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Profiles in Cardiology

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Ernest Henry Starling

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English physiologist Ernest Henry Starling (1866–1927) (Fig. 1) made many important contributions to medical science, but he is remembered mainly for his *Law of the Heart*, published in 1918.[1–3] Starling's classic formulation of this fundamental physiologic concept was an extension of earlier research by European physiologists Carl Ludwig and Otto Franck and American physiologists Henry Newell Martin and William Howell.[4] Born in London in 1866, Starling entered Guy's Hospital Medical School in 1882. At Guy's he was mentored by physiologist Leonard Wooldridge, who had worked in Ludwig's world-renowned Physiological Institute in Leipzig. In 1887, Starling was appointed demonstrator in physiology at his alma mater.

Starling's earliest research focused on what he and his longtime collaborator William Bayliss of University College, London, termed "the electromotive phenomena of the mammalian heart.[5,6] In 1891, Starling and Bayliss reported the first successful recording of the electrical activity of a mammalian heart. They used a capillary electrometer, the only technique to record the heart's electrical impulses until 1902, when Willem Einthoven invented a string galvanometer to record the electrocardiogram. Starling and Bayliss also showed that contraction of the mammalian heart began at the base and proceeded to the apex. In addition to these important observations relating to electromechanical aspects of cardiac function, they developed a technique for measuring intra-aortic and intraventricular pressures more accurately.[7]

When Starling summarized his conceptualization of the mechanisms by which the heart adapted to various physiologic and pathologic stresses in an 1897 lecture, "On the Compensatory Mechanisms of the Heart," he and Bayliss had begun to study the physiology of lymphatic absorption and secretion. Early in the twentieth century their research focused on pancreatic function. In 1902, as a result of these studies, Starling discovered a substance he named "secretin." This discovery was a catalyst for the development of endocrinology.[8] Starling proposed the term "hormone" in 1905 in his Croonian Lecture, "On the Chemical Correlation of the Functions of the Body."[9] A productive researcher, Starling was also a prolific author. In 1912, he published his classic textbook of physiology, a 1423 page book that weighed almost 5 pounds. Starling explained in his preface,

> Throughout the work I have sought to show that the only foundation for rational therapeutics is the proper understanding of the working of the healthy body. . . Ignorance of physiology tends to make a medical man as credulous as his patients and almost as easily beguiled by the specious as the advertising druggist.[10]

After his textbook was published, Starling refocused his research effort on cardiovascular physiology. In 1915, he delivered the prestigious Linacre Lecture at Cambridge University. These lectures were published as separate pamphlets, and Starlings "Linacre Lecture on the Law of the Heart" appeared in 1918.[11,12] Two years later, he explained,

> The heart, freed from all its nervous connexions, has the power of automatically adjusting the force and extent of its contractions to the task which is set it by the two factors determining its work, *viz*: the inflow into the heart from the veins, and the resistance offered to the outflow by the arterial pressure.[13a]

Starling modified the isolated mammalian heart preparation developed by H. Newell Martin of Johns Hopkins during the 1880s in order to vary the arterial resistance.[14] In a series of elegant experiments, Starling studied how changing the preload and afterload affected cardiac output. This research led him to conclude,

> The behaviour of the muscle tissue of the heart thus resembles that of muscular tissue generally, whether skele-

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FIG. 1 Ernest Henry Starling (1866–1927).

> tal or unstriated, in which the contractile stress set up by each contraction is a function of the length of the fibre. The greater the length of the fibre, and therefore the greater amount of surface of its longitudinal contractile elements at the moment when it begins to contract, the greater will be the energy in the form of contractile stress set up in its contraction, and the more extensive will be the chemical changes involved. This relation between the length of the heart fibre and its power of contraction I have called 'the law of the heart.'[13b]

During the rest of the twentieth century, many scientists and clinical investigators extended Starling's observations on cardiovascular physiology. For example, American physician and investigator Tinsley Harrison used Starling's observations to help explain the clinical syndrome of heart failure in the 1930s.[15] American physiologist Maurice Visscher, who worked in Starling's laboratory during 1925–1926, was the coauthor of Starling's last paper on cardiac physiology, published in 1927, the year the British physiologist died.[16] Visscher was an important member of the multidisciplinary team at the University of Minnesota that developed a heart-lung machine in the early 1950s. This work, and similar research at the Mayo Clinic, extended the pioneering experiments of Philadelphia surgeon John Gibbon, Jr., who developed a heart-lung machine that was based on isolated heart preparations that Martin, Starling, and others had invented to study circulatory physiology. In 1970, Jeremy Swan, William Ganz, and James Forrester of Los Angeles reported their technique of bedside hemodynamic monitoring that incorporated principles Starling had articulated decades earlier.[17] Many recent advances in pharmacological therapy for heart failure depend, in part, on discoveries made by and theories proposed by Starling and other researchers almost a century ago.

Starling could not have imagined the many practical diagnostic and therapeutic consequences of his contributions to cardiovascular physiology. Nevertheless, he believed that basic scientific research was a vital component of a complex equation that ultimately results in advances in patient care. In his Linacre lecture on the law of the heart Starling declared,

> For years the 'muscle-nerve physiologist' was reproached by the so-called practical man with spending his time and attention on things which can have little importance in medicine, for the maintenance of health or the cure of disease. And yet it is in the researches on a subject, considered even by some physiologists as wearisome or trivial, that we have found the clue to the behaviour of the heart under all manner of conditions, and the explanation of phenomena which have long been a puzzle to the student of the healthy or diseased organism…In physiology, as in all other sciences, no discovery is useless, no curiosity misplaced or too ambitious, and we may be certain that every advance achieved in the quest of pure knowledge will sooner or later play its part in the service of man.[11a]

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