Why Does the Heart Beat?
The Discovery of the Electrical System of the Heart
Mark E. Silverman, MD; Daniel Grove, MD; Charles B. Upshaw, Jr, MD

Abstract—Why does the heart beat? This question—known as the myogenic versus neurogenic theory—dominated cardiac research in the 19th century. In 1839, Jan Evangelista Purkinje discovered gelatinous fibers in the ventricular subendocardium that he thought were muscular. Walter Gaskell, in 1886, demonstrated specialized muscle fibers joining the atria and ventricles that caused “block” when cut and found that the sinus venosus was the area of first excitation of the heart. By examining serial embryologic sections, Wilhelm His, Jr, showed that a connective tissue sheet became a bundle connecting the upper and lower cardiac chambers, the bundle of His. Sunao Tawara traced the atrioventricular (AV) bundle of His backward to find a compact node of fibers at the base of the atrial septum and forward where it connected with the bundles of cells discovered by Purkinje in 1839. Tawara concluded that this “AV connecting system” originated in the AV node, penetrated the septum as the His bundle, and then divided into left and right bundle branches that terminated in the Purkinje fibers. Martin Flack and Arthur Keith studied the conduction system of a mole and found a structure in the sinoauricular junction that histologically resembled the AV node. They felt that this was where “the dominating rhythm of the heart normally begins” and named it the sinoauricular node in 1907. The ECG of Einthoven soon brought a new understanding to the complex electrical system that makes the heart beat. In 2006 and 2007, we celebrate the 100th anniversaries of the publication of the exciting discovery of the AV and sinus nodes, truly landmarks in our understanding of cardiac structure and physiology.

Key Words: atrioventricular node ■ conduction ■ electrical stimulation ■ sinoatrial node

Whenever any hypothesis is proposed, the system involved should be taken into consideration as a whole. Moreover, a conclusion derived from the anatomical architecture must eventually accord with the results of physiological experiments regarding the system."
—Sunao Tawara, 1906

Why does the heart beat? This provocative question dominated cardiac research in the 19th century.2–4 In the second century, Claudius Galen observed that an excised, denervated heart continued to beat after isolation: “The heart, removed from the thorax, can be seen to move for a considerable time,...adefinite indication that it does not need the nerves to perform its function.”5 William Harvey, in De Generatione Animalium (1651), stated that “the pulse has its origin in the blood. . .the cardiac auricle from which the pulsation starts, is excited by the blood.” Albrecht von Haller, an experimental physiologist at the University of Göttingen, Germany, also postulated irritability of the heart muscle resulting from the intracardiac blood. On the basis of crushed spinal cord experiments in 1812, Cesar Legallois in France believed that the heartbeat was under nervous control.2,3 In the 1830s and 1840s, the discovery of the sympathetic and parasympathetic nerves and ganglia inside and outside the heart, as well as the effect of galvanic stimulation on the nerves and heart, supported his nervous theory.2,4 This ongoing, somewhat fevered, debate, arguing about whether the heartbeat was triggered by inherent excitation by the heart muscle itself or was due to an electrical stimulus from either external nervous or local ganglionic control, was known as the myogenic versus the neurogenic theory.4

Ultimately, this physiological debate would be decided by anatomists who would discover the site of origin of the electrical impulse and its conducting pathway through the heart: first, the Purkinje fibers (1839); then, the bundle of His (1893); then, the bundle branches (1904); next, the atrioventricular (AV) node (1906); and finally, the sinus node (1907).6 In 2006 and 2007, we celebrate the 100th anniversaries of the publication of the exciting discovery of the AV and sinus nodes, respectively, truly landmarks in our basic understanding of cardiac structure and physiology.

Jan Evangelista Purkinje and the Distal Cardiac Conducting System

The story begins in early 19th-century Bohemia (now the Czech Republic) with the discovery of the specialized distal conducting pathway by Jan Evangelista Purkinje (1787–1869)7 (Figure 1). Purkinje was born in Libochovice, was educated in a Piarist monastery, and studied philosophy in Prague. He entered medicine at the University of Prague at 26 years of age. After graduation in 1819, he assisted in anatomy

From the Department of Medicine, Emory University, and the Fuqua Heart Center of Piedmont Hospital, Atlanta, Ga.

