

# Purkinje fibers of the Heart Conduction System

## *The History and Present Relevance of the Purkinje discoveries*

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### SUMMARY

It has been 160 years now since Purkinje published his findings of conduction fibers in the heart in *Archiv f. Anatomie u. Physiologie*, and 166 years since the Polish version of this publication. Even during Purkinje's life some anatomists had studied the morphology of these fibers, but nobody at that time understood the great physiological and medical importance this discovery would have for medicine. This can be seen as late as the 20th century and even today. Purkinje's work triggered a cascade of these discoveries, which led at the beginning of the previous century to the formulation of the basic scheme of the conduction system. Purkinje fibers or Purkinje cardiomyocytes are part of the whole complex of the cardiac conduction system, which is today classified as specific heart muscle tissue responsible for the generation of the heart impulses. From the point of view of their ultrastructural composition, the cells of different parts of the cardiac conduction system are largely similar. In contrast to heart contractile cardiomyocytes, the cells of the cardiac conduction system including Purkinje fibers have a small amount of myofibrils, fewer small mitochondria and thus a light cytoplasm as well as a higher glycogen content, but their T-tubular system is tiny or absent. These cells can be detected with some morphological, histochemical methods. However, the cells of the conduction system are not completely uniform as they differ in size, number of nexuses-gaps, intercalary disks and in some other features in the individual parts of the conduction system. However, these specialized cells work as a whole. Nowadays morphological research concerning all parts of the cardiac conduction system, including Purkinje fibers, is focused on ultrastructural, histochemical and genetic issues, with the aim of preventing and treating disturbances of the conduction system such as arrhythmias with the increasingly popular genetic therapy - and possibly of replacing electrical pacemakers with biological ones. If Jan Evangelista Purkinje had lived nowadays, he would have been surprised and delighted at the degree and extent of research and the clinical application his discovery induced.

**Key words:** Purkinje fibers, morphology, history, present time.

*El.*

*Čas. Lék. Čes., 2006, 145, pp. 329–335.*

The spontaneous activity of the heart depends on specialized myocytes located in the determined parts of the heart. These particular myocytes, which morphologically differ in certain features from the contractile cardiomyocytes, are able to generate spontaneous impulses and conduct them to the whole heart muscle. In the heart these specialized cells are mutually connected and form an anatomical and physiological unit, called the heart conduction system.

### WHAT DID J. E. PURKINJE IN THE HEART?

Jan Evangelista Purkinje was the first person in the world to discover and describe the heart conduction system, in particular its last part (from the point of view of the conduction system behavior), which is called the Purkinje fibers in his honor. The fibers of this last part run on the interior surface of the ventricles to join the working cardiomyocytes. Nowadays these fibers are also called Purkinje heart cells or Purkinje cardiomyocytes.

### HISTORY OF THE DISCOVERY OF PURKINJE FIBERS – PURKINJE CARDIOMYOCYTES

Jan Evangelista Purkinje was born the 18 December 1787 in Libochovice (Bohemia). In 1818 he defended his doctorate and in spring 1823 he became Professor of the University in Vratislav (Previously: Breslau, Germany; nowadays: Wrocław, Poland), where he worked until 1850. It was during this period in Vratislav, between the ages of 35 and 63, that he made his most important discoveries. This very age generally represents the physiological extent of the greatest creative waves of the human being. From 1850 until his death in 1869 Purkinje worked in the Institute of Physiology in Prague, which he had founded and built up. The acquisition of the big Plösl microscope in 1835 represented an important turning point for Purkinje's histological and embryological research. Purkinje published his discovery of a part of the heart conduction system, nowadays called Purkinje fibers – Purkinje cardiomyocytes (1) in 1845 in "*Archiv für Anatomie, Physiologie und wissenschaftliche Medicin*", in the article "*Mikroskopisch – neurolo-*

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gische Beobachtungen". Over 15 pages the author describes neurological fibers and ganglions in various organs. Only the last two pages deal with Purkinje heart fibers. The paper represents, as Purkinje mentions himself, a follow-up to his previous neurohistological works that had been published in Polish (2) in 1839 in *Rocznik wydziału lekarskiego w uniwersytecie Jagiellońskim*. Krakow, Tom II, pp. 44-67. Purkinje had observed the conduction fibers in sheep's hearts. The paper was partly translated from German into Czech by Professors Borovanský and Weigner in 1937 (3). Having gone through the available literature I have not found an accurate and self-contained Czech translation of this paper, so I shall take the liberty of presenting the English (Czech) translation here.

