Concomitant with the development of catheter ablation techniques for the treatment of atrial arrhythmias, there has been renewed interest in the morphologic arrangement of the cardiac conduction system. The first descriptions of the anatomy of the nodes and atrioventricular conduction system appeared nearly 100 years ago. Since then the subject has been controversial, possibly because of the early researchers' imprecise knowledge of histology. The components and structure of the specific conduction system in humans are similar to those found in commonly used laboratory animals. The conduction system is composed of specialized myocytes. Its atrial components, the sinus node and the atrioventricular node, are in contact with atrial myocardium. The His bundle penetrates the right fibrous trigone, then divides into two specialized ventricular bundle branches (right and left), which also are surrounded by a fibrous sheath that separates the specialized myocytes from the ordinary myocardium. Only at the distal ramifications of the bundle branches do the fibrous sheaths disappear, allowing continuity with the ventricular myocardium. Knowledge of the specialized myocardium can help in the development of potentially useful therapies for some forms of cardiac arrhythmia.

Key words: Catheter ablation. Sinoatrial node. Atrioventricular node. His bundle. Myocardium.

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INTRODUCTION

The classic studies of Stannius in 1852 were the first to propose that cardiac conduction was myogenic. About a century ago it was shown that specialized muscular tissue was responsible for the initiation and spread of the heart beat. In 1906, Sunao Tawara confirmed the existence of a muscular bundle described by His back in 1893. Also in 1906, Keith and Flack confirmed the existence of the His-Tawara system. One year later they described the structure of the sinoatrial (SA) node.

Although Purkinje was the first to describe specialized ventricular fibers, he was unaware of their importance in the structure of the heart, and it was Tawara who showed that the muscular bundle described by His was continuous with the ventricular...
Purkinje fibers. Tawara’s studies have recently been translated into English, although the first translation of part of his work into this language was undertaken by Robb in his 1965 textbook. These works are basic reading for all researchers who would study the cardiac conduction system (CS).

**COMPONENTS OF THE SPECIFIC ATRIOVENTRICULAR CONDUCTION SYSTEM**

The muscular bundle connecting the atria to the ventricles was described by His as a «penetrating bundle.» However, His did not observe the histological continuation of this bundle in the right atrium with the atrioventricular (AV) node, the ventricles, or the ventricular Purkinje cells. It was Tawara who recognized this connection while working for his doctorate under the direction of Aschoff. Earlier, in 1893, both Kent and His had described muscular AV connections which were the cause of much confusion for many years. Later, it was observed that these connections were not to be found in healthy hearts, but in those that were diseased.

Following on from the findings of Kent and His, both clinical cardiologists and physiologists searched for the structure responsible for generating the cardiac impulse. It was suspected that this was situated in the area where the superior vena cava and the right atrium joined; under experimental conditions this is the last part of the heart to stop beating (the so-called *ultimum moriens*). In 1907, Keith and Flack distinguished the SA or sinus node in all the mammals they studied, including humans. Its constituent cells were believed to be the site of origin of the cardiac impulse.

The CS arises in the SA node, which is found in the upper anterior right atrium (Figure 1). The AV node is found in a lower, posterior position in the atrium. The CS extends from the AV node to the penetrating bundle of His and then divides into the left and right bundle branches which descend through the interventricular septum, enveloped in a connective tissue sheath that isolates them from the surrounding muscular tissue. Inside the myocardium they are continuous with the Purkinje network (Figure 1).

