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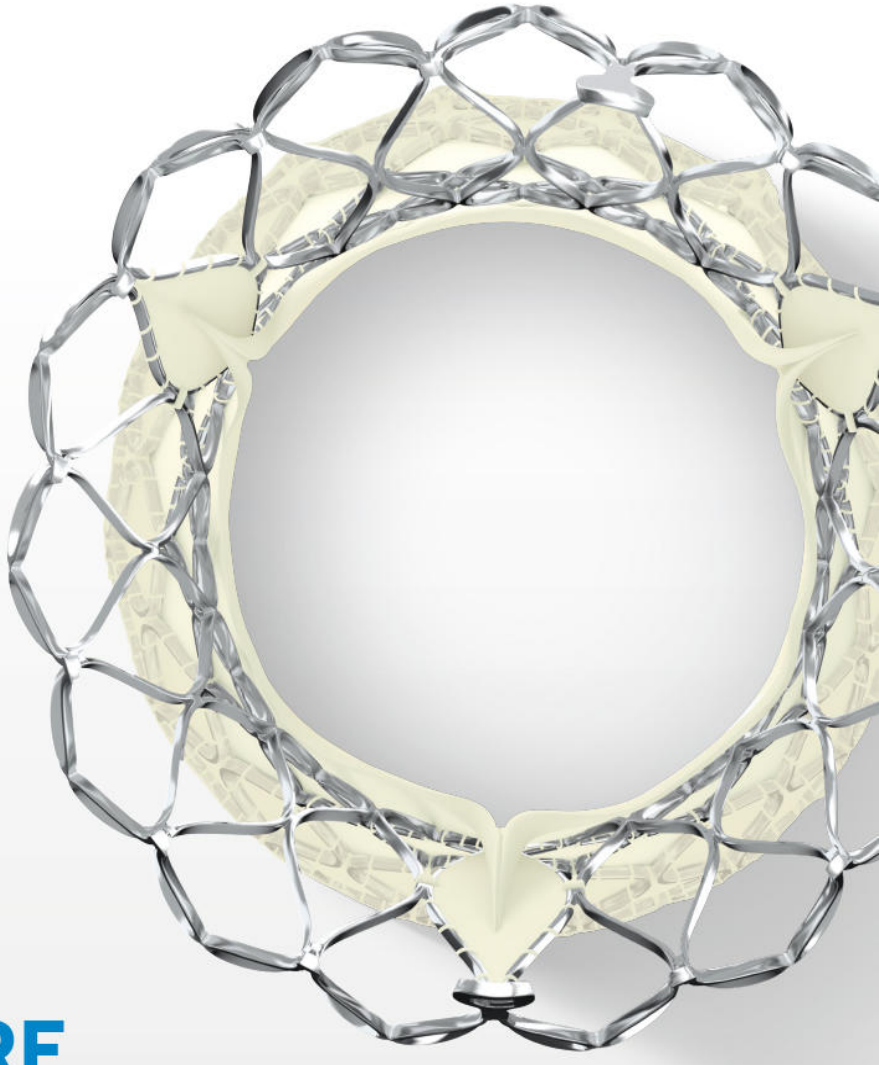

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George Ralph Mines: Victim of Self-Experimentation?

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A life unfulfilled is lamentable; a life unfulfilled of its potentiality is a tragedy. Such was the life of George Ralph Mines (Fig. 1), an enigma in the annals of cardiology. Struck down at the age of 29, Mines left this earth with the key to important electrophysiologic data, but with the door unopened for further exploration. His life, though short, could best be described as an explosively vibrant one characterized by brilliant intellectual achievements and human enjoyment. Why, then, should he have died so young without evidence of a lethal disease?

George Ralph Mines was born in Bath, England, on May 13, 1886. His parents were H. P. Mines and Alice G. Ward. He began his early formal education at Bath College and the Grammar School in Kings Lynn. He matriculated at Sydney Sussex College, Cambridge University, when he was 19 years old and graduated from there in 1908. The years from 1908 to 1909 were important in George Mines's life. During this time period, he received a scholarship at the Allen University, a fellowship at Sidney Sussex, and he married Marjorie Rolfe of Newnham College, an aspiring poet.[1] For the next few years, Mines taught at Needham College and conducted research in the physiological laboratory at Cambridge. His rise in academic circles was rapid and astounding for one so young. At the age of 24, he was elected to the Physiological Society. A year later, he was awarded the Gedge Prize and soon thereafter became Assistant Demonstrator in the physiological laboratory at Cambridge. During his brief tenure at Cambridge, Mines was very productive.[1] He seemed to have boundless energy. With the assistance of a second-year student at Needham named Dorothy Dale, a number of manuscripts were published in the *Journal of Physiology*. The focus of these experiments centered on the various effects of nerve stimulation on the in vitro frog heart and the influence of electrolytic solutions on in vitro frog cardiac muscle function.[2,3]

