Origin and Early Years

Arnold M. Katz

Abstract—Circulation Research, first published in 1953, was created by the American Heart Association as “the authoritative new journal for investigators of the basic sciences as they apply to the heart and circulation.” This review of the early years of the journal highlights the contributions of the first four Editors: Carl J. Wiggers, Carl F. Schmidt, Eugene M. Landis, and Julius H. Comroe, Jr. The success of Circulation Research is seen not only in the high quality of the articles published in its pages but also in the remarkable improvements in prevention and treatment of cardiovascular disease that have occurred over the past half century. (Circ Res. 2001;88:1105-1111.)

Key Words: history ▪ Circulation Research ▪ basic cardiovascular research ▪ Carl J. Wiggers ▪ Carl F. Schmidt ▪ Eugene M. Landis ▪ Julius H. Comroe, Jr

In 2003, Circulation Research will celebrate its 50th anniversary. This brief history commemorates the events leading to the publication of this journal, which are fading into the mists of time, along with the contributions of the first editors. A story emerges that describes a world of science quite different from that of today; although the need to obtain funding and publish studies has changed little over the past half century, the scope, complexity, and especially the pace of research have increased dramatically. Over this period, basic cardiovascular research has also become more visible to the public and more accountable to the organizations that support the increasing costs of discovery. At the same time, interactions with industry have stimulated entrepreneurial ventures that were unimaginable 50 years ago, when Circulation Research began publication.

Origins

Circulation Research was created by the American Heart Association (AHA) shortly after its sister publication, Circulation, was first published in 1950. Circulation was the successor to the American Heart Journal, which since its founding in 1928 had been the official journal of the AHA; both were largely clinical in orientation, most basic research articles being published in physiology journals, such as the American Journal of Physiology. The origins of Circulation Research can be traced to 1944, when the AHA established a Scientific Council to coordinate its research and professional programs. Formal rules and regulations of this Council were first published in 1950 and accepted by the Board of Directors in 1952 after considerable debate regarding the relationship of the Scientific Council to other, more established components of the AHA. The latter included the Section on the Study of the Peripheral Circulation (which became the Council on Circulation), the Council on Rheumatic Fever and Congenital Heart Disease, and the Council for High Blood Pressure Research.

Impetus for a journal dedicated to publication of basic cardiovascular research came from the Executive Committee of the Scientific Council, which at its June 6, 1951 meeting, considered publishing Circulation in “several sections, eg, clinical, physiological, biochemical . . . .” The feasibility of launching a basic science supplement to Circulation was examined at the November 24, 1951 meeting of the Publications Committee, where a tentative title of Circulation – Basic Science Supplement was chosen. For fiscal reasons, bimonthly publication of the supplement was initially recommended because “pharmacological houses do not like to advertise in quarterly journals.” The Executive Committee accepted the recommendation of the Publications Committee and suggested an initial publication date of January 1953.

In April 1952, the basic science supplement to Circulation became Circulation – Research (the hyphen did not disappear from AHA minutes until 1953), and Carl J. Wiggers (Figure 1), then the leader of cardiovascular research in the United States, was selected to be the first editor. When Wiggers presented his plans for the new journal at the May 4, 1952 meeting of the Editorial Board of Circulation, the discussion centered on a likely deficit in publishing the new journal (which would have to be covered by the AHA), and the possibility of approaching the National Heart Institute with a view to their “subsidizing part of the cost.” This led to a formal proposal to the Board of Directors of the AHA, where “after lengthy discussion” at the June 5, 1952 meeting it was moved, seconded, and voted that the AHA subsidize the new journal for 2 years at the rate of $10,000 per year.

The goals of Circulation and Circulation Research are contrasted in a prepublication announcement by the AHA,
which states that Circulation was “specifically for the practicing physician with a definite interest in the heart and circulation [providing] the newest, most authoritative information on all clinical aspects of the cardiovascular field,” while Circulation Research was to be “the authoritative new journal for investigators of the basic sciences as they apply to the heart and circulation—anatomy, biology, biochemistry, morphology, pathology, physics, pharmacology and others.” The latter was intended to “integrate and disseminate new knowledge regarding fundamental problems, on the solution of which rests much of applied research and clinical practice of cardiology.” A briefer distinction between the two official journals of the AHA was stimulated by the Publication Committee, which directed the medical director of the AHA to write to the Editor of JAMA asking the latter to “publish an editorial on the appearance of the new journal.” The result was an announcement in JAMA that distinguished between Circulation and Circulation Research, noting that the former “concentrate[s] . . . on clinical problems and applied research, as distinguished from fundamental research in the cardiovascular field.”

