Richard John Bing, who died on November 8, 2010, at the age of 101, in his home at La Canada, Calif, was one of the most eminent cardiovascular investigators of the 20th century. In reality, however, he had several incarnations: one as a musician and composer of modern music; the other, as a physician scientist of the old school, equally at home at the bedside and in the laboratory. In his later years, he lived through a third incarnation, that of a writer.

First and foremost, however, Richard will be remembered as a pioneer in the diagnosis of congenital heart disease by physiological methods, as the father of the field defined as cardiac metabolism, and as the first to assess coronary flow noninvasively with a radioactive tracer (Rb85), which laid the foundations for nuclear cardiology and, more specifically, positron emission tomography. But Richard did much more.

C. Willis Hurst has described Richard Bing as a Renaissance man. His colleagues remember his colorful personality. I remember my first encounter with Richard at a small meeting in 1974 when he entertained us after dinner by playing improvisations on the piano. We did not go to bed until well after midnight. Little did I know then that Richard was a composer of 20th century orchestral, chamber, and choral music, and that his music was performed by some of the great orchestras, including the Vienna Philharmonic. But I know well that, at that very night, I got hooked on cardiovascular research.

Last year, I had the fortune to write about Richard’s life on the occasion of his 100th birthday. I entitled the article “Richard Bing at 100 – A Lion in Winter.” Richard and I joked that he got to read his own obituary. Not quite so. Following an invitation from the editors of Circulation Research, I now take a fresh look at Richard’s many contributions to cardiovascular research, providing much-needed comment and also encouragement for the present generation of cardiovascular scientists.

His Roots in Germany, Denmark, and the United States

Richard came from a proud heritage. He grew up in the medieval city of Nürnberg in Germany, a city that, at the time, suffused with the life of an educated middle class. His father was a merchant, his mother a singer. For centuries, this middle class provided the underpinning for Germany’s pre-eminence in the arts and the sciences, in commerce and engineering, irrespective of religion or creed. When the Nazis put an end to this fabric in 1933, Richard was still able to graduate from medical school at the University of Munich in 1934, merely because the Bavarians were a little slower than the rest of Germany to adopt the antisemitic laws. Richard then left Germany for Switzerland (where within a year he obtained a second medical degree from the University of Bern) and ended up as a research fellow at the Carlsberg Institute in Copenhagen.

Why Copenhagen? Here is one reason: as a medical student in 1930, Richard was struck by a short movie showing cell division under the microscope. Since then, his dream was to become proficient in the new technique of cell and tissue cultures. The best place to learn cell culture was the Carlsberg Institute. However, before he had settled on his new life’s path, his plans were once again drastically changed. Richard encountered two visitors from the Rockefeller Institute in New York, Alexis Carrel and Charles Lindbergh. Carrel, the surgeon, had won the Nobel Prize at the age of 39; Lindbergh, the aviator, had flown across the Atlantic at the age of 25. With youthful enthusiasm, both men had joined forces for a new adventure: tissue culture and organ preservation with the
aim to engineer organ replacements. They were at least half a century ahead of today’s intense interest in regenerative medicine. It is hard to make out in hindsight whether Richard seized the opportunity to join the odd couple, or whether it was the other way around. In any case, Richard moved to the Rockefeller Institute in 1936 and learned organ perfusion. Not that he ever published with either Carrel or Lindbergh. Instead, his first paper, entitled “The perfusion of whole organs in the Lindbergh apparatus with fluids containing hemocyanin as respiratory pigment,” was a single-author article in Science. What an accomplishment for a young European immigrant! Another important event took place in 1938: Richard’s marriage to Mary Whipple, the daughter of Alan Whipple, chair of surgery at Columbia, and the descendant from a well-established New England family. After standing up to adversity in Germany, Richard truly embraced the American culture and the American life. In the following years, he took up a research apprenticeship on the kidney and hypertension laboratory of Homer Smith at New York University and served in the US Army. More detail can be found elsewhere.

I remember well that Richard never liked the now trendy term “translational medicine.” He lived it, and he was fond of saying: “Love for the patient also means love for science.” Although PubMed lists more than 500 articles, by far, not all of them are original articles. There are two common features to Bing’s best published work. First, conceptually he was often way ahead of the field. Secondly, he had the skill and good fortune to turn adversity into success, especially during the first 40 years of his career. The second 40 years he spent in the relative tranquility of the Huntington Medical Research Institutes in Pasadena, CA. Nonetheless, he published his last first-author original article at the age of 92! Between 1938 and 2001 lie 63 uninterrupted years of work as a scholar and investigator. In this respect, Richard equals the Venerable Dr Routh, the legendary president of Magdalen College in Oxford, from 1791 to 1854. But was there ever before a cardiovascular scientist whose first and last works were more than 6 decades apart? Everything about Richard was interesting: his demeanor, his learning, his wisdom, his wit, and, most of all, his open disdain for pretense.

Time of “Sturm und Drang”

From the time he started medical school (in 1928) until he left the chair of medicine at Wayne State University (in 1969), Richard had moved at least 13 times, 5 times alone in the United States (his Army service not included). These moves often coincided with periods of extraordinary creativity. (The Germans call it “Sturm and Drang” (storm and stress) after a literary movement in the late 18th century.) Into this time fall Richard Bing’s three major legacies in cardiovascular medicine, which I discuss now briefly.

