Profiles in Cardiology

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Julius Friedrich Cohnheim

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Julius Friedrich Cohnheim (Fig. 1), a founder of experimental pathology, made many important contributions to cardiovascular physiology and pathology. His exhaustive monograph on pathology was the second most influential nineteenth century text on the subject (after Rudolf Virchow's classic 1858 book on cellular pathology). Cohnheim was born on July 20, 1839, in Demmin, a small town in the Prussian Province of Pomerania.^{1–3} After receiving his preliminary education in Demmin and the ancient city of Prenzlau, Cohnheim moved to Berlin in 1856 to study medicine. The following year he moved to Würzburg, where he studied histology with Rudolf Albert von Kölliker, a pioneer of microscopic anatomy. Cohnheim returned to Berlin in 1860 where, after receiving his medical degree, he started his dissertation under the supervision of Rudolf Virchow. Impressed by the young Prussian, Virchow appointed him his chief assistant in 1865.

During the 1860s, Cohnheim focused his research on the mechanism of inflammation, a subject of considerable debate at the time.⁴ Cohnheim performed a series of animal experiments in an attempt to gain a better understanding of the complex process of inflammation. He concluded that acute inflammation was the result of leukocytes that circulated to the site of injury and then migrated through capillary walls to form collections of blood cells that contributed to what had long been termed "pus." This theory challenged his mentor Virchow's interpretation of inflammation, but it was

an important contribution that set the stage for later work on the subject.

In 1868, at the age of 29, Cohnheim became professor of pathology at the University of Kiel. By then he had become especially interested in the circulation as well as in venous obstruction and arterial embolism. He also studied the role of collateral vessels in the context of arterial obstruction. The following year he worked for two months in Carl Ludwig's laboratory of experimental physiology at the University of Leipzig. Ludwig's laboratory was a factory of new knowledge where several scientists focused on cardiovascular physiology.⁵ During the last decades of the nineteenth century, the German universities led the world in research and many budding American medical scientists and academic physicians studied there. Some of these (for example, Henry Bowditch, John J. Abel, and Franklin P. Mall) returned home to introduce laboratory training and research into the nation's elite medical schools such as Harvard, the University of Michigan, and Johns Hopkins.^{6,7}

Cohnheim moved to Breslau in 1872 where he helped create a pathological institute at the university. That year he published a monograph *Untersuchungen über die embolischen Processe*,⁸ that summarized the important research on the circulatory system he had undertaken during the previous four years. This rare book includes Cohnheim's theory that infarction of various organs such as the heart and kidney occurred as a result of occlusion of terminal arteries. He also described his experiments that shed light on the pathophysiology of abscess formation. Cohnheim's classic two-volume work on general pathology, *Vorlesungen über allgemeine Pathologie*,⁹ was published between 1877 and 1880; this work was translated into English a decade later.¹⁰ About one-third of the text is devoted to the pathology of the cardiovascular system. By this time Cohnheim's reputation had grown to the point that he attracted students and ambitious young medical scientists from various countries, including William Welch and William Councilman from the United States.

Carl Weigert, who had also trained with Virchow, became Cohnheim's assistant in 1874. Reflecting Virchow's and

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FIG. 1 Julius Friedrich Cohnheim, July 20, 1839–August 15, 1884. From the collection of W. Bruce Fye, M.D., M.A.

Cohnheim's interest in thrombosis and embolism, Weigert focused his research on these problems. Cohnheim encouraged Weigert's studies, which culminated in 1880 with the publication of a classic paper on infarcts.¹¹ Weigert discussed the pathologic appearance of "infarcts" in several organs, including the heart. Based on several years of experiments, he claimed that passive tissue injury was the fundamental mechanism of cellular proliferation in inflammation. He applied his theory to the poorly understood histologic finding of "chronic myocarditis" and concluded that thrombotic or embolic occlusion of the coronary arteries often complicated atherosclerosis in them. If a vessel became occluded slowly and adequate collaterals existed, then the muscle it supplied would be gradually replaced by fibrous tissue. If, on the other hand, the occlusion occurred abruptly, large areas of scar appeared. This paper, based on research that Weigert performed in Cohnheim's pathologic institute, is justly viewed as a milestone in the description of the pathologic aspects of myocardial infarction.¹²

Cohnheim's chapters on the heart reflect his sophisticated understanding of cardiac pathology and physiology. For example, we are now focusing more attention on abnormal diastolic function as a factor in several clinical settings, especially heart failure. Cohnheim characterized diastole as an active process in which the heart acted as a "suction-pump." He described the heart's function in systole as a "force-pump." His text is filled with descriptions of animal experiments that he or his associates and pupils performed to investigate and explain various aspects of cardiovascular physiology or pathology. The subjects that he discussed in detail include the pathophysiology of pericardial effusion, the relationship of coronary embolism and severe coronary atherosclerosis to

sudden death and left ventricular dysfunction (as a result of myocardial necrosis), the causes and consequences of ventricular hypertrophy, the pathophysiology of thrombosis and embolism, and arteriosclerosis. Cohnheim's comprehensive and influential monograph on pathology addressed many other subjects in addition to the cardiovascular system.

Cohnheim described the physiology of cardiac contraction in terms of concepts that we usually attribute to Otto Franck (1895) and Ernest Starling (1918). Indeed, Starling's work was influenced by various publications of the Scottish physiologist Charles Roy, who had studied with Cohnheim and worked in his laboratory.¹³ Cohnheim explained,

The work done by the heart . . . is determined by the quantity of blood reaching the ventricle during diastole, and the amount of resistance to be overcome by the heart in propelling it into the arteries; and because both factors are normally liable to constant variations, the amount of work done by each contraction is also probably a constantly varying quantity.¹⁰

Cohnheim was especially interested in the pathophysiology of valvular heart disease and performed a series of experiments to help elucidate the mechanism of left ventricular hypertrophy or dysfunction in cases of aortic stenosis or insufficiency. He recognized that various other pathologic and physiologic abnormalities could cause ventricular hypertrophy. Cohnheim explained that left or right ventricular hypertrophy might result from "diseases of the vascular system, whether of the greater or lesser circulation, that give rise to increase of resistance."¹⁰ He discussed peripheral resistance in great detail.

In 1877, William Welch, a recent American medical graduate studying in Europe, wrote to his father from Breslau and described his impressions of Cohnheim. Welch, who would become the first pathologist at Johns Hopkins and a leader in medical education, was struck by Cohnheim's intense desire to elucidate the mechanisms of the various signs and symptoms of disease:

Cohnheim's interest centers on the explanation of the fact. It is not enough for him to know that congestion of the kidney follows heart disease or that hypertrophy of the heart follows contraction of the kidney, or that atheroma occurs in old age, he is constantly inquiring why does it occur under these circumstances. He is almost the founder and certainly the chief representative of the so-called experimental or physiological school of pathology. . .¹⁴

Cohnheim moved to Leipzig in 1878 to accept the chair of pathology at the university. But he would live only 6 more years. Beginning in the early 1870s, Cohnheim began to have recurrent attacks of gout. He died suddenly in Wiesbaden on August 15, 1884. During his brief life, Cohnheim had a tremendous influence on pathology and experimental medicine. Long after his death his influence resonated through his

writings and the contributions of his pupils, who established laboratories of experimental pathology modeled after those Cohnheim had developed in Germany.

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