#### **The English (Czech) translation of the Journal formulation**

13. *Directly under the serous membrane (skin) on the interior walls of the sheep heart I observed firstly a network net of grey, flat and gelatinous fibers that partly spreads to the papillary muscles and to other neighboring fibrous trabecular and that partly bridges furrow of the heart walls. Then, during a microscopic observation, I found these fibers are mostly formed by grains (cells) resembling the cells in ganglions, which are tightly joined forming a polyedric shape. In the interior of each grain I found one or two nuclei not of spherical shape, similar to the nuclei of the genuine ganglion grains. In these grains I found fibers that were mutually crosswise connected in the number of 5 to 10 pieces, arranged into longitudinal bundles of grey fibrils. Elastic tissue formed by double fibrils is located among the grains in the interstitium of their walls. When treated with vinegar, these fibrils present transverse strips similar to heart muscle fibrils. It is difficult to say if they represent real fibers or just contours of membranous walls which, like plant cells, surround granular contents; in my opinion the second option is more likely, as after crushing the grains, I could not see any similar free fibrils. On no account can they be compared to nervous fibrils that may be seen in ganglions, weaving ganglion balls round, even though it appears so at first sight. I never managed to find real nervous fibrils in these granular fibers, which would prove the obvious nature of the ganglions.*

*Therefore, I would incline to categorize this new tissue as cartilaginous, although considering its softness, I am in doubt about its effect in the relation to a relatively huge muscle mass of the heart. (Thus, it is currently more likely to me to consider this tissue an independent locomotive apparatus and to regard the membranes surrounding the grains as muscular ones). Moreover, I found similar granular fibers in beef, pig and horse. However, I never managed to find the same in human, dog, rabbit or hare.*

Although a literal translation from the German original aged 160 years into Czech (and English afterwards) seems slightly halting from the point of view of the contemporary professional terminology, it is possible to deduce the following facts:

A) Purkinje excluded that the fibers he found were nervous fibrils and ganglions.

B) After some hesitation he also excluded the hypothesis of cartilaginous origin of the fibers.

C) He finally described the fibers as being of a muscular type belonging to the locomotor apparatus.

Purkinje could not know at that time that these fibers he discovered and described as fibers of being a muscular type, were fibers of the conduction system.

Purkinje's name would possibly have gone out the window if the discoverer of electric currents in the heart contraction (together with Heinrich Müller) a Swiss anatomist and physiologist Professor Rudolf Albert Kölliker (1852) had pointed these fibers out, naming them Purkinje fibers. (4, 5). Since then, this term has been broadly accepted in international literature. The discovery of Purkinje fibers launched an explosion of other morphological, physiologic and

clinical discoveries and papers dealing with this issue, which still reverberates today. Owing to their localization on heart ventricles walls as described by Purkinje, these particular cardiomyocytes are regarded as a final segment of the conduction system that is connected to normal cardiomyocytes ventricular musculature and go as far as the improper chordae tendineae. Purkinje cells have the following important morphological features: 20-70 microns of size, spacious sarcoplasm, small amount of myofibrils localized marginally in the cell. Two years before Purkinje's death (1867) Obermeier described three types of Purkinje cells differing in quantity of sarcoplasm and thus in compactness of myofibrils. Bigger cells predominantly had a cubic shape with fewer myofibrils marginally in the cell; they were connected to spherical cells of middle size having more myofibrils and finally to the cells of a long thin shape having more striated myofibrils. He found Purkinje fibers in hearts of sheep, horses, pigs, cows, geese and pigeons. However, he did not find them in humans, cats, hares, mice or frogs. In the heart of big animals, such as beef cattle, he observed the Purkinje fibers not only under ventricle endocardium but also in the ventricle muscle. (6). Obermeier suggested another name for Purkinje fibers – Purkinje muscles chains ("Purkinje'sche Muskelketten"). Knowledge of the conduction system and Purkinje cardiomyocytes was significantly expanded thanks to the research of a Japanese scientist Tawara. (7). In 1906 Sunao Tawara published the results of his two and half year work in Marburg, concerning the conduction system, in his book: *Das Reizleitungssystem des Säugetierherzens*. Verlag Gustav Fischer, 1906 (200 pages and 10 color tables). Tawara's teacher and consultant, Ludwig Aschoff (1866–1945) behaved very nobly as he did not mention himself as a co-author of the book. He had only written a foreword. Tawara discovered the atrioventricular node (formerly called Tawara or Aschoff Tawara node); he also histologically described in detail Purkinje cells in the atrioventricular node and branches and their transition to the contractile muscle. He was keen to retain the name of Purkinje bundles and thus helped to spread the term to the whole cardiologic world. He excluded some previous opinions regarding Purkinje fibers (cells) as a pathological structure (8). In 1908, in his publication concerning the discovery of electrocardiogram, Einthoven used Tawara's research concerning the atrioventricular conduction system, including its final bifurcation of conduction fibers (or Purkinje fibers) into the heart muscle, in the interpretation of the electrocardiogram (9). One of the first wax and wire reconstructions of the atrioventricular node, branches and bifurcation of Purkinje fibers of the calf heart was effected by Lydia de Witt 1909 (10).

