Richard J. Bing - A Man for All Seasons
A Brief Conversation with Richard J. Bing at 100 Years
Past Truth & Present Poetry

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"a man of angel’s wit and singular learning; I know not his fellow. For where is the man of that gentleness, lowliness, and affability? And as time requireth, a man of marvellous mirth and pastimes: and sometimes of as sad gravity: a man for all seasons."

Whittinton R. cited by Miller (1)

Thinking of a suitable way to characterize the life of Richard J. Bing, who celebrated his 100th birthday this year, I was reminded of Robert Bolt’s “A Man for All Seasons”. This play tells about Thomas More, the author of Utopia, who was a philosopher, writer, and theologian, and who became Henry VIII’s Lord Chancellor in 1529. The phrase, “a man for all seasons”, had been used to describe More by his contemporary, Robert Whittinton, in the quotation that introduces this article. Whittinton’s source is Erasmus’ dedication of The Praise of
Folly in which Erasmus refers to More as a vir... omnium horarum. This phrase also describes Bing who, like More, was a “universal” man who made enormous and diverse contributions to our understanding of science and art.

Richard was born in Nürnberg, Bavaria, on October 12, 1909. Between 1929 and 1934, he attended the Universities of Vienna, Berlin, and Munich. After receiving an M.D. degree from the latter in 1934, he became caught up in the turmoil then swirling through Europe and moved to Bern, Switzerland, where he spent much of his time in DeQuervin’s laboratory studying thrombus formation. In 1935, he received a second M.D. from the University of Bern, after which he joined the Carlsberg Biological Institute in Copenhagen, from 1935 to 1936, he learned how to prepare cell cultures. Here he met Alexis Carrel, a pioneer in cardiac surgery who received the Nobel Prize for his work on sutured blood vessels and organ transplantation, and Charles Lindbergh the aviator, both of whom were working to design a pump that could perfuse isolated organs. Lindbergh’s interest in tissue perfusion was stimulated by the fact that his sister was dying of rheumatic mitral stenosis and the hope that a machine which bypassed the heart could allow surgeons to repair damaged valves in a bloodless field. Richard’s contacts with Lindbergh and Carrel led to the award of a Rockefeller stipend that took him to New York. After returning briefly to Denmark to complete his obligations at the Carlsberg Institute, he emigrated to the United States into World War II. As he lacked the medical license needed to serve in the US Army Medical Corps, he became an assistant resident in medicine at the Johns Hopkins School of Medicine. This allowed him to pass the National Board examination in medicine, which made him eligible for a commission in the army. He joined the United States Army Medical Corps in 1943 as a Lieutenant, and served in the chemical warfare corps in Maryland and then in Germany, rising in rank to Lieutenant Colonel. After his discharge in 1945, he was recruited as an Assistant Professor of Surgery to Johns Hopkins where, in 1947, he was promoted to Associate Professor of Surgery with a joint appointment in Medicine. In 1951, he moved to the Medical College of the University of Alabama at Birmingham, serving as Professor of Medicine and Professor of Clinical Physiology. From 1956 to 1959 he was Professor of Medicine at the Washington University School of Medicine in St. Louis. He became Chairman of the Department of Medicine at Wayne State University in Detroit in 1959, and in 1969 he moved to the University of Southern California as Professor of Medicine and Director of Experimental Cardiology at the Huntington Medical Research Institutes.