**Morphological-macroscopic areas of interest**

Several macroscopic areas of interest help to locate the cardiac CS. The SA node, which is sub-epicardial (Figure 2a), is wedged into the juncture between the musculature of the superior vena cava and that of the atrial appendage. Its base is opposite the terminal crest. The distance between the SA node and the epicardium is 0.3±0.1 mm. In about 10% of persons, the node does not extend towards the inferior vena cava but lies in a horseshoe shape around the lower part of the orifice of the superior vena cava. The AV node is found at the base of the atrial septum at the apex of a triangular area first illustrated by Koch. This triangle is situated on the endocardial surface of the right atrium (Figures 2b and c), is bordered anteriorly by the insertion of the septal leaflet of the tricuspid valve, and posteriorly by a fibrous tendon known as the tendon of Todaro. This tendon is the fibrous subendocardial continuation of the Eustachian valve, and inserts into the atrial musculature separating the orifice of the coronary sinus from the fossa ovale. The apex of this triangle is formed superiorly by the junction of the anterior and posterior borders mentioned above, corresponding to the central fibrous body (CFB) of the heart. The base of the triangle is formed by the orifice of the coronary sinus together with the vestibule of the right atrium supporting the septal leaflet of the tricuspid valve. This base is known to electrophysiologists as the septal isthmus, and it is here where radio-frequency ablation of the slow pathway is performed in patients with AV nodal reentrant tachycardia.

The continuation of AV conduction occurs via the penetrating bundle of His, the only part of the conductive axis that perforates the CFB. The CFB is formed by the union of the connective tissue of the aortic and mitral heart valve leaflets with the septal leaflet of the tricuspid valve—the so-called right fibrous trigone—and the membranous part of the interventricular septum. In many mammalian hearts, the trigone is fibrous, but bovine hearts have a central mass of bone or cartilage (the *os cordis*). In contrast, the fibrous tissue of sperm whale CFB is very loose. The membranous portion or septum, which can range in length, is a good guide for locating the AV bundle of His. This ap-
pears above this membranous portion after crossing the right fibrous trigone (Figure 2d), and then divides into the left and right bundle branches. The right branch passes through the septal musculature at the base of the medial papillary muscle of the right ventricle. It then becomes a thin cord that penetrates deep into the septomarginal trabeculation or moderator band connecting the medial and anterior papillary muscles. The origin of the left branch lies below the commissure between the right and non-coronary cusps of the aortic valve; it then descends through the subendocardium of the interventricular septum (Figure 2d). Its path is sometimes visible owing to the shiny fibrous lamina that sheathes it. The proximal part of the left branch is much longer than that of the right. Occasionally a third branch called «dead-end tract» is seen in fetal or infant hearts, and this continues the bundle of His in an anterio-superior direction towards the root of the aorta.

Structure of the nodes and the atrioventricular conduction system

Studies in which the histological techniques employed were similar to those used by Tawara and later workers such as Davies and Truex et al have shown that the CS of humans is arranged in a manner quite like that of other mammals (with slight variations between species and between hearts). Tawara reported the separation of the specialized myocardium from the normal or working myocardium by a thin sheet of connective tissue visible under the light microscope, and on this the criteria proposed by Aschoff and Mönckeberg for histological identification of the specialized myocardium are based. Simply put, specialized myocytes stand out from working myocytes when viewed under the light microscope, and can be «followed» from one histological section to the next. In his monograph, Robb preferred to define...
the conductive tissue with the term «connecting» rather than «conducting» system, because histological preparations better define cell morphology than function. He also observed differences in the texture of the specialized myocardium depending on the freshness of autopsy material and the fixing and staining methods used. Tawara\textsuperscript{2} was aware of this and pointed out the heterogeneity of specialized myocyte morphology even in histological sections of the heart. Within a given species, the most obvious differences are related to the age of the individuals examined.\textsuperscript{10} In recent years different molecular and immunohistochemical markers have been used to locate the conductive tissue in embryonic hearts of humans and other mammals. However, no specific marker has been found that can highlight this tissue in adult humans.

In the normal human heart, the SA and AV nodes do not meet the criteria of Aschoff and Mönckeberg\textsuperscript{18,19} because they are not electrically insulated from the surrounding myocardium by connective or fatty tissue. Rather, they enter into contact with atrial working fibers after a small area composed of transitional cells.