It has already been said that Purkinje fibers are part of the conduction system. Individual parts of the conduction system are located in different places of the heart, e.g. in the right atrium wall, in the interventricular septum and in the wall of both ventricles.

*At this point a question arises: are all parts of the conduction system morphologically similar or partly similar, or they are fundamentally structurally different?*

#### **PARTS OF THE CONDUCTION SYSTEM – CRONOLOGICAL DEVELOPMENT DISCOVERIES**

As it has already been said, Purkinje presented the first part of the conduction system in the shape of the final network of heart fibrils on the interior wall of sheep ventricles in 1845. The atrioventricular bundle was the second discovered part of the conduction system (11). It is called after its discoverer, an internist His Junior (1893), the His bundle. A similar discovery was made by Kent (1892–1893), who found a muscular connection between atria and

ventricles and dissected the atrioventricular node (12). However, he was not convinced of the importance of these bundles. The last structure of the conduction system, the sino-atrial node (13), was discovered by Keith and Flack in 1907.

So-called atrial conduction pathways, also referred to as atrial preferential pathways or internodal pathways connecting the sinoatrial and the atrioventricular nodes, are still a matter of contention (14–16). The question is whether these pathways are formed by conductive substance or just by working cardiomyocytes. These pathways were known as early as the beginning of the 20<sup>th</sup> century. They consist of an anterior pathway of Bachman (1916), running from the anterior margin of the sinoatrial node, surrounding the vena cava superior and in the anterior part of the interatrial septum running to the atrioventricular node (17). The middle preferential pathway (Wenckebach – 1907) runs from the proximal surface of the sinoatrial node to the dorsal part of the atrial septum up to the limbus fossae ovalis, where it joins the anterior pathway, and together they join the atrioventricular node (18). Finally, there is the posterior (inferior) preferential pathway (Thorel – 1910) that detaches from the caudal of the sinoatrial node, running caudad along the crista terminalis and in its inferior part entering the atrioventricular node (18).

#### MORFOLOGICAL STRUCTURE OF THE INDIVIDUAL PARTS OF THE CONDUCTION SYSTEM

##### *Sinoatrial node - SA node*

Nowadays we generally use the term “sinoatrial node”. However, from the embryologic point of view, the term “sinuatrial” would be more correct, as it is created in the part of an embryonic heart part, sinus venosus. The node is situated on the junction of the anterior circumference of the vena cava superior and the right auricle, in sulcus terminalis. It is spindle-shaped, 5–9 mm long, 3–5 mm wide. It spreads from the prominence of the right auricle up to torus inter-venosus and, in some cases, as far as to the area of sinus coronarius. There can be interspecific variations of the localization of the node (20). The node is formed by thin fusiform cells, arranged in winding shape, with a tendency to a longitudinal arrangement along sulcus terminalis. The cells of the interior layer are circularly arranged surrounding the SA artery that runs through the center of the node. The sinoatrial node enveloping the sinoatrial artery reminded Söderström (1948) of an enormous adventitia (21). Pacemaker cells of the node – **nodal cells**, have very little of striated myofibrils, a centrally placed nucleus and a slightly eosinophilic cytoplasm. They are smaller than atrial cardiomyocytes - 3–9 microns wide, 15–20 microns long. They are surrounded by a net of interstitial tissue containing mostly collagenous fibrils with some elastic fibers. The number of fibers increases with age. Transitional cells with more than 50 % of myofibrillar content can be found marginally in the node. They have marked Z, H, M zones and lines and are bigger than nodal cells, about 10 microns, and have more nexuses (gap junctions) as well. As for their structure, they are between typical contractile muscle cardiomyocytes with a great amount of contractile myofibrils, and nodal cells with a small quantity of myofibrils.