Correspondence to Mark E. Silverman, MD, 1968 Peachtree Rd NW, Atlanta, GA 30309. E-mail marksil@comcast.net

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and physiology and conducted research in pharmacology, including self-experimentation with digitalis and belladonna. In 1823, at 36 years of age, he became professor of physiology and pathology in Breslau in East Prussia, where he created the world’s first Department of Physiology in 1839. Purkinje remained in Breslau for 27 years before returning to Prague, where he was the chair of physiology.7,8

An erudite man who wrote poetry and spoke 13 languages, Purkinje also was active in the Czech nationalist movement and translated the poetry of his close friends Goethe and Schiller. Purkinje was a pioneer in many fields, describing the Purkinje effect on vision (decreasing light intensity affects red and blue objects differently) and other visual effects; the Purkinje nerve cells in the cerebral cortex; the sweat glands in the skin; the effect of pancreatic extracts on protein digestion; the visual and cardiac effects of digitalis toxicity; the use of a microtome to make thin slices; ciliary motion in higher organisms; the nervous influences on the secretion of gastric acid; in vivo capillary microscopy; and new aspects of the psychology of dreams. He also was the first to study the science of fingerprints and to use the terms plasma and protoplasm. After a remarkably productive career, Purkinje died in 1869 at 82 years of age.

In 1839, Purkinje discovered a net of gray, flat, gelatinous fibers in the ventricular subendocardium of the sheep heart. The fibers were composed of numerous corns with nuclei gathered tightly in a polyhedral form.8 Initially, Purkinje believed that they were cartilaginous fibers; 6 years later, however, he decided that they were muscular. Their conductive function would not be understood until the work of Sunao Tawara in 1906.1

Walter Gaskell and the AV Conduction of the Cardiac Impulse

Walter Gaskell (1847–1914), the son of a barrister, was born in Naples, Italy, and grew up in northern England (Figure 2). While an undergraduate studying mathematics at Cambridge University, he came under the influence of Michael Foster, a major figure in 19th-century British physiology.4,9,10 In 1874, Foster guided Gaskell to work with Carl Ludwig in Leipzig, where Gaskell studied the vasomotor control of blood flow in skeletal muscle arteries and demonstrated that sensory nervous stimulation could cause arterial dilation. After returning to Foster’s laboratory at Cambridge in 1875, Gaskell produced the definitive work on the anatomy and function of the efferent sympathetic nerves and the antagonistic effects of the autonomic nervous system on the heart.9,10

Among Gaskell’s many contributions, his understanding of impulse formation and cardiac conduction in the early 1880s is of special note. Working with an isolated strip of tortoise ventricular muscle devoid of ganglia or nervous connection, Gaskell showed that the strip continued to pulsate at a rate similar to the intact heart. He concluded, “The rhythmic capacity of every part of the heart depends not upon the presence of ganglion cells but rather upon the persistence of a primitive condition of heart muscle.”11 In the slowly beating tortoise heart, he was able to demonstrate that conduction of the heartbeat proceeded in a coordinated fashion as a mus-
cular peristaltic wave, spreading from the sinus venosus to the sinus-auricle (the atrium near the sinus venosus), then to the auricle-ventricle (the atrium near the AV groove), and from there to the ventricle. He noted that different areas of the heart were more apt to generate rhythmicity than others, with the sinus venosus as the dominant generator of automaticity. From his extensive experimentation, Gaskell concluded that the beat of the heart “starts from that part which is most rhythmic, i.e., which beats spontaneously at the quickest rate, and travels as a wave of contraction over the rest of the heart at rates of speed which vary in different parts according to the nature of the muscular tissue.”

In 1882–1883, Gaskell repeated key experiments originally performed by Hermann Friedrich Stannius in 1852 and Luigi Luciani in 1873, in which a ligature was placed between the atria and ventricle of a frog heart. Luciani, an Italian physiologist who also had worked in Ludwig’s fertile laboratory, had observed grouping of ventricular beats that he called a “periodic rhythm.” Luciani’s 1873 publication “On the Periodic Function of the Frog Heart” was the first graphic representation of AV block. Luciani did not fully recognize the significance of his discovery, although he believed that increased resistance to impulse propagation played a significant role.

By placing a ligature in the AV groove and cutting away portions of atrial tissue, Gaskell created various degrees of block between the atrium and the ventricle. With increasingly deeper cuts, the ventricle would respond only to the second, then the third, etc, beat of the atrium, a rhythm that Gaskell called “partial block.” With complete transection, the ventricle stopped completely, only to begin again at a slower rate independent of its atrium. He called this phenomenon “complete block,” a term first used by George J. Romanes, his coworker at the Cambridge Physiology Laboratory who had showed that cutting the muscular rim of the jellyfish blocked its contraction. Gaskell concluded that impulse propagation slows at the junction between the atrial and ventricular chambers. In 1883, he attributed this delay to “undifferentiated embryonic muscular tissue” which he thought had greater rhythmicity but slower conductivity. He noted similar thin tissue with a lack of cross-striations and abundant, large nuclei in the sinus venosus region. In 1886, he found muscular connections in the frog and tortoise hearts that formed a ringlike sheet that, when cut at specific locations, blocked the coordinated contraction of atria and ventricles.

