Walter Holbrook Gaskell was a nineteenth-century British physiologist whose investigations from 1874 to 1889 became central to our current understanding of cardiac physiology. His many cardiac contributions include the following: 1) the recognition of certain inherent properties of cardiac muscle; 2) the experimental proof that led to the acceptance of the myogenic theory of the origin of the heartbeat; 3) the mapping of the anatomy of the sympathetic nervous system; 4) the understanding of the dual autonomic control of the heart; 5) the discovery of the vasodilating effect of sympathetic stimulation on blood flow through skeletal muscle arteries; and 6) the introduction of the concept of heart block. Gaskell's elucidation of the sequence of cardiac contraction and atrioventricular block and his concepts of rhythmicity, excitability, contractility, conductivity and tonicity provided the physiologic explanation necessary for the future understanding of cardiac rhythm disturbances. (J Am Coll Cardiol 2002;39:1574–80) © 2002 by the American College of Cardiology Foundation

“The law of progress is this:—The race is not to the swift, nor to the strong, but to the wise—the secret of evolutionary success is the development of a superior brain.”

—W. H. Gaskell (1,2)

Walter Holbrook Gaskell (Fig. 1) was a nineteenth-century British physiologist whose investigations from 1874 to 1889 dispelled certain entrenched views and became central to our current understanding of cardiac physiology. His many cardiac contributions include the following: 1) the recognition of certain inherent properties of cardiac muscle, which he termed “rhythmicity, excitability, contractility, conductivity and tonicity”; 2) the experimental proof that led to the acceptance of the myogenic theory, as opposed to the neurogenic theory of the origin of the heartbeat; 3) the mapping of the anatomy of the sympathetic nervous system; 4) the understanding of the dual autonomic control of the heart; 5) the discovery of the vasodilating effect of sympathetic stimulation on blood flow through skeletal muscle arteries; and 6) the introduction of the concept of heart block (2–6).

EARLY LIFE AND CAREER

Gaskell was born November 1, 1847, in Naples, Italy, where his family was spending the winter for the sake of his father’s health (5). His father was a barrister, and his family lived in northern England with substantial inherited wealth. After early education at Highgate School in London, he entered Trinity College, Cambridge University in 1865, majoring in mathematics and graduating with academic honors in 1869. There he was greatly influenced by Michael Foster, an inspiring physiologist whose talent for recruiting and mentoring young physiologists served to develop the internationally respected Cambridge School of Physiology (7). The following year, Gaskell began undergraduate medical studies at University College Hospital, London. After completing his medical studies in 1874, he decided on a career in physiology. Foster advised him to work for a year under Carl Ludwig, the great German physiologist, whose introduction of the kymographic recording method was integral to the investigation of the heart. In Ludwig’s well-equipped laboratory in Leipzig, Gaskell studied the vasomotor control of the blood flow in the skeletal muscle arteries, demonstrating that sensory nervous stimulation could cause arterial dilation (2,7). His continuing interest in the nature of the sympathetic control of cardiac and arterial function led to his definitive work on the anatomy and function of the efferent sympathetic nerves, published in 1885, which served as the foundation for all future investigations in this area. His studies also proved the antagonistic cardiac effects of the autonomic nervous system, especially the cardioinhibitory role of the vagus nerve and its control of the heartbeat (2,3).

Gaskell returned to Cambridge in 1875 and obtained his medical degree in 1878, though he never practiced medicine. He joined Foster’s research team (Fig. 2) and in 1883 became a university lecturer in physiology, a position he held until his death. Gaskell received many honors during his career, including the Croonian Lecturer of the Royal Society in 1881, Fellowship in the Royal Society in 1882 and its Royal medallist in 1889, the Baly medallist of the Royal College of Physicians in 1895 and honorary doctorate degrees from Edinburgh and McGill Universities. For his work on the autonomic nervous system, he was awarded the
INVESTIGATIONS ON RHYTHMICITY,
THE ORIGIN OF THE HEARTBEAT
AND THE SEQUENCE OF CONDUCTION