First, he ventured with the catheter where no one had ventured before, into the hearts of “blue babies.” Richard established sound physiological principles for the diagnosis of congenital heart disease by introducing both pressure recordings and oximetry runs for shunt calculations. As Bing himself once wrote, “In science as in art, events should be related to the time they were created, in order to do them justice and to see them in perspective.” At the time Bing started cardiac catheterization at Johns Hopkins University in 1945, Helen Taussig relied on physical examination, ECG, and fluoroscopy for the diagnosis of congenital heart disease. There existed only two cardiac catheterization laboratories: one of them directed by the pioneers Andre Counard and Dickinson Richards at Bellevue Hospital in New York; the other directed by Lewis Dexter at the Peter Bent Brigham Hospital in Boston. In the period of 5 years, Bing delineated, in rapid succession, the hemodynamic features of 20 different forms of congenital heart disease, from the tetralogy of Fallot to the Taussig–Bing anomaly, a form of complete transposition of the great arteries. The early articles were published more or less alternately in the Journal of Clinical Investigation and in the, now long defunct, Bulletin of the Johns Hopkins Hospital, in the latter for the mere convenience of having the editorial office down the hallway. It was Bing’s aim to elucidate physiological principles (such as adaptation to hypoxia, or the development of pulmonary hypertension), but, he told me once: “The chips always came down in the operating room where Blalock had to have a diagnosis.” Because, at the time, the tetralogy of Fallot, patent ductus arteriosus, and coarctation of the aorta were the only operable malformations of the heart and great vessels, a false diagnosis before surgery invariably had fatal consequences!

The second major legacy was more of an unplanned nature. While performing right heart catheterization in patients, he had frequently noticed that the catheter tip entered a region of the heart where the pressures were lower than in the ventricles and where the blood was very dark. It took a few simple experiments to ascertain that the catheter had entered the coronary sinus. This discovery coincided with Richard’s reading of an article by C. Lovatt Evans, physiologist and collaborator of Ernest Starling at University College in London, who had measured substrate usage in an isolated heart/lung preparation. Bing recognized the importance of his observation by measuring first arteriovenous differences for O₂, then coronary flow, and changes in substrate concentrations across the heart muscle. Although analytical methods were cumbersome at the time, a new branch of the tree of cardiovascular physiology began to sprout. In a series of articles, reviewed by him in his famous Harvey Lecture, Bing and his coworkers established that the human heart extracts almost all O₂ delivered on the arterial side, that an increase in O₂ supply can only be achieved through an increase in coronary blood flow, and that human heart muscle is able to meet its energy needs through the oxidation of a variety of substrates, mainly fatty acids, but also glucose, lactate, ketone bodies, and amino acids. In his work, he characterized the conditions that determine substrate preferences and looked at disease states such as the failing heart and the heart in diabetes. When asked in 2009 why he did not follow up on cardiac metabolism at a time when biochemists had already put together all the metabolic pathways, he answered me with a rhyme, in German, meaning “been there, done that.”

Richard’s third major legacy related to the noninvasive assessment of coronary flow and, with it, the birth of nuclear cardiology. While Chairman of Medicine at Wayne State
University, he collaborated with George Clark, a physicist at the Massachusetts Institute of Technology, on a new method to measure coronary blood flow in vivo by a radioactive tracer method. On Clark’s advice, he used the positron emitter Rb\(^{84}\) and coincidence counting. Although Bing only sporadically followed up on the fundamental observation, others did. Thus, Bing became an inventor of positron emission tomography (PET) of the heart, now widely used for the noninvasive assessment of regional myocardial blood flow and metabolism. As in many of his endeavors, Richard was able to see more than the horizon.

**Adding Ever More Colors to the Rainbow of Experimental Cardiology**

Richard liked the broad term “experimental cardiology,” not the least because it gave him the freedom to change fields when he felt he had reached the end of a particular line of investigation. So, when he left cardiac metabolism disappointed because it did not reveal a clue to the cause of nonischemic heart failure, he turned to ever more molecular questions: the contractility of actomyosin threads and topics including protein metabolism in hypertrophy and failure, coronary microcirculation, lipid metabolism in isolated perfused coronary arteries, experimental myocardial infarction, diltiazem, perfluorochemical emulsions as oxygen carriers, lysophosphatidylcholine and atherosclerosis, NO, eNOS, prostacyclin, iNOS, oxidation products of NO, cyclooxygenase inhibitors, and many others. He published his last original article as first author in 2001 at the age of 92, on NO, prostanoids, cyclooxygenase, and angiogenesis in colon and breast cancer. Several other articles and books followed in the years thereafter. A book on the history of cardiology went through two editions and is of special value because it contains the accounts of an eyewitness to the evolution of our discipline from vague concepts to sound physiological principles. It is a delight to read.

With Richard Bing’s death, the cardiology community has lost one of the last direct links to the early years of clinical and experimental cardiology. Richard’s legacy will continue in the International Society for Heart Research, the forerunner of which he helped found in 1967, together with cardiovascular scientists from both the West and the East. Like a hunting lion, Richard was at his best when he pounced on a new idea, like a lion pounces on his prey. Furthermore, he exalted when we could ask him: “Tell us how it was?” He always had a good story to tell. And he did his story telling with consummate passion, especially in his beloved series, “Past Truth and Present Poetry” for Heart News and Views, the newsletter of the International Society for Heart Research. Because he was so very old, we thought Richard would be around forever. Now, the lion in winter is a lion at rest.

**Heinrich Taegtmeyer**

*Department of Medicine/Cardiology*  
*University of Texas School of Medicine at Houston*  
*Houston, Texas*

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**References**

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Heinrich Taegtmeyer

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