Richard’s life as an investigator was interrupted by the entry of the United States into World War II. As he lacked the medical license needed to serve in the US Army Medical Corps, he became an assistant resident in medicine at the Johns Hopkins School of Medicine. This allowed him to pass the National Board examination in medicine, which made him eligible for a commission in the army. He joined the United States Army Medical Corps in 1943 as a Lieutenant, and served in the chemical warfare corps in Maryland and then in Germany, rising in rank to Lieutenant Colonel. After his discharge in 1945, he was recruited as an Assistant Professor of Surgery to Johns Hopkins where, in 1947, he was promoted to Associate Professor of Surgery with a joint appointment in Medicine. In 1951, he moved to the Medical College of the University of Alabama at Birmingham, serving as Professor of Medicine and Professor of Clinical Physiology. From 1956 to 1959 he was Professor of Medicine at the Washington University School of Medicine in St. Louis. He became Chairman of the Department of Medicine at Wayne State University in Detroit in 1959, and in 1969 he moved to the University of Southern California as Professor of Medicine and Director of Experimental Cardiology at the Huntington Medical Research Institutes.

Richard’s appointment to the Department of Surgery at Johns Hopkins brought him into contact with Helen Taussig and Alfred Blalock, then among the world leaders in congenital heart disease. Here he established the third cardiac catheterization laboratory in the United States, and the first dedicated to the study of congenital heart disease. This collaboration led to the description of the “Taussig-Bing Malformation”, which is characterized by a ventricular septal defect and transposition of the great vessels in which the aorta arises entirely from the right ventricle and the pulmonary artery, while arising mainly from the right ventricle, is levoposed and partially overrides the ventricular septum.

It was at Johns Hopkins that the inadvertent passage of a catheter into the coronary sinus led this young clinical investigator into the field of cardiac metabolism. This occurred when Richard realized that blood samples taken from the coronary sinus would allow him to measure arterio-venous differences of substrates and metabolites across the human heart. After recognizing the importance of this accidental discovery, he determined its safety and began a lifelong study of the metabolism of normal and diseased human hearts.

As is often the case, Richard’s successes in research led to his being offered positions of increasing administrative responsibility that encroached on his ability to work as a creative scientist. His move to Alabama in 1951 provided an opportunity to study the metabolism of diseased human hearts, but required that he also become director of the cardiac clinic. In 1956, when he moved to Washington University, he became Director of the Internal Medicine Service at the affiliated Veteran’s Administration Hospital and, in 1959, when he assumed the Chair of Medicine at Wayne State School of Medicine, he became director of a major clinical program at a large inner-city hospital. In spite of his increasing clinical and administrative demands, in 1964 he pioneered the use of positron emitters to measure coronary blood flow and to image the human heart. His final move, to the Huntington Medical Re-
Richard Bing receiving his honorary degree from the University of Bologna in 1978. This photo was published in the Journal of Molecular and Cellular Cardiology, Volume 20, Caldarera C., “Professor Richard Bing and the award of his Honorary degree.” p. 1079, Copyright Elsevier, (1988), and is reprinted with permission.

search Institutes of the University of Southern California, allowed him to return his focus to the laboratory.

As a major contributor to what has been the greatest century of progress in the history of medicine, Richard left an indelible mark on cardiology. One can gain an appreciation of this history by reading the list of Richard’s publications that is available on the web (2) along with articles that add personal reminiscences about Richard’s life (3-6). The most significant of Richard’s scientific accomplishments were in areas related to cardiac metabolism, where he made many important contributions to cardiology, including the demonstration (i) that the heart is an omnivore, which means that the heart can obtain energy for its incessant mechanical activity by oxidizing fat, carbohydrate, and protein, (ii) that under most conditions fats are the preferred substrates, and (iii) that the heart’s oxygen demand is so great that virtually all of the oxygen delivered via the arterial blood is extracted before the coronary venous blood enters the coronary sinus. Richard’s studies extended beyond areas related to metabolism. In the early 1950s, he published studies on the heart’s contractile proteins and subsequently added his voice - and his data - to the then fierce dispute regarding a possible change in the molecular weight of cardiac myosin in failing hearts; not surprisingly, Richard’s finding that there was no such change proved to be correct.