The subject of the exact site of origin of the heartbeat dominated late nineteenth-century cardiac physiology (7). William Harvey first noted in his De generatione animalium, published in 1651, that “the pulse has its origin in the blood...the cardiac auricle from which the pulsation starts, is excited by the blood” (8). In 1839, German physiologist Robert Remak, a pupil of Johannes Müller, discovered the presence of groups of ganglion cells in the sinus venosus of the frog, comparable to similar ganglia in the respiratory center that were thought to regulate the muscles of respiration automatically (9). Müller suggested that these sinus venosus cells initiated and perpetuated the heartbeat in response to sympathetic stimulation (10). This location was further supported by the 1852 studies of Hermann F. Stannius, who tied a ligature around the sinoatrial junction of a frog’s heart, causing standstill of the atria and ventricle while the sinus portion still contracted (11). In 1872, Luigi Luciani also found evidence that the rhythmic activity of the frog heart was most highly developed in the vena cava and sinus venosus.

At the Cambridge Physiological Laboratory between 1879 and 1883, Gaskell investigated the nature of the heartbeat and the sequence of contraction by employing a new method of suspension for his studies on the excised frog and tortoise hearts (9,12,13). In this method, the contractions of the atrium and ventricle were registered simultaneously by two levers attached by silk threads, one to the right atrium and the other to the apex of the ventricle. The heart was suspended and held firmly by a screw-clamp in the sinoatrial groove or atrioventricular (AV) groove. He altered the “excitability” of the tissue by heat transferred from a galvanic current passed through a wire coil. In the early 1880s, using his isolated, slowly beating tortoise heart preparation, which facilitated visual observation, Gaskell noted that conduction of the impulse traveled in an orderly fashion as a muscular peristaltic wave beginning in the sinus venosus, moving next to the “sinus-auricle” (the atrium near the sinus venosus), then to the “ventricle-auricle” (the atrium near the AV groove) and from there to the ventricle. Gaskell concluded that heart muscle itself possessed rhythmicity independent of the ganglia and that different areas were more “rhythmic” than others (9). He also observed that the dominant generator of the heartbeat—that tissue possessing the highest cardiac rhythmicity—was located in the sinus venosus and suggested that it provided a discrete cyclic stimulus, a major departure from the prevalent view that the motor impulse was continuous and the cardiac muscle able to respond only intermittently. Gaskell wrote: “We come, then, to the conclusion 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” (9).
From his studies, he evolved the following laws of the development of cardiac rhythm (9,13):

1. “The power of independent rhythmical contraction decreases regularly as we pass from the sinus to the ventricle; ...”
2. “The rhythmical power of each segment of the heart varies inversely as its distance from the sinus; ...”
3. “The rhythmicity of the cardiac muscle varies inversely as its conductivity.”

In 1907, Arthur Keith and Martin Flack were the first to discover the anatomic location of the sinoatrial node. Using the electrocardiographic technique introduced by Willem Einthoven in 1903, Thomas Lewis was able to show, in 1910, that the spread of excitation advanced throughout the heart. He verified that the sinus node of Keith and Flack was indeed responsible for the origin of the electrical impulse, and that the electrical wave spread through defined conducting pathways (14).

**EXPERIMENTALLY INDUCED RETROGRADE CARDIAC CONDUCTION**

Gaskell was able to produce retrograde cardiac conduction; he was, perhaps, the first to do so. In his observations on the heart of a large skate, he noted that the heartbeat vigorously and “with great regularity, in the order auricle, ventricle, conus” (arteriosus) (13). He was able to reverse the normal anterograde direction of cardiac conduction by touching the muscular conus arteriosus, equivalent to the ascending aorta, with the sharp point of a knife. Immediately, “the rate of the contractions started from the conus end was somewhat quicker than the normal rate from the sinus end...[and] a contraction wave is...started in it which when it reaches the ventricle, causes a contraction of the ventricle, and in due sequence of the auricle” (13). By gently stimulating the sinus venosus, the normal order of anterograde cardiac conduction was restored.

