigs, calves and cattle. In these species, the bluish appearance of the cytoplasm contrasted sharply with the more intense reddish staining of ordinary cardiac muscle. The number of fasicles also represented a distinguishing feature. These criteria proved of little value in cats, monkeys and man where the singly arranged Purkinje fibers did not always stain differentially and
lacked a continuous connective tissue sheath to delimit them from adjacent muscle. In fact, this sheath is so well developed in the ungulates, that it has been studied extensively by the injection of various dyes. However, with higher magnification the larger Purkinje fibers in man were readily identified by their clear central area and sparse peripherally placed myofibrillae. They were able to identify Purkinje fibers in 14 of 20 human hearts. Because of an evident overlap in the diameter of Purkinje and cardiac muscle fibers, they computed an average measurement on the basis of 25 fibers of each. Only those fibers were selected which included nuclei in the plane of the section and these were measured in their widest portions. Purkinje fibers were found to be twice the mean diameter of cardiac fibers in all animals except man. In cattle the cardiac fibers averaged 15.5 microns as compared to 43.6 microns for the Purkinje fibers, whereas in man, the comparison was 16.1 to 20.6 microns. Examination of longitudinal sections revealed regions of continuity between Purkinje and cardiac fibers. Purkinje fibers stained with Best carmine glycogen consistently revealed an excess of glycogen. They emphasize the state of tissue preservation in specimens to be studied and conclude that much of the confusion over this subject arises from a failure to appreciate individual and species difference of Purkinje fibers. The so-called "typical Purkinje fiber" is a popular fallacy, since it is often based on the appearance of the typical fiber in another species.

**Materials, Methods and Findings**

**Microscopic studies.** Four adult hearts were examined by consecutive serial sections. Six others were studied by taking a series of sections through areas known to contain the component structures of the conduction system.

All hearts studied were essentially normal except for a few with moderately severe atherosclerosis. Serial blocks were cut through the crest of the auriculoventricular septum and along the course of the bundle branches. Sections were 8 to 12 microns in thickness. Sec-
tions were stained with hematoxylin and eosin except for every fifth section which was stained by the Van Gieson method.

The auriculoventricular node is roughly flask-shaped and is located on the right side of the interauricular septum between the orifice of the coronary sinus and the right border of the membranous septum of the ventricle (figs. 1 and 2). It measures approximately 8 by 4 by 0.6 mm. The node converges toward, and its anterior portion penetrates, the central fibrous body (trigonum fibrosum) where it forms a slender muscle bundle, the bundle of His, which measures 1 to 4 mm. in width and approximately 15 to 20 mm. in length. The bundle is roughly triangular on cross section. It bridges the crest of the interventricular septum within the lower part of the membranous septum of the ventricle and just below the mesial portion of the aortic fibrous ring. Just before reaching the left border of the membranous septum, it
bifurcates (fig. 2). The right bundle branch dips caudally beneath the tricuspid valve in the groove between the mesial and anterior cusps (fig. 1). It descends to enter the myocardium of the right side of the septum (fig. 5), gradually emerging so that it becomes subendocardial at the base of the anterior papillary muscle (fig. 1) where it is often visible to the naked eye. Frequently the overlying muscle bundles of the myocardium run obliquely across it, thus helping to define it more clearly. The right bundle seems to form a continuous arc which merges imperceptibly into the bundle of His. It measures approximately 1.5 mm. in width and averages about 40 mm. in length. The left branch (fig. 2) forms a broad membranous ribbon 3 to 6 mm. in width as it leaves the bundle below the aortic fibrous ring and just to the right of the right semilunar valve of the aorta and becomes almost immediately subendocardial. It blends so intimately with this lining that it is most difficult to dissect out intact. As it descends, it gradually fans out into numerous diverging fasciculi and is somewhat longer than the right branch. In most hearts, the left branch divides into an anterior and posterior ramus. These observations are in accord with recent observations of Kisten 42 and Lev 43, 44

The auriculoventricular node (fig. 3) appears as a compact mass of fine interlacing muscle fibers which are roughly ovoid in transverse section. These fibers are smaller than those of the adjacent auricle. The fibers of the auriculoventricular bundle (fig. 4) are somewhat larger than those of the auriculoventricular node but smaller than those of the ventricular myocardium and stain somewhat paler. As the bundles descend, more and more Purkinje fibers (fig. 6) make their appearance.