In 1967, Richard was present at the founding meeting of the International Study Group for Research in Cardiac Metabolism and, not surprisingly, was elected its first President. When, in 1976, the ISGRCM became the International Society for Heart Research, Richard was elected its Life President. Along with Lionel Opie, he founded the Journal of Molecular and Cellular Cardiology which became a centerpiece of this society.

The honors and awards that Richard has received are too numerous to list in this article. Among the honors that meant the most to him were an Honorary degree in Medicine and Surgery from the University of Bologna (7) and the naming of what I consider the most important prize given by the ISHR: The Richard Bing Young Investigator Award.

Music played a large role in Richard’s life. He took piano lessons as a child and studied piano in the master class of the conservatory in the Nürnberg Gymnasium; however, the major focus of his musical efforts was composition. He wrote a Missa that was performed at Saint Steven’s Cathedral in Vienna and broadcast on National Public Radio. Commenting on the differences between medicine and music, Richard wrote: “As compared to composing music, the path of medical research is like a slow-motion film, sometimes little progress for weeks, days of experimentation that may lead to nothing … This search for success in cardiac research was at times wearing. It was then that I sought refuge in composing music. It was a refreshing change, like traveling to a new and exciting country; I felt renewed” (8). Richard’s other non-scientific efforts include Cardiology, The Evolution of the Science and the Art (2nd Ed, New Brunswick, Rutgers NJ, 1999), The Winds of Time and other Stories (Xlibris, Bloomington IN, 2005), and Fifteen Lives and a Cat’s Story (Xlibris, Bloomington IN, 2004); the latter is a collection of short stories which concludes with words of wisdom that Richard generously attributes to Louis, his cat.

In 2000, Richard concluded an interview when, responding to the question: “How do you wish to be remembered?” he stated: “I would like to be remembered as a decent human being, full of controversy…” (3).

Looking back over the almost 50 years that I have known Richard as a colleague and friend, I can attest to the invariable kindness, gentleness, and decency of this remarkable man. When I first met Richard, he was a giant and I was a pup. Yet even
A BRIEF CONVERSATION WITH RICHARD J. BING AT 100 YEARS

On the advent of his 100th birthday (October 12, 2009), it was my great privilege to ‘interview’ Dr Richard J. Bing by e-mail correspondence. In addition to his many contributions to cardiovascular medicine (see the lead article in this issue, “Richard J. Bing, A Man for All Seasons” by Arnold Katz), Dr Bing has been a lifelong contributor to the ISHR – from his role as first president of the International Study Group for Research in Cardiac Metabolism (forerunner of the ISHR) in 1967, to the 41st installment of his history of science series, “Past Truth & Present Poetry”, found on page 7 of the current issue. The Society is grateful for Dr Bing’s continuous support, and we wish him well as he celebrates 100 years of a life well lived in the service of the heart.

HN&V: As every member of the ISHR knows, you were instrumental in the formation of the International Study Group for Research in Cardiac Metabolism in the 1960s (which later became the International Society for Heart Research), and you served as the first President of the Society and first Editor (with Lionel Opie) of the Journal of Molecular and Cellular Cardiology. What was the reasoning behind the formation of this Society? What can you remember about the early days and initial meetings?

RJB: I recall that I went to London the year when ISHR was founded, to talk to the publishers. It was a very successful trip because a young man took me thru London, and he was an expert in old London history. As we were talking about the future of ISHR, we also watched a spoon dance in a London pub. Also, I met the spark plug of ISHR, Eörs Bajusz, who impressed me as a quiet yet intense person - a real pioneer. I was then asked to become the first president and I had some fruitful discussions. The birth of ISHR was a natural outcome for some of us who thought that the big groups such as the American Heart Association and the American College of Cardiology were not primarily concerned with fundamental aspects of cardiology, and there was no organization which exclusively stressed the scientific molecular aspects of the heart. Then he was never condescending - he made it clear that we were colleagues in the search for truth. Never shy about entering a debate, and always fierce in arguing his point of view, Richard’s goal was to find the best answer that could be provided by the data then available. Who was right and who turned out to be wrong was never an issue; in these debates all that mattered was what the evidence demonstrated. Having worked at the forefront of both science and art, Richard is one of a select few who can justly be said to have lived a vir... omnium horarum - a life for all seasons.