He stimulated the right vagus nerve in the tortoise with an electric current. This slowed the sinus rhythm, permitting the appearance of a ventricular rhythm, slower than the sinus rate and previously “entirely concealed until the sinus rhythm was...[slowed] by the action of the vagus nerve.” Retrograde cardiac conduction followed with “a regularly beating heart, in which every contraction starts from the ventricle and passes through the auricle to the sinus” (13). He also slowed the sinus rate by the application of a cold salt solution to the sinus venosus, and at the same time he sent a warm blood solution through the coronary arteries to develop and to speed up the ventricular rhythm, previously suppressed and concealed by the dominant sinus rhythm. The results were similar to those outlined above after right vagus nerve stimulation with the appearance of a dominant ventricular rhythm and retrograde cardiac conduction. “Thus the automatic sinus rhythm can be obscured by a quicker ventricular rhythm just as the automatic ventricular rhythm can be obscured by a quicker sinus rhythm” (13).

**THE MYOGENIC VERSUS THE NEUROGENIC THEORY OF THE SPONTANEOUS HEARTBEAT**

In the wake of Galen’s second-century observation that the excised heart will continue to beat, physiologists hotly debated whether the mechanism that induced the heartbeat was myogenic or neurogenic in origin. The myogenic theory, traced to William Harvey in 1628 and Albrecht von Haller in 1757, held that the heart muscle itself—perhaps stimulated by the blood—generated the impulse to contract. The neurogenic theory, proposed by Giovanni Borelli in 1680, stated that nervous influences, derived either from extracardiac nervous connections or from local ganglionic cells within the heart muscle, sent a continuous stream of impulses along nerve fibers to stimulate the heart muscle—first to the atrium, then, after a delay passing through ganglia at the AV junction, to the ventricle. Contraction was intermittent owing to the nature of the atrial and ventricular muscle (3,8,9). The neurogenic theory was more widely believed until Gaskell’s logical experiments tilted the argument in favor of the myogenic theory.

In order to show that all parts of the muscular heart tissue possessed the automatic power of rhythmical contraction, Gaskell turned to the tortoise heart, from which he cut a strip of ventricular muscle that was clearly isolated from nerve structures and devoid of ganglionic cells. He noted rhythmic pulsations of the strip at a rate similar to that of the normal intact heart and found that it could continue to beat rhythmically for as long as 100 h. Based on his studies and the experiments of Stannius, Gaskell concluded that “the beat of the heart of cold-blooded vertebrates depends upon the rhythmical power of the muscular tissue of the large veins and sinus being greater than the rhythmical power of the other parts of the heart, and that in all cases the greater or less rhythmicity of any part of the heart depends upon the nature of the muscular fibre of which that part is composed, and not upon the presence or absence of ganglion cells” (9,13).

Although the myogenic versus neurogenic debate was not immediately resolved in favor of a myogenic origin of the heartbeat, and would be much better understood only when the anatomy and function of the sinoatrial and AV nodes and the cardiac conduction system were eventually discovered, Gaskell’s work, published fully in 1883, was persuasive and considered a watershed of cardiovascular physiology (7,8,12,13).

**INVESTIGATIONS ON AV BLOCK**

In 1882 and 1883, experimenting with the tortoise heart, Gaskell repeated the provocative 1852 frog heart study of Stannius (9,11). Like Stannius, Gaskell placed his “first ligature” between the sinus venosus and right atrium, resulting in standstill of the atrium and ventricle but still
allowing the sinus venosus to continue its regular beat. After a variable time, the atrium and ventricle began to beat again, at first slowly, and then gradually increasing in rate, still not reaching the rate of the sinus venosus rhythm. This suggests that the ligature initially caused complete sinoatrial block and atrial and ventricular standstill, followed by the gradual acceleration of an independent, ectopic atrial escape rhythm. A similar phenomenon occurred when a ligature or cut was placed anywhere on the atria, the difference being that the cardiac standstill was longer and the rate of the escape rhythm was slower when the ligature or cut was made closer to the ventricle. If another ligature—the “second Stannius ligature”—was then placed in the AV groove during the atrial and ventricular standstill, the ventricle began to beat rapidly initially, while the sinus venosus maintained its regular beat and the atrial standstill continued. The ventricular rate slowed progressively to a standstill; after a variable time, the ventricle began to beat again slowly, gradually increasing to a steady rate, but at no time was quicker than the rhythm of the sinus venosus. The “second Stannius ligature,” or cut, apparently caused junctional or ventricular tachycardia followed by ventricular standstill. Later, we infer, a gradual acceleration of an independent, ectopic junctional or ventricular escape rhythm occurred. Because the atria were in standstill, we cannot state the degree of AV block, but in another experiment Stannius demonstrated significant AV block: “If you put the ligature on a healthy frog exactly at the AV groove of the heart, both the atria and ventricle remain in rhythmical contractions. The contractions of both are not at the same time nor the same rate; most of the time there are two to three contractions of the sinus venosus and atria to one contraction of the ventricle” (11). This description suggests to us the presence of complete AV block or advanced second-degree AV block.