Viewed through a microscope, nodal cells contain a small amount of irregularly arranged myofibrils and mitochondria. The sarcoplasmic reticulum is ramified but poorly developed. There is no transversal tubular system. Junctions between the cells are formed mostly by desmosomes or by few fasciae adherentes and several nexuses. Intercalary discs cannot be seen. Myofibrils form only 40 % of the whole cell volume (22). For basic data about the node structure see citations (23–31).

##### *Atrioventricular node – AV node*

The atrioventricular node is localized between the coronary sinus mouth and the septal leaflet of the tricuspid valve in Koch triangle. It can easily be revealed by dissection. It is 5–7 mm long and 2–5 mm wide. Its cells can be microscopically distinguished from the atrial muscle. Their structure is plexiform, they are nearly of the same size as atrial cells, but their cytoplasm is lighter than in atrial and ventricular myocytes. They are characterized by their striated structure and intercalated disks. Inside the node we find larger amounts of elastic and collagenous connective tissue than in atrial and ventricular muscle, but less than in the sinoatrial node. The node is divided into two zones: a superficial one, formed by transitional cells and normal cardiomyocytes and a deep (compact) one. The cells of the compact zone are similar to nodal cells. Small nodal cells gradually transfer to bigger Purkinje fibers of the atrioventricular bundle. The electronogrammes of nodal cells of the AV node show a smaller number of irregularly arranged myofibrils, a poorly developed sarcoplasmic reticulum and no tubular system. Cell junctions are formed by a lot of desmosomes and few nexuses. We can more frequently see the fasciae adherentes than in sinuatrial cells, but not so often than in atrial and ventricular myocytes. For basic data about the atrioventricular junction area see citations (32–38).

#### ATRIAL PREFERENTIAL PATHS (PATHWAYS)

##### *Atrial Preferential Paths (Pathways)*

*Are they part of the conduction system?*

Impuls excitation preferentially and the quickest by so-called preferential pathways. These pathways consist of muscular fibers, fibers similar to Purkinje cells and fibers similar to nodal cells, however these last ones are sporadic (39). Some authors (40–42) do not recognize these pathways from the morphologic and physiologic point of view as conduction system pathways. They argue that these preferential pathways mostly consist of working heart muscle cells that do not constitute a pathway. The pathways in individual hearts differ in their running, according to the muscle arrangement. They are considered to be muscular atrial bundles – trabeculae formed by contractile cardiomyocytes. This opinion is based on the definition of a pathway tract (43–44), in the formulation of Aschoff 1910 and Mönckeberg 1910.

1. Fibers in a pathway tract should be identical.
2. There should be formed a casing of connective tissue surrounding the bundle – features of an isolated cable.
3. There must be continuity, joining one fiber to another.

The given pathways do not fulfil these conditions. Emberson with Challice 1970 and Bojsen-Moller with Tranum-Jensen 1972 described a so-called “sinoatrial ring node” – SARB. They used cholinesterase staining in mammals, such as a rabbit, to find an open ring of atrial cells going through one elliptical branch by the cauda of sinuatrial node, along sulcus terminalis and through the second branch over the head of sinuatrial node and septum up to the atrioventricular node (45, 46). The question is whether this ring partly overlaps with internodal pathways or not.