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cardiology. For me, these were golden years because the founding members recognized the primary importance of fundamental research.

**HN&V:** You have been writing your wonderful series, *Past Truth & Present Poetry*, in the Society newsletter, *Heart News and Views*, for the past 13 years. How did it come about that you began this series, and why is a knowledge of the history of medical science important to young physicians and scientists?

**RJB:** Dr Ruigrok initiated my authoring the “Past Truth & Present Poetry” series of articles in the ISHR newsletter in 1996 [see *HN&V* 15:1, “From the Editorial Office” by Tom Ruigrok]. A knowledge of the history of medicine is important because of the individual pioneers: their struggle, their fate, and their courage of conviction. Younger people should know of the men and women who made their field great. It is important to listen to the interplay between individuals in the spirit of the time. This interplay can lead to tragedy or victory. Younger scientists should know that they are not alone in their struggles.

**HN&V:** You have served as a mentor for countless physician scientists throughout the years. Who were your mentors and how did they influence your career?

**RJB:** My mentors were Allen O. Whipple, Homer W. Smith, Alexis Carrel and Alfred Blalock. All four of them influenced me by promoting me in rank and giving me their confidence. Carrel encouraged me to go into research, and Blalock made it a reality. Whipple and Smith helped me to get through the initial bumps of an early career in science. [See also: *HN&V* 11:2 “An Odyssey in Science and Medicine” by Richard Bing].

**HN&V:** Everyone is familiar with Charles Lindbergh, the famous aviator, and with the subsequent personal tragedy and political controversy in his life. Based on your personal and working relationship with Lindbergh, what would you like to add to this image of the man?

**RJB:** Lindbergh was extraordinary, kind and helpful to me and I would be an ogre if I did not express my thanks to him.

**HN&V:** Throughout your illustrious career you have moved every few years, and you have influenced, and been influenced by, researchers and physicians at many excellent hospitals and research institutions. How do you think this exposure to a wide variety of experiences and approaches contributed to your growth as a physician scientist, and would you recommend this path to young scientists?

“I knew Charles Lindbergh well and worked with him in 1936 when I was a young M.D. and a fellow at the Rockefeller Institute, now the Rockefeller University, in New York City with Dr Alexis Carrel, the well known experimental surgeon and Nobelist. Lindbergh became interested in medical science because he tried to find a cure for his sister-in-law, Elizabeth Marrow who had severe mitral stenosis. Why, he reasoned, would it not be possible to construct a mechanical device capable of circulating blood through parts of the body, bypassing the heart, leaving it bloodless and accessible to the surgeon. Therefore, what he had in mind was essentially a heart-lung bypass. It was not until the 1950’s that Gibbon in Philadelphia, after long animal experimentation, built and used the first heart-lung bypass system on a patient with congenital heart disease.”

A fascinating part of the history of molecular biology was played by the group at Caltech with Max Delbrück, and his group was referred to as the “Phage Group”. Max Delbrück was its center and its driving force. Delbrück did not approach the secret of genetics by means of biochemistry as Avery had done; Delbrück had worked with Niels Bohr in Copenhagen, Denmark, and believed with Bohr that the riddle of genetics could be solved by physics. Delbrück conceptualized the riddle of life with the replicating of phage within the black box of the cell. But the evidence of the importance of biochemistry in the exploration of genetics was overwhelming and in 1950 Luria, Delbrück’s partner and co-worker, suggested sending James Watson to Europe to learn nucleic acid chemistry.

RJB: I moved around too much. One only receives academic glory by remaining on in one place alone. I do not recommend this unsteadiness to others.