These experiments were the first to demonstrate the existence of specialized muscle fibers joining the atria to the ventricles and provided the necessary foundation for the discovery of Wilhelm His, Jr.

Wilhelm His, Jr, and the Connecting Bundle Between the Atrium and Ventricle

Wilhelm His, Jr (1863–1934), is remembered eponymically for his discovery of the conducting pathway between the AV node and the bundle branches (Figure 3). Born in Basel, Switzerland, the son of a famous anatomist and embryologist, he grew up in Leipzig, Germany, a noted center of science and culture. As a child, he showed talent as a violinist. After early schooling, his father arranged for him to study in Basel, Geneva, Bern, and Strasburg so that he could be widely exposed to great educators. After receiving his medical degree in 1888 from the University of Leipzig, His became an assistant in a clinic where several coworkers were investigating whether disease affected the heart through its ganglia or muscle. He proposed approaching the problem by using embryological techniques taught to him by his father. By following the development of the cardionervous system in different classes of vertebrates, he was able to show that the heartbeat begins before cerebrospinal nerves or ganglia develop. These studies provided strong support for the myogenic theory at a time when the neurogenic theory was still in sway.

His also was perplexed about how the stimulus conducted from 1 segment of the heart to another. He was aware of Gaskell’s work showing that conduction passes through a muscle bridge from atrium to ventricle with a delay at the AV groove in the frog and tortoise hearts. By examining serial sections of the heart during different stages of embryological development, His showed that a connective tissue sheet inserts between the upper and lower portions of the heart to form a complete ring. He followed serial sections in this connective tissue ring as it went through increasing stages of growth, searching for a bridge connecting the upper and lower chambers. In 1893, while in Leipzig, he described the conducting bridge that would become known as the His bundle: “I have succeeded in finding a muscle bundle which
unites the auricular and ventricular septal walls. . . . The bundle arises from the posterior wall of the right auricle near the auricular septum, in the atrioventricular groove; attaches itself along the upper margin of the ventricular septal muscle . . . proceeds on top of this toward the front until near the aorta it forks itself into a right and left limb." His presumed that the specialized bundle connected the atrium directly to the ventricular muscle but did not perform any experiments to show its purpose, commenting, "I cannot state with certainty whether this bundle actually conducts the impulses from the auricle to the ventricle, as I did not perform any experiments dealing with the severing of the bundle." He also experimented on rabbits, however, and was able to show that severing the bundle could result in asynchronous contraction of the atrium and ventricle.

His left the field of embryology and AV conduction to become a professor and expert in the metabolism of uric acid and gouty arthritis in Dresden (1901), Basel (1902), Göttingen (1906), and finally Berlin (1907), where he was professor of internal medicine and director of a clinic.

Sunao Tawara and the Discovery of the AV Node

The late 1860s brought great governmental and societal change to Japan. Japan had been dominated by an isolationist regime until modernization opened the door to Western thought in 1867. Medical education was affected as the new Japanese government adopted a German-influenced system attracting professors from Germany to teach in Japan. In exchange, Japanese students were sent to Germany. Sunao Tawara (1873–1952) was born on the island of Kyushu, Japan, in 1873 and was adopted as a young child by a physician-uncle (Figure 4). After graduating in medicine from the University of Tokyo, where he showed an interest in anatomy, he was directed to Marburg, Germany, in 1903 to work at the Institute of Pathologic Anatomy of Ludwig Aschoff, an internationally recognized pathologist and a proponent of the myogenic theory. At that time, Aschoff was especially interested in the pathophysiology of the failing heart with an emphasis on its nervous control, myocardium, and valves. Tawara was asked to perform a histological examination of 150 hearts with myocarditis, a laborious study that led to the discovery of the nodules of rheumatic myocarditis, later named Aschoff bodies. As part of the study, the region of the AV bundle was carefully examined. This led Tawara to obtain a more comprehensive study of the anatomy of the conduction system. His monumental discovery and insight, made in just 3 years and published in 1906, is introduced by his statement, "I intend, for the first time in medical history, to propose an integral and consistent explanation concerning the atrioventricular bundle and the Purkinje fibers." Through the tedious task of combing through serial sections, following the path of similar histology, Tawara was able to trace the AV bundle of His backward where it ended in a compact meshwork of fibers resembling a “knoten” (node) at the base of the atrial septum. Distally, he found that the bundle of His divided into 2 bundle branches that connected with a fanlike group of “subendocardially scattered characteristic muscular bundles.” Tawara, with the help of Aschoff, quickly realized that these peculiar fibers could be the same “network of gelatinous fibers” discovered by Purkinje 58 years earlier. He confirmed his suspicion in sheep and other mammalian hearts just as Purkinje had done.