In the SA node, Keith and Flack\textsuperscript{5} distinguished between the sinus and working cells. Tawara\textsuperscript{2}, however, indicated the difficulties he encountered in differentiating AV node cells from those of the bundle of His. He therefore proposed that the difference between them was purely anatomical. On the basis of this definition, the portion of the CS completely sheathed by the CFB is termed the penetrating bundle or bundle of His (Figure 3a). The atrial portion from the proximal conduction system to the bundle of His is called the AV node (Figure 3b). This anatomical distinction is logical because the insulation of the penetrating bundle of His prevents it from making direct contact with the electrical activity of the afferent atrium. Any atrial activity must therefore be previously directed through the AV node.

The intrinsic function of the SA node is to be the source of the cardiac impulse. The SA node in humans is an arched or fusiform structure. Histologically it is composed of cells slightly smaller than normal working cells which are arranged in bundles. These mix together with no spatial order, stain weakly, and are

**Fig. 3.** Sagittal histological sections of the sinoatrial (SA) node of the human (a;×10) and pig heart (b;×40) stained with the van Gieson method. Note the contact between sinus cells (SC) and working atrial cells (WAC). Sinus cells are characterized by being clearer and embedded in a greater amount of connective tissue (red). c: van Gieson-stained section of the mid-zone of the triangle of Koch. Note the shape of the compact AV node and the transitional cells (TC) in contact with the convex surface of the compact node. d: Masson’s trichrome-stained section showing the penetrating bundle of His surrounded by fibrous tissue (green) from the CFB.

SNA indicates sinus node artery; CFB, central fibrous body; TV, tricuspid valve.
embedded in a dense connective tissue matrix (Figures 3a and b). With age, the amount of connective tissue increases with respect to the area occupied by the nodal cells. On the periphery of the node, specialized cells are mixed with those of the working myocardium (Figures 3a and b). In addition, multiple radiations or extensions interdigitating with the working atrial myocardium have been described. These penetrate intramyocardially into the terminal crest, and the superior and inferior vena cavae. The SA node is arranged around an artery known as the sinus node artery, which can run centrally or eccentrically inside the node. In 29% of human hearts this artery ramifies inside the node. The SA node is also intimately associated with the autonomic nervous system. It has been suggested that the majority of these nerve fibers are parasympathetic, the sympathetic fibers being concentrated around the node’s blood vessels.

The inherent function of the AV node is to delay the cardiac impulse. In humans, this node has a compact portion and an area of transitional cells. The former is semi-oval and lies over the CFB (Figure 3c). In the sections close to the base of the triangle of Koch, the compact part of the node divides into two extensions or prolongations. The artery vascularizing the AV node is usually found between these. The length of these extensions varies from one heart to another. The size of the transitional cells is intermediate between those of the AV node and the atrial working cells. They are surrounded by a greater quantity of connective cells than that covering the working cells, but they are not insulated from the adjacent myocardium. Rather, they form a kind of bridge between the working and nodal myocardium, and collect electrical information from the atrial walls, transmitting it to the AV node.

Controversy surrounds how the impulse from the SA node reaches the AV node. Some authors have suggested the existence of specialized tracts between them. Our studies do not support this idea but favor the hypothesis that the working muscle fibers themselves (and their geometric arrangement in the atrial walls) are responsible for conduction being more rapid in some areas of the atrium than in others.

The AV node continues distally with the penetrating bundle of His (Figure 3d), although there are slight differences in terms of cellular arrangement between these two structures, including the arrangement of the bundle of His cells in a more parallel fashion. The explanation for this might be morphological: the bundle of His starts to be surrounded by the connective tissue of the CFB, thus becoming a conducting tract that takes information to the ventricles.

The AV node of the dog is smaller than that of humans, but has a longer penetrating bundle of His. Some authors interpret this to mean that a portion of the AV node of the dog lies within the CFB. In the rabbit, other authors describe part of the bundle of His as though it formed part of the AV node, but this is a mistake (Figures 4a-d). The most outstanding morphological difference between the AV node of the dog and those of the rabbit and humans is that the former is not covered by transitional cells. In rats (with a resting he-

Fig. 4. This composite figure shows the atrioventricular (AV) node plus the bundle of His and its right and left bundle branches in the rabbit. Horizontal bar in b represents 1 mm (same for all images). Masson’s trichrome staining. A indicates aorta; TT, tendon of Todaro; RV, right ventricle; LV, left ventricle; TV, tricuspid valve.
art rate 10 times faster than that of dogs or humans), the AV node is proportionally comparable to that of the dog, but the CFB is smaller.