One of us (E.S.H.) 45, 46 devised a unique apparatus (fig. 7) which will produce a photographic record of undistorted serial sections at 6 micron intervals through a block of tissue containing the auriculoventricular node, bundle of His, and bundle branches. By project-

![Fig. 5. Photomicrograph of the right bundle branch in cross section (X16). Hematoxylin and eosin. RBB, right bundle branch.](image1)

![Fig. 6. Photomicrograph of Purkinje fibers in oblique section (X100). Van Gieson’s stain. Ordinary cardiac muscle is seen to the right. P, Purkinje fibers.](image2)
ing the completed film as a motion picture, it is possible to follow the course and changing relationships of the component structures from level to level in an uninterrupted sequence. Specimens which have been fixed in formalin are immersed in a solution of 80 per cent alcohol in which 2 Gm. of lead acetate per 100 cc. have been dissolved (eight hours). They are then transferred to 95 per cent alcohol containing 0.5 Gm. of lead acetate per 100 cc. De-

hydration is completed in the usual manner with minor modifications. The tissue (fig. 7 a) is mounted in the vise of a sliding knife microtome. The knife is mounted at one end of the sliding carriage and is equipped with a suction tube (b) which will remove and dispose of each section as it is cut. Any or all sections may be saved if desired for study at high magnifications. The vacuum line is compressed by a normally closed clamp (c) which is released by a dog (d) at the proper interval. The stain is conducted by gravity from a reservoir through a rubber tube to a small channel in a plastic bar (e and e'). The fluid emerges through a small pore on the under surface of the bar where it slowly accumulates to form a hanging drop. A second and similar channel in this plastic bar is attached to a water siphon and will remove the excess stain. The plastic bar is mounted on the sliding carriage in such a way that it will pass directly over the speci-

AURICULOVENTRICULAR CONDUCTION SYSTEM

Fig. 7. Diagram of apparatus for making a motion picture record of consecutive serial sections through the conducting tissue.
number of exposures can be made at each new level. The whole apparatus is powered by a one third horse power electric motor.

The essential procedure embodies a distinct departure from the usual method of preparing and studying serial sections, that is, the stain is applied not to the displaced sections, but to the intact surface of the block. Attention can therefore be directed to the details of the exposed surface in their normal relationship to the remainder of the specimen. Furthermore, serial sections prepared by routine methods always suffer some distortion due to compression during cutting or as a result of inequal spreading. Such inaccuracies do not occur with the present method. The resultant section is stained in varying shades of sepia due to the lead sulfide precipitated by the action of the sodium sulfite staining solution upon the lead acetate impregnated tissue.

A motion picture of the conduction system was prepared by this technic. The film allows one to follow the course of the bundle of His as it leaves the auriculoventricular node, crosses the septum and then bifurcates. The bifurcation is depicted rather dramatically. As the last section of overlying tricuspid valve is removed, the right branch makes its appearance and the bundle and both branches are revealed.

**DISCUSSION**

Despite the question posed by Glomset and his associates, the accumulated evidence tends to reaffirm the myogenic theory of conduction. Due to inadequate nerve-staining technics, the exact distribution of the sympathetic (in particular) and parasympathetic nerve fibers to the heart has not been established sufficiently well to prove or disprove either theory. Nettleship and Hirsch reported on the extent of nerve degeneration following ganglionectionomy in lower animals. The former demonstrated degeneration and fragmentation of ventricular nerve trunks and the ventricular epicardial network following bilateral stellate and middle cervical ganglionectionomy. Similar structures in the auricles were spared. There also occurred degeneration of the apical portion of the endocardial plexus, simple nerve endings in the fat and from one half to three fourths of the coronary artery plexuses. Thoracic dorsal root ganglionectiony produced similar changes. Following total vagotomy, the epicardial plexus of the ventricle was spared, but degeneration occurred in the auricular trunks, endocardial, aortic and pulmonary plexuses. Section of the vagus proximal to the nodose ganglion spared myelinated fibers of the auricles but not those terminating about the epicardial ganglia. Electrocardiographic studies were not a part of these experiments. The fact that similar procedures are performed in man for various reasons without any resultant heart block would seem to discount the neurogenic mode of conduction. Logically it would appear highly improbable that conduction should be mediated through the muscular route in practically all animals except man. One might hypothesize that in view of the unique function of the heart which requires its fibers to lengthen and shorten forcefully approximately 100,000 times each day, that the most efficient mode of conduction might occur in a tissue which is also capable of such changes in length without interfering with its conducting function.

The authors feel that the technic described herein demonstrates more clearly than any other the cardiac conduction system. The motion picture record clearly refutes certain of the morphologic claims of the neurogenic exponents. This technic will be applied in subsequent studies in an attempt to demonstrate in moving sequence the histologic picture of bundle branch block and the vascular supply to the conducting tissue.

**SUMMARY**

The question and evolution of the myogenic versus the neurogenic theory of cardiac conduction is reviewed at length.

Gross and microscopic studies of the auriculoventricular conduction system were carried out in a total of 60 adult human hearts. Results of these studies are in accord with the myogenic concept of cardiac conduction.

**SUMARIO ESPAÑOL**

Estudios gruesos y microscópicos del sistema de conducción auriculoventricular fueron obtenidos en 60 corazones humanos. Una técnica
única es introducida que produce un record fotográfico serial en secciones no distorsionadas de un bloque conteniendo el nódulo auriculoventricular, el paquete auriculoventricular y sus ramificaciones. Proyectando la película terminada como una cinta cinematográfica el curso y las relaciones variables de las estructuras del componente pueden ser observadas de un nivel a otro en una secuencia no interrumpida. El concepto miogénico de conducción cardíaca y el concepto neurogénico son revisados en detalle.

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