#### ATRIOVENTRICULAR BUNDLE (HIS BUNDLE), RIGHT AND LEFT BRANCH

We should be grateful to Tawara (1906) for emphasizing the morphological unit of transfer of the atrioventricular node to the atrioventricular bundle, branches and Purkinje fibers. The atrioventricular bundle consists of two parts: a so-called penetrating bundle, going through the fibrous figure, and a ramifying bundle, lying

astride on the ventricle septum muscle, under the membranous septum. The left branch runs from the bundle as a continuous layer of fibers along the whole length of bifurcation, whereas the right branch seems to be a direct follow-up of the ramifying bundle. The right branch passes under the septal endocardium to the musculus papillaris anterior and fragments to the net of Purkinje fibers for the walls of the right ventricle. The left branch splits under the septal endocardium into the anterior and posterior fasciculi and both of them pass to Purkinje fibers of the ventricle. Some authors recognize three rather than two fasciculi: anterior, medial and posterior. The cells of both parts of the atrioventricular bundle and branches in human are smaller than the cells of the working myocardium (37). However, in bigger mammals, such as cows and sheep, the cells of atrioventricular bundle and branches resemble larger Purkinje cells. The cells in the bundle and branches are longitudinally oriented and separated by collagenous fibers. James and Sherf (1971) described in electronogrammes in dogs and humans that the atrioventricular bundle consists of large cells similar to Purkinje fibers, containing few myofibrils and a light perinuclear zone (16). In addition they found 2 types of transitional cells there: large ones and narrow ones. In the proximal part of the bundle they described the cells identical to the sinuatrial bundle cells. Here, in the SA node, they called them P cells. The cells in question are nodal cells microscopically appearing as pale. However, cardiologic literature did not accept this term and consistently continues to use the term of "nodal cells" for the SA and AV node cells. They cannot be mistaken with Purkinje fibers. Later on, James et al. (1974) described the ultrastructure of branches (47). According to them, the left branch consists of typical Purkinje fibers (cells) that are mixed with cells resembling working cardiomyocytes. The cell junctions are made of intercalated disks that contain long nexuses. The right branch is mostly formed by working cardiomyocytes. Typical Purkinje fibers (cells) were very rare in the right branch. Vassal-Adams (1983) does not recognize these findings and considers the whole atrioventricular system, including the node, quite heterogeneous (48). It cannot be clearly specified into separated cell types. All these heterogeneous cells are connected with intercalated disks.

#### **PURKINJE FIBERS (PURKINJE CELLS, PURKINJE CARDIOMYOCYTES, RAMI SUBENDOCARDIALES**

They represent the terminal part of the conduction system. They consist of the AV bundle and branch. Under the ventricle endocardium the branches fragment into the net of fibers discovered by Purkinje. These are formed by cells with a small amount of fibrils and a great quantity of glycogen in reverse. Purkinje fibers in human reach only the interior myocardium layer, whereas in certain animals they extend to the whole myocardium (6, 49). The fibers are connected to the working myocardial cells by intercalated disks, with or without the transitional cells. One fiber transfers the impulse on thousands of working cardiomyocytes. This arrangement guarantees a synchronous action of working cardiomyocytes during the contraction.

There is no uniform description of Purkinje cells in the literature. Thus, in the paper of Obermeier already, a description of three types of Purkinje cells (see the chapter about history) may be found.

Another description of 3 types of Purkinje cells was given in 1973 and 1987 (50, 51):

Type I. – The cells of this type are situated in the area of the atrioventricular bundle bifurcation and in the proximal part of branches. They contain a small amount of myofibrils and the cells are smaller (6 microns of diameter) than in type II.

Type II. – These are the biggest Purkinje fibers (10–20 microns

of diameter) and are situated in the ventricular myocardium (32). They are also located in the ventricular subendocardial layer and in false chordae tendineae.

Type III. – These are present in the junction between the big Purkinje cell and the myocardium cell and are bigger than working cardiomyocytes. They have few mitochondria and no T system. We call them transitional form of Purkinje cell (8-12 microns of diameter).

The size of Purkinje fibers is also given in various forms. There are interspecific variances, but there are also differences in data from different authors. The size of Purkinje fibers in whales is about 19–94 microns whereas in humans it is about 10–46 microns (32).