In November 1952, before publication of the first issue, the number of manuscripts submitted to Circulation Research “exceeded expectations,” but in mid-1953 Wiggers commented on a “shortage of papers.” In early 1954, he stated that “an insufficient number of articles [was] received” for him to recommend that the journal be published monthly. Happily, the Executive Committee of the Scientific Council continued its support for Circulation Research and voted in December 1953 to increase the size of what had remained a bimonthly journal. A decrease in the number of subscriptions, from 2431 in 1953 (the initial target had been 2400) to 1830 in 1954, led the publisher to observe that “[m]any subscribers complain that the journal is too technical” and that pharmaceutical manufacturers are not particularly interested in publishing in Circulation Research. In spite of these concerns, the AHA continued its support, voting that this journal should continue publication, even at a loss.

The Formative Years: Carl J. Wiggers

Carl Wiggers, the first in a series of distinguished editors (Table I), was born in Davenport, Iowa in 1883 and received his medical degree from the University of Michigan in 1906.3,4 He was a first-rate clinician5 who served as Head of Physiology at Western Reserve University from 1918 to 1953. His research, which touched on most of the important discoveries in cardiovascular physiology during the first half of the 20th century, laid the foundations for both hemodynamic physiology and clinical hemodynamics; for this reason, he was viewed as the “Dean of Cardiovascular Physiology.”5 Wiggers described the relationships between pressures throughout the heart and vascular system, the heart sounds, and the ECG; he provided an elegant description of the cardiac cycle that is often referred to as the “Wiggers’ Diagram.” He was also one of the pioneers in cardiac electrophysiology, describing the vulnerable period and its relationship to ventricular fibrillation. He examined the mechanisms responsible for irreversible shock and identified the cause of the early pump failure of the ischemic heart as failure of excitation-contraction coupling. Wiggers’ seminal contributions to hemodynamics were instrumental in the rapid clinical application of cardiac catheterization after World War II.

Wiggers became Editor of Circulation Research when he retired as Chair of Physiology at Western Reserve. He wrote in his autobiography:

I was warned that editors can neither make new friends nor retain old ones. I was shown a cartoon depicting a captive editor surrounded by a ring of cannibals, variously labeled contributor, reader, publisher, and printer. Javelins were being hurled at the editor, presumably to tenderize his flesh preparatory to putting him in the stew pot. Nevertheless, since my pachydermal covering had thickened with the years, I resolved to take the risks.3

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<th>Table 1. Editors of Circulation Research</th>
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<tr>
<td>Carl J. Wiggers 1953–1957</td>
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<td>Carl F. Schmidt 1958–1962</td>
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<td>Eugene M. Landis 1963–1966</td>
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<td>Robert M. Berne 1971–1975</td>
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<td>Francois M. Abboud 1981–1986</td>
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<td>Eduardo Marbán 1999–present</td>
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Figure 1. Photograph of Carl J. Wiggers (right), taken by the author at a meeting of the American Physiological Society in Atlantic City in the mid-1950s. At the left is Anton J. Carlson, whose position as intellectual leader in Gastrointestinal Physiology during the first half of the 20th century was similar to that held by Dr. Wiggers in Cardiovascular Physiology.
Wiggers continued: “After five years of service I discovered that all of these hazards are a myth. On the contrary, an editorship is a gratifying experience.”

