Editorials

Reflections on the Founding Editor, Carl J. Wiggers

Eugene Braunwald

The opportunity provided me by Dr Marbán, on the occasion of the fiftieth anniversary of Circulation Research, to reflect on my early contacts with the journal, naturally brings to mind 1953, the year of its founding. It was an exciting time for cardiovascular research. The United States had largely recovered from the trauma of World War II, and an internal enemy, cardiovascular disease, had replaced the external enemies as the greatest threat to the nation. The National Heart (now the National Heart, Lung, and Blood) Institute had recently been established, and the American Heart Association had been reorganized to sharpen its focus on scientific activities. Substantial financial support for cardiovascular research and training was becoming available for the first time, and a variety of technologies that had been developed or perfected during the war were being applied to the study of the heart and circulation. The American Heart Association, which had published Circulation since 1950 (and before that, the American Heart Journal), foresaw the expansion of cardiovascular research and wisely established the first journal devoted entirely to this subject.

At the time, physiology was the unchallenged “queen” of the cardiovascular sciences, and Carl J. Wiggers, the unchallenged “king” of cardiovascular physiology. He was the obvious choice to be the founding editor of Circulation Research, and the Heart Association was fortunate that he was stepping down from the chairmanship of Physiology at the (then) Western Reserve University Medical School and could devote his considerable energies, intellect, and prestige to this activity. Circulation Research became established rapidly as a prestigious scientific journal, and soon branched out from cardiovascular physiology to embrace biochemistry, pharmacology, anatomy, biophysics, and other basic science disciplines related to the heart and circulation. Certainly, in the early 1950s, there was no shortage of high-quality journals of physiology, pharmacology, biochemistry, etc., which contained, scattered among their pages, studies that dealt with the heart and circulation. However, an interdisciplinary journal focused on a single organ or organ system was a new concept. For the first time, interdisciplinary communication was encouraged and thereby interdisciplinary collaboration was fostered, leading to the development of a new field—Cardiovascular Science. Soon, other areas followed the lead of Circulation Research and interdisciplinary journals in other fields, such as Neuroscience and Behavioral Science, emerged.

Carl J. Wiggers

Carl J. Wiggers’ research was well known and highly respected. He had instant name recognition and seemed a natural choice to start this new journal. I was in the first year of my first postdoctoral research fellowship, and it was thrilling for me to receive an acceptance letter for my very first paper from Dr Wiggers and to see it published in the second volume of Circulation Research. I was equally pleased when the major products of my subsequent fellowships were also published in the journal. My colleagues and I benefited enormously from the revisions that Wiggers demanded. He was a hands-on editor who personally reviewed every manuscript submitted to the journal and put his imprint on each study that was published.

Wiggers was a true hero and demi-God to my generation of aspiring cardiovascular investigators. I heard him lecture many times, but my two personal meetings with him are etched into my memory. In the first, in 1956, I presented to him the results of our experiments in Stanley Sarnoff’s laboratory at the NIH on the determinants of myocardial oxygen consumption. He asked searching questions and made excellent suggestions about the interpretation of the results. Although he was very interested in the work, he refused to consider it for Circulation Research, because of his absolute rule of not allowing more than three authors on a paper. (Ours had five, and to the relief of the research fellows, Sarnoff was unwilling to reduce the number; the series was published in the American Journal of Physiology.) In my second encounter, later in 1956, I found myself seated next to Wiggers on a flight from Washington to a congress in Havana; I described our experiments on the circulatory effects of quantified, controlled valvular regurgitation. Again, he asked tough but fair questions that helped me to prepare two papers, which he accepted.

From these personal contacts, I became interested in this great man and learned that he was born in Davenport, Iowa, in 1883 and received his medical degree from the University of Michigan in 1906. After serving as an instructor of Physiology in Michigan, he became an Assistant Professor at Cornell and trained in the laboratory of the great Professor Otto Frank (of Frank-Starling fame) in Munich. Frank had perfected optical manometers and capsules for the precise measurement of intracardiac pressures and volumes, instruments that were to serve Wiggers well throughout his
professional lifetime. He became chair of Physiology at Western Reserve in 1918, a position he held until 1953 when he became editor of *Circulation Research*.