Purkinje cells, as is universally accepted, contain few myofibrils. The Z line may be larger but may be absent as well. The T system is absent or just poorly developed and mitochondria are small with few cristae. Myofibrils in Purkinje fibers work as passive cytoskeletal components (52, 54). They are different in composition of myosin from the cells of working myocardium, as they contain not only two light chains but also an accessory type of myosin with an intermediate molecular weight (53, 55). Unlike working cardiomyocytes, where the sarcoplasmic reticulum is joined with the sarcolemma of the T tubule (interior coupling) and with the peripheral sarcolemma (peripheral coupling), Purkinje fibers that do not have T tubules are joined with the peripheral sarcolemma only (56). Purkinje fibers are PAS positive as they contain a considerable amount of glycogen, which is typical for the conduction system cells (50,49). A large quantity of glycogen in Purkinje fibers is metabolized by the way of anaerobic enzymes. Thanks to this property, these cells are more resistant to hypoxia than the ventricle myocardium cells (57). An activity of acetylcholinesterase was found in the conduction system, including Purkinje cardiomyocytes; however, no such activity was detected in working myocardium cells (58). There is interspecific variety in connection of Purkinje fibers with working ventricular cardiomyocytes, among different animals and between animal and man as well. The difference is in presence or absence of transitional cells between Purkinje fibers and working cardiomyocytes. Such a connection between a Purkinje cardiomyocyte and a transitional cell guarantees a high resistance of coupling and a quick conduction on the working myocardium. This arrangement is well marked in rabbits and pigs (59). On the contrary, no transitional cells were detected in human and cattle hearts. The Purkinje fibers detected here only got smaller on passage to the myocardium. In the cattle heart, Purkinje fibers under the ventricular endocardium form a two-dimensional net that converts into a three-dimensional one on its passage to the myocardium. At the beginning, Purkinje fibers in myocardium are surrounded by a connective tissue - which gradually disappears, so that a contact of the Purkinje fibers with ventricular myocytes can be realized. Only in the area of 2 mm under the epicardium was this connection not found (60). This electrical coupling between Purkinje fibers and working cardiomyocytes may be disturbed in acidosis, hypoxia and hyperkalemia (61). Ectopic impulses, disturbances in conduction of an impulse and reentry tachycardias can emerge in Purkinje fibers in the peri-infarctuous area (62–64). The electrical impulse is more quickly transferred by Purkinje fibers (2–3 m/sec) than by ventricular cardiomyocytes (0,3–0,4 m/sec). That is thanks to a group of proteins – connexins C40,C43, C45. If the connexins are knocked out, a disturbance appears in conduction of impulses through the AV node and Purkinje fibers, including the spatial conduction of impulses (65, 66). A confocal laser microscope is used in mapping normal and abnormal dynamics of Ca<sup>2+</sup> in Purkinje conduction cells (67). An accumulation of Ca<sup>2+</sup> in the cytosol in the present of cardiotonic agents leads to tachyarrhythmias in the Purkinje cells but not in the working ventricular cardiomyocytes (68). Lately, the genes influencing the development of





**Picture 1.** Conducting system (Purkinje fibres) of the left cardiac ventricle. Photograph of the dissection from the Institute of Anatomy, 1<sup>st</sup> Medical School, Charles University, kindly allowed by Professor Seichert and Doctor Nařka

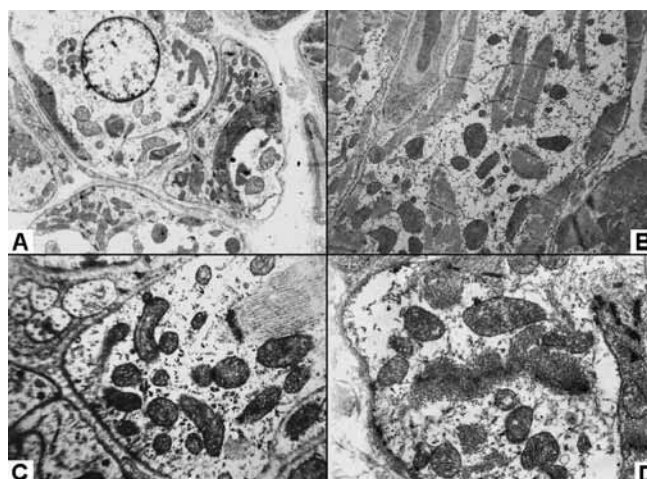
the His-Purkinje system and disturbances of the conduction system cells, have been explored in transgenic animals – expression of the lacZ gene (69, 70). The His – Purkinje system starts working as soon as before the septation of the heart.