Mines's life as a researcher from 1912 to 1914 can only be described as peripatetic and frenzied. His work took him from Plymouth to Naples and then, in 1913, to Roscoff, France, where his continued research at the Biological Station led him to the concept of the vulnerable period of the ventricle, the period where the cardiac muscle he was studying was prone to fibrillate during electrical diastole. This work would remain unpublished until after his death in 1914. His travels also took him to various university laboratories, including that of Brodie at Toronto and McGill in Montreal. At the University of Toronto, Mines was appointed assistant to Professor Brodie, a position he held for only a few months. During this time, an academic search for the position of Professor of Physiology at McGill University was underway, and he was recruited to lecture to the McGill faculty. His depth of knowledge in the area of physiology coupled with his research productivity so impressed them that he was offered the position of Professor and Chair of the Department of Physiology. It was now 1914. Unfortunately, he was to die within months of his appointment.[1]

In the laboratory, Mines proved himself a master of ingenuity and mechanical expertise as exemplified by his construction of the various types of apparatus used in his research protocols. He was truly in his element in the physiology laboratory, much as a conductor is at home in front of a symphonic orchestra. Incidentally, he also had a great interest in the piano: so much so, that before turning to physiology, he seriously considered a career in music. This gift for music was transmitted to his daughter Anatole who became a professional viola player.[1]

Mines's investigations into cardiac muscle physiology led to two seminal contributions in electrophysiology. The first of these contributions was his work in the area of reentrant rhythms in cardiac muscle. In his paper, "On Dynamic Equilibrium in the Heart," Mines, utilizing frog, tortoise, and electric ray muscle, described a phenomenon that he aptly named "reciprocating rhythm."[4] He attributed this rhythm to a circulating excitation of conduction tissues in the cardiac muscle of his experimental models, which he determined to be unidirectional in nature; one path conducting in an antegrade direction (atrium to ventricle), the other conducting in a retrograde di-

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FIG. 1 George Ralph Mines (1886–1914). (*Source*: Physiological Laboratory, Downing Street, Cambridge, U.K. Used with permission.)

rection (ventricle to atrium). In addition, Mines noted that this reciprocating rhythm could either be terminated or triggered by an extrasystolic beat and that this might be a possible cause of some of the clinical paroxysmal tachycardias. In this experiment, Mines noted that the motion of the tissues caused by this reciprocating rhythm resembled that of fibrillating mammalian hearts, and that this mechanism might serve as the explanation for this lethal dysrhythmia.[4]

His other major contribution to electrophysiology was his work that eventually led to the posthumous publication in 1914 of a paper entitled "On Circulating Excitations in Heart Muscles and Their Possible Relation to Tachycardia and Fibrillation." In this study, Mines modified the usual method of inducing ventricular fibrillation in animal hearts that utilized repeated shocks from an induction coil. His method involved the application of single shocks timed to occur at specific periods during the cardiac cycle. The rabbit served as the mammalian heart model. Mines developed an apparatus that allowed for the administration of the electrical impulse to the rabbit heart via a Morse key. He found that in a number of experiments, only a single activation of the Morse key was required to trigger fibrillation depending on the timing of the impulse delivery, and that this timing appeared to be crucial in determining whether fibrillation would occur. He further determined that this point in time, when fibrillation occurred, was immediately after the refractory period. This was the first time this zone of vulnerability to fibrillation had been identified.[5] In 1923, DeBoer described the reentry phenomenon and also demonstrated how an electrical shock applied to the heart of the frog could result in ventricular fibrillation if applied late in systole.[6,9] Louis Katz reported in 1928 that premature ventricular contractions could produce life-threatening dysrhythmias if they occurred on the T wave.[7,9] It was not until 1940 that Wiggers and Wegria reported their findings in the *American Journal of Physiology* in a paper entitled "Ventricular Fibrillation Due to Single Localized Induction and Condenser Shocks Applied during the Vulnerable Phase of Ventricular Systole."[8,9] This was the first time the term "vulnerable phase" had been used in the literature, 26 years after Mines's posthumous paper.

Mines's death occurred under a shroud of mystery and speculation. He was discovered in an unconscious state in his laboratory at McGill University on November 7, 1914, still attached to his physiologic monitoring equipment. He was transported to the Royal Victoria Hospital for further management. After a transient period of consciousness late that night, he suddenly died before midnight. A complete postmortem examination led to no conclusive diagnosis of the cause of death. In fact, the autopsy failed to reveal any evidence of structural alteration of his vital organs. It has been speculated that Mines may have been a victim of self-experimentation. In retrospect, this speculation was fueled by Mines's own words in his October 6, 1914, Founder's Day address to the faculty of McGill University one month before his death. In his address, Mines spoke of two other researchers who had become well known for their self-experimentation. One was Head, who had severed his own arm nerves in his quest to understand the origin of skin sensations, and the other was Washburn, who reportedly swallowed a stomach tube in order to study the physiology of digestion in his work with his partner, Cannon. The inclusion of these two researchers' names in his address may have been a veiled reference to his own intense desire for knowledge obtainable through self-experimentation.[1]

In the light of the autopsy findings and the circumstances under which he was found in his laboratory, the possibility arose that a fatal ventricular dysrhythmia was the precipitating cause of his demise. Also, since the events leading to his death occurred in his laboratory, the further possibility arose that the dysrhythmia may have been self-induced. There is no definite proof of this, but despite all attempts to the contrary the nagging question still remains: Did George Ralph Mines die of a lethal ventricular dysrhythmia and could this have been self-induced?

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