Tawara’s genius was to realize the function of the Purkinje cells and that there was an electrical pathway, the “atrioventricular connecting system,” as he named it, that originated in the AV node, penetrated the fibrocartilaginous portion of the septum as the His bundle, and then divided into defined left and right bundle branches as it descended downward to reach the terminal ramifications of the Purkinje fibers (Figure 5A and 5B) He commented that “the connecting system also represents a transporting or conducting pathway. Because the pathway is not a ductal, but a continuously related protoplasmic cord, conduction of excitation impulses surely must take place there.” Finally, he summarized, “The system is a closed muscle bundle that resembles a tree, having a beginning, or root, and branches. . . . The system connects with the ordinary ventricular musculature for the first time at the terminal ramifications.” Tawara credited R. Retzer and K. Braeunig for their independent description of the right and left bundle branches in 1904.

Before Tawara’s discovery, conduction through the His bundle was assumed to be slow because of the observed long interval between atrial and ventricular contraction and the presumption that it was embryologic tissue. Because His
assumed that the bundle connected directly to the base of the ventricle, physiologists taught that the base contracted before the apex of the ventricle. Tawara believed otherwise, postulating that connective tissue insulation allowed a rapid velocity of conduction through the His bundle to the Purkinje fibers. He thought that each segment of the connecting system had different functional abilities and that the apex of the ventricular muscle was the first to be stimulated, followed by an orderly sequence of muscular contraction spreading upward from the apex to the base of the ventricle. Thus, he also introduced a new understanding of the physiology of the heart muscle and its electrical control. Because he thought that the conducting bundles were muscular tissue (not nerve tissue) surrounded by connective tissue, he stated that his work supported the myogenic theory.

The important anatomic and physiological implications of Tawara’s work were immediately recognized by Ludwig Aschoff, his mentor, who arranged for its publication in monograph form. As Sir Arthur Keith later commented in his autobiography, “With the discovery of the conducting system of Tawara, heart research entered a new epoch.” In 1999, Robert Anderson, in an introduction to the English translation of Tawara’s book, wrote, “The anatomic studies of Tawara laid the basis for the development of the science of cardiac electrophysiology.”

Tawara returned to Japan in 1906 and became a distinguished professor of pathology at the University of Kyushu and was twice president of the Japan Pathology Association. He was a modest man. One of his teachers later wrote, “There are some who often talk very proudly about their academic achievements. However, this kind of presumptuousness was foreign to Tawara. He very seldom spoke about his achievements, and then only at the strong request of his students.” In 1908, Willem Einthoven referred to Tawara’s monograph as the theoretical basis for interpreting the ECG. Tawara received the Imperial Prize of the Japan Academy for his brilliant work on the conduction system, and he was awarded a special medal by the emperor. Tawara died in 1952 of dementia.

Arthur Keith, Martin Flack, and the Discovery of the Sinoauricular Node

The discovery of the origin of the impulse that controlled the heartbeat is generally considered to be the contribution of Sir Arthur Keith and Martin Flack, although Walter Gaskell (1883), H.E. Hering (1900), and Karel Wenckebach (1903) also deserve some of the credit. Arthur Keith (1866–1955) was born in rural Aberdeen, Scotland, the sixth son of a farmer (Figure 6). He was an indifferent student until medical school at the University of Aberdeen, where he excelled, graduating in 1888 with highest honors. He won prizes in anatomy that included Darwin’s book *On the Origin of Species*, which would prove influential. After a posting to a mental hospital in Perth and a year in general practice, he went to Siam (now Thailand) as the medical officer for a gold mining company and a plant collector for a botanical survey. In Siam, he began his studies of monkeys and apes, the beginning of a lifelong passion in anthropology and paleontology that would eventually bring him international recognition and a knighthood in 1912. In 1892, intent on a career in comparative anatomy, he returned to England from Siam to study various species at University College, London. In 1895, he visited His in Leipzig; that same year, he was appointed senior demonstrator of anatomy and curator of the Museum at the London Hospital, where his career flourished over a 13-year period. While there, he developed his interest in the structure and development of the heart and the functional anatomy of the respiratory system. He was appointed to the conservatorship of the Hunterian Museum at the Royal College of Surgeons in 1908, serving for 25 years in this position. He published many important books on anthropology, lectured widely, and wrote popular books for the nonscientist, gaining national and international recognition for his work. His final years were spent as the Master of the Buckston Browne Research Farm, fittingly close to the home of Charles Darwin, whose work had been an inspiration to him. Keith died in 1955. In 1903, Keith became acquainted with the work of James Mackenzie, a general...
practitioner in Burnley, England, who had a strong bent for clinical research. Mackenzie had developed a kymographic device to record venous and arterial pulse waves so that he could analyze irregular cardiac rhythms in his patients.22,23 Mackenzie moved to London in 1905, where he soon became the leader of the emerging field of British cardiology. He was knighted in 1915. Keith corresponded with Mackenzie, who responded: “You are the man I am looking for; I have hearts which I observed in patients over a long series of years and now I want someone to examine them. Will you do it?” Keith quickly accepted the offer.22 In 1 heart, Keith noted a localized complex of unusual tissue at the junction of the right atrium and superior vena cava. Not yet knowing about the work of Tawara, he failed to realize its significance.