#### SUBSIDIARY PACEMAKER CENTRES – ECTOPIC CENTRES

From the electrophysiological point of view, numerous authors have convincingly demonstrated that in the heart there are centers of formation of subsidiary and ectopic rhythms. These were described in the area of coronary sinus on the false chordae tendineae and in ventricles, by the ramification of Purkinje fibers, on sleeves of pulmonary veins or in the ring surrounding the tricuspid or mitral valve (71–74). Recently, ectopic impulses registered from the pulmonary veins have been closely studied as well (75, 76). In this content, Professor Šteiner (77) has lately pointed out the Purkinje's and his student's Raeschel's priority in describing myocardial fibers on pulmonary veins. However, it is very difficult from the morphological point of view to identify these centers. For now, only a description of the myocardial muscle arrangement on pulmonary veins is known (78, 75). Only some individual cells with a morphological resemblance to conduction cells have been found so far, e.g. in the area of sinus coronarius (79, 80).

*Although some controversial contentions exist, from the given overview is clear that Purkinje fibers are morphologically very similar to the cells of other parts of the conduction system. The main list of identical features is given in the summary.*

Considering all the facts given in this paper, the frontier between the normal myocardium and the conduction system (specialized myocardium) seems to be clearly apparent. Nevertheless, Anderson and his colleagues (42) recently published controversial opinions on the anatomical definition of conduction systems. He gives the following opinion presented at the Novartis symposium 2002 about the conduction system: not only are all myocardial cells in the postnatal heart able to transfer the impulse, but in addition all of them have a potential of being congenitally special as for the conduction system. Even the myocardium, described as “working”, is significantly heterogeneous, considering its morphology, ultrastructure and genes. Nevertheless, the incontestable fact is that some cells are more specialized than others and form a conduction system. That is not just an academic question, as fatal arrhythmias may occur in the event of disturbances of the system caused either by physiologists or



**Picture 2.** Electronmicroscopic pictures of the conducting cardiac system.

A: a nodal cell from the sinoatrial node; B: a nodal cell from the atrioventricular node; C – a Purkinje cell (Purkinje fiber); D – a cell from the sinus coronarius area (a possible ectopic center).

Cells from all parts of the conducting system have a strong resemblance in ultrastructural terms.

by a pathological event such as myocardial infarction. Embryologic research shows that some primordial areas in the heart convert to the postnatal conduction system. Discovery of the genes and their localization in the developing heart invokes the following issue: would they be effective in distinguishing and accurately topographically determining the conduction system? It is debatable whether the areas differentiable by the way of transgenes, such as minK-LacZ or Engrailed2-LacZ, which is also known as CCS-LacZ, can be considered part of the conduction system. It is questionable, since these areas are significantly larger than the components defined and verified to be part of the conduction system. Another arguable issue is whether some acetylcholinesterase positive cells, at certain places (such as retroaortally or in the tricuspid valve), can be considered conductive or whether they have just a nodal phenotype – they do not work as postnatal conduction system. During the embryonic stage in the primitive heart, in the shape of a simple tube, its every cell is endowed with rhythmicity. However, only a part of them become cells of the conduction system. There are also interspecific problems, as the conduction system is more distinctly modeled in mammals in comparison to lower classes of vertebrates. There is a whole range of questions to be answered. From these several comments it is clear that research into the conduction system will proceed. Genetic therapy of disturbances of the conduction system will definitely be one of the future ways. Cell therapy, whether it is by means of embryonic stem cells or adult mesenchymal cells, is promising. Biological pacemakers, created in these ways could replace contemporary electric pacemakers (71).

#### P.S.

When studying historic materials I was surprised and puzzled after having read the sentence by Professor Chodounský (5), a assistant of Purkinje's, in his memoir book “Jan Evangelista Purkinje, his Impact on the Czech Culture “ from 1927. When describing Purkinje's funeral he wrote on page 110:

*It has to be remarked that Professor Treitz was the one and only faculty member of the Prague Medical School who came to the churchyard of Vyřhrad*

It would be unworthy of the Alma Mater not to pay its respects to this genius.

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