HN&V: What period of time do you consider to be the most productive with regard to your research, and what factors contributed to that productivity?

RJB: The time I spent at Hopkins and Alabama was the most productive, because at Hopkins I had access to the ferment of early surgery and at Alabama I could follow my own trends.

HN&V: Over the course of your lifetime, you have seen many changes in the conduct of medical research – with amazing technological advances and the advent of the computer era. What do you see as the greatest challenge that you consider to be the most productive with regard to your research, and what factors contributed to that productivity? and at Alabama I could follow my own trends.

HN&V: You are not only a renowned cardiologist and researcher, but also an accomplished composer, having written over 250 works for chorus or chamber ensembles, as well as your Missa for full orchestra and chorus. What attracted you to both science and music, and what do you see as parallels and areas of divergence between musical composition and research science?

RJB: I will answer with a quote from an article I published last year in the magazine, Leonardo, which says it best: “Writing music and doing medical research have a common denominator: the creative impulse. Therefore, those of us who are blessed and cursed with this creative urge are motivated to venture in different directions. Writing music is my hobby, being a physician and scientist is my profession. Both are challenges that make life an exciting adventure.”

HN&V: You have written, “I judge my life by the degree of happiness I have received from my work, from my music, and from my family. I have been fortunate in having all my life done what I love most: pursuing the science of medicine and creating music. These have formed the anchor that has given my life stability and a continuous sense of value.” What do you consider your most important legacy?

RJB: I consider my most important legacy the demonstration that one can succeed despite difficulties with obtaining funds and by asserting oneself against ignorance and the ill-will of non-scientists.

Evolution is a popular subject because it deals with mysteries of the origin and future of our species. What is the origin of man? Did he come out of Africa? Is there a blind watchmaker who succeeds in putting together viable mutations? What is the role of adaptation and of natural selection? New scientific definitions have been invented; a scientific jargon that is so different from the original writing of Darwin. Fortunately, within recent years, new facts have come to light mostly through study of the mitochondria, their evolution and contributions to the development of our species. I shall pay tribute to Otto Warburg, an ingenious contributor to our knowledge of mitochondrial function.

Mitochondria are living signposts of evolution. Mitochondria can move, fuse, and divide within a cell. They can occupy as much as 25% of the volume of the cytoplasm. The mammalian mitochondrial genome consists of a circular, double-stranded DNA molecule that has 15,000 base pairs. This is about 1/10,000 of the smallest animal nuclear genome. They possess their own maternally inherited DNA, different from the DNA of the cell nucleus. How did this happen? There is valid evidence that mitochondria once were independent cellular structures which were engulfed by other cells and now live a symbiotic existence within the cells that engulfed them. Smaller bacteria started to live in larger ones but maintained their own chemistry. Thus, the small endocytosed bacteria became mitochondria.

The DNA of the engulfed mitochondria encodes proteins which are essential for the existence and function of these cellular organisms.

Mitochondrial DNA is of special significance for human phylogenetics. It is inherited from the mother, who gets it from her mother and so on for thousands of years. Thus, mitochondrial DNA can be used to trace maternal genealogy. Among Europeans, almost everyone can trace their maternal genealogy to a few women who lived between 100,000 and 200,000 years ago. They join the clan mothers of other parts of the world. They eventually fused to one woman: the mitochondrial Eve. The idea of a separate mitochondrial DNA was expressed by H.G. Wells in 1935: “As the sperm has activated the ovum, its head burrows actually into the substance of the ovum, leaving the tail outside to wiggle for a while and then perish.” Little or none of the male DNA reaches the egg. Knowledge of the maternal inheritance of mitochondrial DNA has been essential in exploring human phylogenetics.