When the histological trajectory of the conduction system is followed towards the penetrating bundle of His, the latter is seen to turn towards the left in many human hearts, and emerge on the muscular crest of the interventricular septum. Surrounded by connective tissue from the CFB, the length of the bundle of His can vary before splitting into the left and right bundle branches. The former branch cascades over the left side of the interventricular septum (Figures 5a and c). The division of the bundle of His resembles a jockey squatting above the muscular crest of the interventricular septum, and descends longitudinally under the endocardium of the left ventricle (Jones’ trichrome, ×5). d: note the covering connective sheath (blue) of the left branch (Jones’ trichrome, ×10). A indicates aorta; E, endocardium; TV, tricuspid valve.

Subendothelial injection of India ink is one of the methods used to observe these fibrous sheets and to demonstrate the subendocardial course of the right and left bundle branches and their ramifications in ungulate hearts (Figures 6b and d). Our studies on the hearts of sheep and calves show these to vary somewhat from human hearts. Calf hearts are more similar to human hearts in that the fascicles of the left bundle branch are usually three in number and originate in the upper part of the interventricular septum (Figure 6b). However, sheep hearts show only two fascicles, and these appear halfway down the length of the septal wall. In both sheep and calf hearts, small muscular trabeculae cross the ventricular cavity—the so-called «false tendon»—which inside them carry distal ramifications of the His branches towards the papillary muscles and the adjacent ventricular walls. On the right side of the heart, the moderator band of both the sheep and calf heart is more slender than that of humans, but inside it always contains an offshoot of the right bundle branch (Figure 6e).

In ungulate hearts the subendocardial Purkinje network is elliptical in arrangement, both in the left and right ventricle (Figure 6e). In addition, from its contour arise branches that penetrate the ventricular walls, leading to new branches or anastomoses with other branches (Figure 6e). However, intramural branches of the Purkinje network have not been demonstrated in the human heart.
A controversial point regarding the Purkinje network is the existence of transitional cells between the working ventricular myocardium and the Purkinje fibers. The anatomical and immunohistochemical studies of Oosthoek et al., show that, in bovine hearts, there is a very small zone of transitional cells where the Purkinje fibers lose their connective tissue cover. However, such cells have not been observed in the sheep heart. When the Purkinje fibers lose their connective tissue cover, electrical impulses pass from the CS to the working myocytes of the ventricles. The spatial orientation of the working myofibrils in the ventricle walls determines the anisotropic nature of ventricular conduction (Figure 6f).

CONCLUSIONS

Although differences exist between species, the structure of the nodes, as well as that of the remainder of the human AV conduction system, is similar to that of commonly used laboratory animals. The SA node, the structure that generates the cardiac impulse, is situated at one extreme of the right atrium. Impulses from it travel posteriorly in the atrial walls through an intricate but precise spatial arrangement of working atrial fibers until reaching the end of the atrium. At this end, transitional cells of the AV node receive the impulse and delay it prior to its transmission via the bundle of His. The latter crosses the insulating fibrous plane between the atria and ventricles, and transmits the impulse via two branches (the right and left bundle branches) towards the corresponding ventricles. Each of these branches is insulated by a connective sheath of working ventricular myocytes. This arrangement allows contact between the specialized and working myocytes only at the distal ramifications of the bundle of His. In this way, the AV conduction system, largely described by Tawara nearly 100 years ago, is structured to impart order to the transmission of cardiac impulses. Knowing the structure and location of specific conductive tissue within the heart could help provide solutions to different disturbances in cardiac rhythm.

REFERENCES