In late 1905, Mackenzie sent Keith a paper written by H.E. Hering in Prague on the pathway of the His bundle. Mackenzie asked Keith if he could confirm its presence in human hearts. Keith was unable to corroborate its presence, going so far as to write back to Mackenzie that he had “given up the search for His’ bundle—having come to the conclusion that there is not and never was any such thing—at least not in the position described as His’ bundle.”22 Mackenzie then sent Keith a paper by Ludwig Aschoff describing Tawara’s research in Marburg on the AV node and conducting system. In his autobiography, Keith relates: “I was unable to corroborate its presence, going so far as to write back to Mackenzie that he had “given up the search for His’ bundle—having come to the conclusion that there is not and never was any such thing—at least not in the position described as His’ bundle.”

Mackenzie then sent Keith a paper by Ludwig Aschoff describing Tawara’s research in Marburg on the AV node and conducting system. In his autobiography, Keith relates: “I was able in heart after heart to verify the existence of Tawara’s system. The auricles, I found, were joined to the ventricles by an elaborate system which, beginning in a root like structure in the auricular septum, ended as an arborization in the ventricles. The ‘bundle of His’ was but a small segment of the Tawara system.” In a letter sent to Mackenzie on March 11, 1906, Keith candidly states, “I must be a duffer not to have seen it before—let alone question its existence.”22

In the summer of 1906, Keith enlisted Martin Flack (1882–1931), a medical student at the London Hospital and the son of a neighbor, to work in a laboratory that Keith had set up in his summer cottage in the English countryside of Kent. Keith was interested in finding the elusive anatomic origin of the cardiac impulse. Aware that Gaskell, Hering, Engelmann, Wenckebach, and others had proposed that excitation originated near the junction of the superior vena cava and the sinus venosus in animals, Keith and Flack embarked on a microscopic study to find the exact site. While Keith and his wife were bicycling, Flack discovered an unusual structure at the junction of the superior vena cava with the right auricle in the heart of a mole that differed from the surrounding muscle cells. When Keith returned, he excitedly noted that it resembled the AV node described by Tawara that he had also seen in the Mackenzie hearts. Furthermore, the structure connected with the vagal and sympathetic nerve trunks, had a special arterial supply, and was located in the area of primary excitation suggested by Gaskell and others. This also was found to be present in all other mammalian specimens. From their anatomic findings, they concluded, “The fact, therefore, that there is a constant differentiation of certain fibers in this region, which, moreover, are in close connection with the nerves affecting the heart’s rhythm, leads us to attach great importance to these fibers, and we feel justified in expressing the opinion that it is in them that the dominating rhythm of the heart normally begins.”23 Their findings were published in the Journal of Anatomy in 1907, and for some time afterward, it was referred to as the sinoauricular node of Keith and Flack. Eventually, it became known as the sinus node and the pacemaker of the heart.

The long-sought-after site of origin of the cardiac impulse and its conduction from the AV node through the ventricle was finally completed. Meanwhile, in 1901, Willem Einthoven in Utrecht had introduced his string galvanometer, which recorded and measured the electricity of the heart.25 In London from 1910 to 1915, Thomas Lewis applied the Einthoven electrocardiogram to the exposed heart to verify the location of the sinus node by its primary electrical negativity. He also traced its excitatory pathway throughout the atria and ventricles, thereby providing a confirmatory correlation of this complex electrical system and the answer to the question, Why does the heart beat?26

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None.
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