It is impossible to write of the evolution of mitochondria without considering the whole of evolution. Adaptation is the key to mutation and mutation is the backbone of evolution. The causal relationship between adaptation and mutation is a much discussed subject. How does adaptation result in the development of new species? The influence of adaptation on the preservation of species has been recently confirmed by observation of bacteria living on opposite sides of a canyon in Israel. This canyon possesses a hot slope facing south to the sun and a cool northern slope always in the shadow. Bacteria inhabiting the southern slope have evolved a different composition of cell membranes, which makes them withstand heat. Similarly, some fish living in Lake Titicaca at the altitude of 12,530 feet possess a higher oxygen-binding hemoglobin than their cohorts at sea level.

Recently, workers at Stanford found quite clearly an adaptation signal in the genome but this does not explain the effect of adaptation on the genome. Do genetic mutations start out at random and are the beneficial ones selected and perpetuated? Here we encounter the hypothetical handiwork of a blind watchmaker, whose busy hands produce innumerable potential mutations. The viable forms are then cut out for survival by the scissors of natural selection. Yet there are still those of us who believe that there must be a watchmaker with perfect vision, who “does not play dice”, but uses adaptation which results in fitness. Many reject an uncertainty principle in evolution.

It is not surprising that mitochondria were first described and named in Germany in the middle of the 19th century, after Paul Ehrlich introduced fixation and staining methods. In the middle of the 19th century, Schultzes published a 27-page long article about “little muscle bodies and what you have to define as a cell”. Mitochondria were defined as “Muskel Körperchen” (“small muscle bodies”). Historically, it is an interesting paper, not shy to condemn or praise contemporary scientists. These “Muskel Körperchen” were later called mitochondriab by Benda from Berlin. Ashe writes, “I concluded that these granular bodies constitute a cellular element for which I proposed the name “thread bodies or mitochondria”.

It took many years to define mitochondria as the “powerhouse of the cell”. They metabolize carbohydrates and fats to generate water and ATP in steps, referred to as complexes. Reducing elements in the form of electron donors are taken from the Krebs cycle while those from fats are recovered from beta oxidation. The electrons are transferred via NADH or succinate dehydrogenase to a series of five complexes with ubiquinone and cytochrome C acting as electron carriers between the complexes. Nature accomplishes this in a step-wise fashion. Instead of “1 + 1 = 2”, nature’s way is: “1 + 0.2 + 0.2 + 0.2 + 0.2 + 0.2 + 0.2 = 2”. The eventual goal is the creation of energy for the formation of high energy phosphates.
Otto Warburg

Warburg (1883-1970) was one of the most influential scientists of the 20th century, not only because of his contributions but also because of his role as a teacher and role model. Two of his pupils received the Nobel Prize, one of whom was Hans Adolf Krebs, who worked with him for some years. Warburg was born into a distinguished family: his father was a well-known physicist and his mother was of South German stock. His family included a famous art historian, and another relative was a well-known banker. As a high school student, he was prone to mischief. One school report writes, "The pupil Otto Warburg has repeatedly taken part in gross misconduct." Through his father, he became acquainted with Emil Fischer, a leading organic chemist, and the physicist, Walther Nernst.

Warburg decided to become a biologist during his work in the Naples biological station. There he started his work on oxygen consumption of the sea urchin egg. His first work showed that after fertilization, the oxygen consumption of the sea urchin egg increases.

During the First World War, Warburg served in an elite cavalry regiment. At that time, he received a letter from Albert Einstein, who was concerned about his safety. He wrote, "You’ll be surprised to receive a letter from me... I entreat you... that you may assist us in our endeavors to safeguard your life... Yours sincerely, Albert Einstein." After the war, he joined the newly founded Kaiser Wilhelm Institut für Zellphysiologie in Berlin where he remained for the rest of his life.

Warburg accomplished much of his work by improving the technique of manometry and spectroscopy. The Warburg Apparatus is an example. The apparatus differs from early manometers in that the volume of the gas space remains constant so that the pressure is the only variable when a gas is formed or removed at constant temperature, and thus it measures the rate of gas exchange. I recall how the hypnotic clicking of the apparatus contributed to the atmosphere of the laboratory.