Wiggers took the opportunity in his Foreword to remind the readers of the “basic purpose” of a scientific journal:

... it is not a primary function [for a journal] to serve as a medium for personal advancement of its contributors. If an investigation has failed to yield new facts which are interesting or interesting facts which are new, the investigator should suppress the urge to convert an unsuccessful or unconvincing research into a published communication. Research is a gamble in which the laws of chance favor the loser, and the loser must remain a good sport. [If] the experimenter has sincerely convinced himself that reluctant nature has been forced to yield one of her secrets through the use of new strate- gems, our readers will not usually be content with mere statements of the fact but will want some evidence as to the degree of reliability which may be placed on the results and the reasonableness of conclusions that are derived from them. ...6

Wiggers was well aware of the importance of clear writing, noting in his Foreword: “Readers are greatly influenced in their judgment of a research project by literary style; a poor presentation can easily damage the best investigation.”6 In describing the balance between presenting too much and too little, Wiggers wrote: “A good paper, like a good glass of beer, should neither be largely foam nor flat; it should have just the right head of foam to make it palatable.”3

**Growth and Stability: Carl F. Schmidt**

Carl F. Schmidt, the second editor, was born in Lebanon, Pennsylvania and received his medical degree from the University of Pennsylvania in 1918. Schmidt was a pioneer in studies of the renal, pulmonary, cerebral, and coronary circulations. With A.N. Richards at the University of Pennsylvania, he was among the first to recognize the dynamics of renal glomerular function. He subsequently turned to studies of the cerebral circulation, developing several innovative methods to measure blood flow that allowed him to recognize the overarching importance of arterial pressure in controlling blood flow to the brain.7 At the same time, his group described the role of CO₂ as a cerebral vasodilator. Early in his career, Schmidt went to China where he served as an Associate in Pharmacology at the Peking Union Medical College. There, with K.K. Chen, he sought to identify active drugs from among a huge number of remedies listed in the Chinese *Materia Medica*. When Schmidt and Chen challenged a Chinese druggist to identify a potent drug in this group of native herbs, they were given a sample of an herbal remedy called ma huang, from which they made a decoction, which they injected into an anesthetized dog. They observed a tremendous, long-lasting rise in arterial blood pressure and subsequently identified the active ingredient as ephedrine.8

Schmidt, much of whose work had been made possible by his development of new methods to measure blood flow, quoted Carl Ludwig’s aphorism: “Die Methode ist alles” in his introductory editorial. Following Wiggers’ precedent in offering advice to authors, Schmidt warned of the dangers of...
methodological error at a time of increasing pace and support for cardiovascular research:

The new editor, like his predecessor, used to dream of the time there would be better support and encouragement for research in the physiological sciences, and when our clinical contemporaries would render more than lip service to the theme that the practical advances of tomorrow depend on the activities in the laboratory today. Now these dreams have come true, and we find some unanticipated flaws in the fruit that looked so luscious.9

Schmidt noted that a “tendency toward superficiality, speed and quantity” could worsen methodological errors. He observed that clinical investigators have “full blown research facilities . . . splendidly appointed and manned by the cream of the crop of young medical graduates [for whom] the tedious procedures of calibrating and progressing one step at a time are likely to be discarded in favor of more immediately productive activities.” Faced with significant clinical and military duties (this was the time of the “doctor draft” in which everyone served), clinical investigators were stated by Schmidt to lack the time “for relaxed study and contemplation . . . they are apt to lack information or even interest in the perspective, purpose and scope of the research.” He continued: “Add to this a desire to share the distinction of appearing first in the list of authors and one has all the ingredients for a series of papers in which the same methods, even the results of the same experiments, appear over and over under different captions, sometimes in different journals, and eventually the mass of accumulated data comes to be accepted as proof of its validity.”9

Schmidt suggested that “these tendencies toward superficially and haste [which] are also seen in basic science departments and institutes . . . are the outgrowth of the project basis for financing research activities [which] places a premium on published evidence of worthiness for further support.”9 He observed:

Neither the committees which act on applications for funds nor those who search for prospective department heads are much impressed by extensive attempts at finding flaws in methods already in use. Therefore the able, intelligent young researcher is apt to select a laboratory with a large output of published work over one in which the old-fashioned habit of caution and self-criticism still prevails, and thus a vicious cycle is brought into operation.9

He also proposed to curb multiple authorship, citing Wiggers when he stated that “four names on the title . . . are enough for practically any paper.”9

The initial success of Circulation Research is documented in Table 2, which details the flow of manuscripts during the first 9 years of publication.10,11 During this period, the number of submissions more than tripled and the number of published pages increased 2.5-fold. The “raw” acceptance rate showed a significant downward trend; when corrected for the increasing number of journal pages (and assuming that manuscript length remained the same), the acceptance rate probably fell from more than half of submissions to less than one eighth. This success led, in 1962, to monthly publication of this journal.