Wiggers’ research encompassed every important aspect of cardiovascular physiology. He described in detail the electrical, mechanical, and acoustical events of the cardiac cycle. The “Wiggers Diagram” has been the centerpiece of all textbooks of physiology and cardiology for more than eight decades. This diagram is etched into the minds of generations of students, physicians, and scientists and has not required material amendment since 1920. He clarified virtually all aspects of normal and abnormal cardiovascular hemodynamics, contributed importantly to the elucidation of the mechanisms responsible for irreversible shock and for ventricular fibrillation, and described approaches to the prevention and treatment of these conditions. Wiggers created a “school” of cardiovascular physiologists; more than 100 of his trainees became leaders in the field—department chairs and institute and laboratory directors. Although he served briefly, and by his own admission unhappily, as Dean of his medical school, he was hailed as the “Dean of Cardiovascular Physiologists” when he received the Lasker Award in 1955, during his editorship of the journal.

**Wiggers and Starling**

As I and many others of my generation experienced, Wiggers was generous of his time as editor, and he was reputed to be a tough but very supportive mentor. However, he was also quite competitive, especially early in his career. Ernest H. Starling, Jodrell Professor of Physiology at University College, London, was the leading cardiovascular physiologist early in the twentieth century, ie, he was Wiggers’ predecessor at the “top of the pyramid” of cardiovascular scientists. During the second decade of the century, Starling and his collaborators perfected the canine heart-lung preparation, which allowed independent control of preload, afterload, frequency, temperature, and some aspects of the humoral environment while pressures and volumes were measured. Starling greatly expanded upon and extended to the mammalian heart observations made on the frog heart in the nineteenth century by the German physiologists Carl Ludwig and Otto Frank. In his famous Linacre Lecture, “The Law of the Heart,” delivered in 1915, Starling stated that “the energy of contraction, however measured, is a function of the length of the muscle fiber at the onset of contraction.”

The younger Wiggers (Starling was 17 years his senior) was basing his research career on the anesthetized, open chest but otherwise intact dog and was highly critical of Starling’s heart-lung preparation, which was then in vogue. In his Harvey Lecture, with its own hardly modest title, *The Present Status of Cardiodynamic Studies on Normal and Pathological Hearts*, delivered in 1920, Wiggers stated: “Are the experimental conditions in the heart-lung preparation better or more controllable [than in the intact circulation]? The very fact for which these experiments are lauded, viz., that each factor—venous inflow, arterial resistance and rate—may be controlled at will, makes them a source of trouble . . . I believe that in many instances it is possible to set the ‘normal’ conditions so that absolutely diverse propositions may be clearly demonstrated with equal facility.”

Thus, the future founding editor of *Circulation Research* delivered the opening shot of a controversy that has continued in the pages of the journal since its inception. I refer, of course, to the two differing approaches to cardiovascular research represented by the work of these two patriarchs of modern cardiovascular science—the reductionist versus the holistic. Although the dog heart-lung preparation and the open-chest anesthetized dog do not differ much on the surface, Starling’s approach was reductionist while Wiggers’ was holistic. In order to gain control of the conditions under which the heart contracts, Starling was forced to sacrifice the more physiological neural and humoral milieu of the intact circulation. In order to retain the latter, Wiggers was forced to sacrifice precise control of the conditions under which the heart contracted, ie, the preload and afterload.

As cardiovascular research has unfolded in the 50 years of *Circulation Research*, the pendulum between the reductionist and holistic approaches has swung back and forth. During the early years and undoubtedly influenced profoundly by Wiggers and his “school,” there was a great preponderance of papers on the intact circulation. Gradually, but progressively, these were superseded by work on strips of isolated cardiac muscle or vascular wall, then on cells isolated from these tissues, subcellular organelles, the proteins of which they are composed, and most recently the genes that encode these proteins. An enormously rich understanding of the components of the cardiovascular system has been derived from this reductionist approach.

Has Starling triumphed in his controversy with Wiggers? I don’t think so.

Contemporary cardiovascular scientists increasingly recognize that despite the enhanced appreciation of the myriad individual components that make up the circulation, a better understanding of the system in which these components operate is urgently needed. It has become quite clear that an organism’s function is not simply the sum of the functions of its individual genes and their products but also depends on the interactions between these products. There is increasing interest in how these interactions are integrated to modify the behavior of the cells, tissues, and organs that comprise the circulatory system. This is leading to a resurgence in research on the circulation as a system. The present (and tenth) editor of *Circulation Research*, Eduardo Marbín, has wisely noted this important trend and has encouraged it in a section of the journal on “Integrative Physiology.” We appear to be reaching a balance between the reductionist and holistic approaches to research on the circulation on the circulation, and the scientists utilizing each are growing more tolerant of each other. Both Carl Wiggers and Ernest Starling would be very pleased at the state of research on the circulation as *Circulation Research* enters its second half century.
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Circ Res. 2003;92:253-254
doi: 10.1161/01.RES.0000059302.68970.F0
Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2003 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/92/3/253

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