In 1913, Warburg described “grana” within the cell, which are the focus of respiration (the mitochondria). This confirmed his idea of “structure-bound” processes in the cell. He also discovered that cyanide inhibits respiration. Since cyanide reacts with heavy metals, Warburg concluded that heavy metal catalysts are involved in respiration. He also tested the effects of carbon monoxide on respiration and found its inhibitory action. He associated this effect with the competition of hemoglobin for oxygen and carbon monoxide.

The contributions of Otto Warburg in biology are numerous and seminal; for example, his work on respiratory enzymes and on the respiration of cancer cells. In 1924, Warburg proposed that “molecular oxygen reacts withivalent iron, whereby there results a higher oxidation state of iron... Molecular oxygen never reacts with the organic substances.” His early work on the role of iron in the respiratory chain has become of paramount importance, as evidenced by recent studies using more sophisticated techniques that have resulted in a major discovery about iron and electron transport; the discovery of metalloprotein containing iron in a non-heme form, which is found in clusters.

Otto Warburg’s father was Jewish, while his mother was an “Aryan”. According to the Nazi Law, he was a “mischling”, belonging to an inferior race and subject to the racial laws of the Third Reich. It is a miracle that he remained in Germany during World War II, and was allowed to continue his work. The explanation was offered that Hitler, being afraid of cancer, believed that Warburg could find a cure for the dreaded disease, and therefore let him work. Although he could not teach, Otto Warburg continued his work during the war in a laboratory outside Berlin. Warburg died in November, 1970 of a pulmonary embolus. Krebs called him eccentric in personal style, aristocratic in outlook in the Greek sense of aristocracy and, in consequence, masterful in his work.

Evolution has honed mitochondria into life sustaining cell structures. Once independent organisms, they now work for the cells that engulfed them. Their work furnishes energy for the existence of cells, organs, and organisms. They have preserved their ability for some independence, they can divide and they carry genetic material from the past to present day. Was it the blind watchmaker who did these wondrous things or was it a presence beyond reality who created the perfect mosaic of life? We can exclaim with the 17th century Danish anatomist Stensen: “What one sees is beautiful, more beautiful is what one knows, but by far the most beautiful things are beyond our knowledge. For who can contemplate the wonderful structure of the organism without asking the question: Who is its author?”

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Richard J. Bing, M.D.
Dear Colleagues,

Hereewith please find the second part of my account of William Harvey’s life and work.

I must admit that my interest in Harvey stems in part from the fact that he was a scholar of classics (as I am). He was fluent in Greek and Latin. He studied classical literature and was a passionate reader of Greek and Roman authors. Both of his books, De Motu Cordis and De Generatione Animalium, were written in Latin. I always remember that the principal of my middle school used to say that the best engineers and scientists come from humanistic schools that emphasize classical subjects. I think he was absolutely right, because classical studies teach one how to think and how to express oneself.

For all practical purposes, physiology was born in the 17th century, and Harvey was one of its fathers. Harvey was a revolutionary. He was the first scholar who dared question traditional beliefs about the heart and the circulation that dated back to Galen, 1500 years earlier. He rejected the common approach of his time (and of the entire Middle Ages), which was to blindly rely on Aristotle and Galen (this approach can be summarized in the mantra “ipse dixit” (“he himself said it” [so it must be true])). This stemmed from his refusal to believe uncritically what he was taught and from his insistence on relying not on the words of Galen, but on his experimental observations, following his reason to its logical conclusions.