Before the understanding of the cardiac conduction system was known, Gaskell attributed the slowing of the impulse propagation at the junctions between the sinus venosus and the atrial and ventricular chambers to the presence of undifferentiated embryonic muscle tissue, which he believed had greater rhythmicity but slower conductivity. He later commented: “...in the intact heart... depression of conductivity takes place at the two natural blocking points, namely, the sino-auricular and auriculo-ventricular junctions” (9). He noted a distinct delay of the contraction wave as it passed over the AV groove. He termed this a “natural pause,” a finding now recognized as the normal AV conduction delay seen on the electrocardiogram as the PR interval. He was able to create a greater delay of the contraction wave by removing a portion of the atrial muscle (Fig. 3). He termed this phenomenon “a commencing block, i.e., a simple delay in the rate of the passage of each contraction wave” (13). After cutting away more and more atrial tissue, greater degrees of AV block occurred (Fig. 4). He explained: “...if the block is more severe, then, instead of every contraction passing the blocking point, only every second contraction is able to pass, and therefore a contraction of the ventricle follows upon only every second auricular contraction. With a still more severe block it is possible to see only every third or every fourth contraction able to pass, and therefore to see the ventricle beating to every third or fourth contraction of the auricle” (9). He called this rhythmic phenomenon “partial block.” He continued: “Finally, if the cut is more severe still, then the block becomes absolute, and no contractions are able to pass; consequently...the ventricle[s] remain absolutely still until they commence to beat with their own independent rhythm” (9). He termed this phenomenon “complete block.” Gaskell credited his fellow worker in the Cambridge Physiological Laboratory, George J. Romanes, as the first to use the term “block.” Romanes was studying the movement of the Medusae, or jellyfish, and noted that the muscular swimming movements of its bell propelled the jellyfish through the water. By cutting the muscular rim of the swimming bell, he was able to “block” its motion and thus the movement of the jellyfish. Romanes used the term “block” throughout his study to “express any artificial hindrance to the passage of contraction” (7,8). Gaskell appropriated the same term in describing a portion of his experiments on the heart muscle of the tortoise, and he was the first to differentiate between the types of heart block.

OTHER EARLY CONTRIBUTIONS TO AV BLOCK

In 1873, Luigi Luciani, an Italian physiologist working in Ludwig’s laboratory, tied a ligature above the AV groove in a frog heart, causing cardiac pauses and a “periodic rhythm” (15). Although Luciani did not fully comprehend the nature of the pauses, he concluded that “the resistances...determine the periodic rhythm.” Alfred Galabin first demonstrated AV block in a human in 1873 by recording of the apex impulse in a patient with a slow heart rate (16). In 1899, Karel Wenckebach in Utrecht was the first to describe group beating in a human, a phenomenon which he termed “Luciani periods.” Wenckebach, with the help of frog experiments by Theodor Engelmann, also unraveled the complex AV relationship that has subsequently become known as “Wenckebach periodicity” and “type I AV block” (17). The anatomic basis for AV conduction disturbances was established by Wilhelm His, Jr., who found a muscle bundle connecting the atrium and the ventricle in 1893, and by Sunao Tawara, who traced the His communication backwards and discovered the AV node in 1906 (18,19).

LATER LIFE

Gaskell was a large, unassuming man of genial disposition who was beloved by many and appreciated by younger physiologists for his encouragement and advice. Ideas were said to pour out of him. His lecturing style was incisive, and he spoke with an infectious enthusiasm (4,6).