**Maturity: Eugene M. Landis**

Eugene M. Landis, the third editor (Table 1), was born in Hope, Pennsylvania in 1901 and received M.D. and Ph.D. degrees from the University of Pennsylvania in 1926 and 1927, respectively. As a medical student, he developed a lifelong interest in capillary function; his work with A.N. Richards at Pennsylvania and August Krogh in Copenhagen stimulated him to measure capillary pressure directly, a monumental discovery, which Krogh stated: “open[ed] up the possibility of an intimate understanding of capillary physiology far beyond anything to be imagined before.”12 The close relationship that once existed between medicine and physiology is seen in Landis’ move from Professor of Medicine at the University of Virginia to Professor of Physiology at

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<th>Year*</th>
<th>Volume</th>
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*1953–1961 data based on References 10 and 11.
†Normalized to pages published in Volume 1.
Rapid Publication: Julius H. Comroe, Jr

Julius H. Comroe, Jr, the fourth editor (Table 1), was born in York, Pennsylvania in 1911; like Schmidt and Landis he received his medical degree from the University of Pennsylvania where he became Chairman of Physiology and Pharmacology at the Graduate School of Medicine. In 1957, he became director of the new Cardiovascular Research Institute at the University of California, San Francisco, and Principal Investigator of a very large and highly productive Program Project. His work, which encompassed both respiratory and cardiovascular physiology, included seminal studies of the pulmonary chemoreceptor reflexes. His interests included the process of scientific discovery in Medicine. He was a dedicated teacher and developed several educational programs for the American Physiological Society. Just before assuming my first faculty position in 1964, I paid Dr. Comroe a courtesy call and mentioned something about my “teaching load.” I vividly recall him rising angrily from his chair stating that teaching was to be viewed as a privilege and not a burden; I still cringe when I recollect his words, which I never forgot.

Comroe’s “inaugural editorial” departed from the earlier practice of presenting philosophical comments on science and offering advice to authors. Comroe focused instead on means to accelerate editorial review and the publication of accepted articles. The need for rapid publication, of course, reflected the accelerating pace of biomedical research. Comroe, however, noted the hazard of excessive emphasis on speed when he wrote: “Some of my associates have asked me ‘Why do you want to rush articles into print?’ I wish to speed into print only those articles that have been judged to be meritorious by competent editorial boards; I do not wish to see Circulation Research become the ‘Acta Retracta.’”

A personal anecdote illustrates Comroe’s attentiveness to good scientific writing: In one of my early papers on the cardiac contractile proteins, I had written that an experiment had “revealed” a finding; Comroe, referring to a well-known striptease artist, wrote in the margin of my manuscript: “Sally Rand reveals.”

Comroe made two other innovations. One was to begin each article with a right-hand page, which was intended to facilitate removal of individual articles for filing. The second was to use the otherwise blank left-hand pages to publish “Classic Pages” (selections from classical articles). The latter provided fascinating vignettes for readers of Circulation Research in the late 1960s and early 1970s and are well worth rereading today.

Comroe’s emphasis on rapid publication highlights one of the major changes in cardiovascular science since 1953. The accelerated pace of discovery can be appreciated in a personal story, which centers on a paper I published in Circulation Research in 1955. The idea for this study, which I coauthored when I was a second-year medical student, came from my father who, as a student in Wiggers’ department in 1918, had published a now classical paper describing left ventricular volume curves, but in which it had not been possible to eliminate the contribution of volume changes in the right ventricle. The advent of right heart bypass, which allowed blood to be drained from the right ventricle, offered us the opportunity to construct pressure-volume loops for the left ventricle. Wiggers’ loan of the glass onometers that had been used to record ventricular volume in the 1918 experiments allowed us to publish experiments that are still occasionally cited. The point of this story is simple: imagine today a first-line journal publishing data based almost entirely on 35-year-old methodology!