In 1875 he married Catherine Sharpe Parker. They had four daughters and a son, named John Foster Gaskell, in honor of Michael Foster. The family settled near Cam-
bridge where he remained for the rest of his life, residing first at Grantchester and later at Great Shelford, where he built a hilltop home—The Uplands—opposite the hill on which stood Michael Foster’s home.

During his youth, he engaged in rowing, cricket, tennis and swimming. Later he enjoyed yachting, fishing, whist and bridge. Throughout life, he always took a somewhat leisurely course during both work and play activities. His

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Figure 3. Appearance and measurements of the tortoise heart when excised and suspended, February 27, 1882 (13). (I) Measurements before Gaskell began the experiment. (II) Measurements after experimental cutting of the right atrium by Gaskell, dividing it into two parts, As and Av. We measured pulse rates, cardiac intervals, atrial and ventricular pulse wave durations and ventricular pulse wave amplitudes from the atrial and ventricular tracings of Figure 4 before and after the experiment. After cutting deeply into the right atrium, 2:1 AV block develops between As and Av. The As pulse rate remains 7.5 beats/min, but the Av and V pulse rates fall to 3.75 beats/min. The V pulse wave amplitude and duration increase with the ventricular bradycardia due to the increased ventricular stroke volume. The As-Av interval increases 0.7 s after the atrial cut, whereas the Av-V interval increases 1.0 s and alternate Av and V pulse waves are blocked. The beginning of the As pulse wave is obscured by the V pulse wave; it is assumed that the As pulse wave duration is the same as the measured Av pulse wave duration. A = right atrium; As = pulse wave of the atrium near the sinus venosus; Av = pulse wave of the atrium near the AV groove; As-Av interval = time from the onset of the As pulse wave to the onset of the Av pulse wave; Av-V interval = time from the onset of the Av pulse wave to the onset of the V pulse wave. B = upper part of the tortoise body; F = forceps attached to the aorta; L = two silk ligatures with hooks at one end (one ligature is tied to the right atrium and the other is tied to the apex of the ventricle; the two hooks are attached to levers of the kymograph); S = sinus venosus; V = ventricle. The figure has been lightly retouched for clarity.
main hobby was gardening, and he converted a large area of his 15 acres of sloping hillside at Great Shelford into a charming terraced garden. From 1889 until his death, he pursued the evolutionary origin of vertebrates, unsuccessfully trying to prove that vertebrates originated from invertebrates. This argument, which was not well received, was published in his 1908 book “The Origin of Vertebrates” (1,5). His final years were also saddened by his wife’s debilitating nervous illness, but he continued his work until the very end. Gaskell suffered a cerebral hemorrhage September 4, 1914, and died at Great Shelford three days later at the age of 66. A final tribute to him stated: “It is safe to say that to no physiologist does medicine owe a debt greater than that which it owes to Walter Holbrook Gaskell, for, in the course of his work on the sympathetic nervous system, he laid for all time the foundations of the pathology of the heart” (4).

CONCLUSIONS

In his 1909 introduction to the inaugural issue of Heart, the first English language journal devoted to the study of heart disease, Gaskell wrote, “The experimental sciences of Phys-
iology, Pathology, and Pharmacology are more and more directly influencing the study and practice of medicine...slowly but surely the results of experiments gained in the laboratories are being applied to man. Medical study is losing its empiric character, and is founding itself on the well ascertained facts of Physiology and its cognate sciences, Pathology and Pharmacology” (20).

Gaskell’s comments were prescient. His own elucidation of the sequence of cardiac contraction and the experimental production of AV block, along with his concepts of rhythmicity, excitability and conductivity, would provide the physiologic explanation necessary for the future understanding of cardiac rhythm disturbances. James Mackenzie and Karel Wenckebach, utilizing jugular and arterial pulse studies on patients at the end of the nineteenth century, and Thomas Lewis, who would apply Einthoven’s electrocardiogram beginning in 1909, soon followed in Gaskell’s physiologic path to introduce the clinical analysis of cardiac arrhythmias that we continue to use today (2, 21).

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