A second story, which demonstrates (in deference to Comroe I eschew the word “reveals”) how little attention was once paid to rapid publication, centers on the discovery that muscle contraction is activated by a rise in cytosolic calcium. This fundamental discovery is generally credited to a 1947 study by Heilbrunn and Wiercinski, who found that when physiologically significant cations were injected into muscle cells, only calcium elicited contraction. The remarkable lack of concern for rapid publication at that time is evident in a statement, published 4 years earlier in Heilbrunn’s 1943 textbook An Outline of General Physiology, that cited “unpublished observations” as support for the statement: “... if various cations are injected into muscle fibers, the effect of the calcium ion [to activate contraction] is outstanding.” In fact, Heilbrunn and Wiercinski were not the first; Ebashi points out that in the 1930s, Chambers and Hale, Keil and Sichel, and Kamada and Kinosita had all published...
evidence that calcium is the intracellular trigger of muscle contraction.

Changing Philosophy of Research

Many of the concerns regarding the role of the investigator expressed by the early editors of *Circulation Research* were summarized in 1950 by Louis N. Katz, who was among those present at the 1951 meeting of the Executive Committee of the Scientific Council of the AHA, where the idea of publishing this journal appears to have originated. In an article published in 1950, my father succinctly stated the philosophy of scientific investigation at the time *Circulation Research* was founded:

Research is a dignified profession to be pursued only by the consecrated and inspired, in quietude, at a leisurely pace, and away from prying eyes. It cannot be placed on a business footing where one new fact is to be returned for each quantum of dollars invested. I have actually heard some persons propose to set up a committee to find out what needs to be done in discovering a cure for some specified malady. I have heard them suggest gathering all the eminent scientists together and putting them to work so that the cure will come in their lifetime. Of course these individuals, worried about themselves, would like to hurry the process. Since industry has been successful by harnessing men together, the uninitiated naturally believe that research results can be accomplished in the same way. Unfortunately this is not necessarily so. Great discoveries are not produced on the assembly line. Only duplicates can be so manufactured. The original must come about through the deliberate activity of a creative mind. And a creative mind works best away from artifices and prodding. Great discoveries evolve—they are not delivered on call.24

Conclusions

The success of *Circulation Research* is apparent not only in the many seminal studies that have been published in its pages but also in the contribution of the journal to what is surely one of the most remarkable half centuries of discovery in the history of Medicine. Evidence that *Circulation Research* has met its original goals is seen in the almost 60% fall in age-adjusted mortality from cardiovascular disease that has occurred since 1953, an achievement that attests to the practical importance of basic research.

A.V. Hill, whose work on the energetics of muscle earned him the Nobel Prize, observed in 1927 that the discovery of X-rays was an accidental byproduct of basic research:

Imagine fifty years ago a prize offered to anyone who could photograph the inside of the body in a living child. He and anyone who tried to win the prize would only have been laughed at for their pains. Certainly those who set out to win it would have been most unlikely to succeed. Success came from a totally different direction, from the work of men [on the conduction of electricity through gases] who to their severely practical brothers may have seemed to be investigating things of little importance. Often, in science as in life, it is the byproducts which turn out in the end to be more important than the things we set out to find. . . . One never knows where scientific investigations will lead, but experience has made it certain that a disinterested and honest study of nature, an attempt to understand the real facts behind the shadow, will lead at intervals to discoveries of the first importance for the comfort and well-being, mental, moral, and material, of the race.25

This view of the importance of basic research was echoed by Comroe, who wrote:

. . . crucial discoveries, essential to later medical miracles, were often made by those not directly concerned with diagnosing or curing or preventing disease . . . the work of many of these was judged to be impractical, impossible, irrelevant or absurd at the time of discovery.8

Comroe’s conclusion was based on a study of what in 1977 were judged to be the “top ten clinical advances in cardio-pulmonary medicine and surgery,”78 although he observed that the public—and many physicians and scientists—often equated important discoveries to the work of a single individual, “[the efforts of] scores or hundreds of competent scientists was essential to provide the basic knowledge necessary for the widely known clinical advance. . . .”26

The last word belongs to Wiggers, who stated:

. . . every disease is an experiment that nature performs, and its signs and symptoms are the manifestations of abnormal function. Medical students during their training in physiology should be inspired with the ambition not merely to interpret such clinical signs, but to see through them on the basis of evidence furnished by experimental work.4

Acknowledgments

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References

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