In 1628, when Harvey published De Motu Cordis, the medical world was still under the pervasive influence of Galen, who lived in the second century A.D. It is both astounding and befuddling to realize that medical knowledge was controlled by one man for one-and-a-half millennia. Galen was the personal physician of the Emperor Marcus Aurelius, and the most prolific writer of antiquity. He was to medicine what Ptolemy was to astronomy. His theory, which was widely accepted up to the 17th century, postulated that all blood was made in the liver from digested food. Blood – Galen said - leaked continuously from the liver, like water coming down from a fountain; then this blood went to the periphery through the veins and nourished all tissues. (So, according to Galen, blood flows in the veins centrifugally, not centripetally.) Galen also asserted that the tissues absorb and use all blood, so that the liver has to continuously replenish it; thus, there is no circulation, no “recycling”. According to Galen, the function of the right heart is just to nourish the lungs; it is but a different kind of “vein”. Galen further asserts that some of the venous blood finds its way from the right to the left side of the interventricular septum, through what he called “pores” (although these pores were never seen, everybody believed for 1500 years that they were there). Once the venous blood is in the left ventricle, it mixes with the “pneuma”, a spiritual essence inhaled from the air in the lungs. The function of the lungs is to bring in the pneuma, which mixes with the blood and makes it become arterial; the blood is then warmed up by the “innate” heat of the heart, and this mixture is pushed into the arteries to the body. Again, since there is no recirculation, blood must be continually produced in the liver.

To us, free thinkers of the 21st century, it is astounding that these extravagant ideas were not challenged for one-and-a-half millennia. It is a good demonstration of the power of the principle of authority, the mindset that dominated the Middle Ages.

These myths were demolished by Harvey in his book, De Motu Cordis (Figure 1) (the full title of this book is “Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus”[“Anatomical Exercise About the Movement of the Heart and of the Blood in Animals”]). It is one of the most important books ever written, possibly the most important book in the history of medicine (certainly it is so for a cardiovascular scientist). It has changed the history of mankind. De Motu Cordis
did for physiology what Vesalius’ “Fabrica” had done for anatomy in 1543—i.e., it debunked galenism. In De Motu Cordis, you can see the experimental spirit. You can see the beginning of a new way of looking at medicine, of using your own senses and experience and your own reason, rather than relying on the words of Galen or Aristotle. It is a small book—only 72 pages, 5” x 7” inches. It was written in Latin, which at that time was the language of the erudite, and published in Frankfurt, Germany (Harvey hoped to avoid troubles at home by publishing his findings abroad). Figure 1 shows the cover of the original edition of De Motu Cordis. There are only a very few original items left.

In the first part of the book, Harvey studied the movement of the heart. He showed that the heart fills passively and contracts actively, and that during contraction, it expels blood. Then he showed that the expansion of the arteries (the pulse) is synchronous with, and is caused by, the contraction of the heart and by the force of the blood pushed by the heart. You may say: “But that’s obvious”. That’s obvious to us. Incredible though it may appear, for 1500 years everybody thought that the pulse is caused by active expansion of the arteries, or according to the Greeks, by expansion of the “pneuma” that Galen had postulated. By dissecting animals (particularly reptiles, where the heart rate is very slow), Harvey also showed that the atria contract before the ventricles (he described this atrio-ventricular sequence in an interesting manner, stating that the atria “arouse a somnolent heart”). He also pointed out that the pulmonic and aortic valves keep blood from going back into the right and left ventricle, respectively, and the mitral and tricuspid valves keep blood from going back into the atria. In defense of descriptive science, up to this point, all of Harvey’s notions were based on his dissections of animals and description of phenomena, but not on real experiments. (It was what nowadays we would call “descriptive science”; had he submitted his findings to today’s top-tier journals, he probably would have had a tough time!)

Harvey started doing experiments when he addressed the second part of the problem: how does blood go from the heart to the tissues and, then, how does it return to the heart? That’s when, for the first time, he used measurements—or quantitative evidence. The introduction of quantitative evidence into physiology was one of Harvey’s fundamental contributions to medicine. He was the first person to actually use measurements in studies of physiology. He asked himself: “If Galen is right—if the blood is being continuously made from food by the liver—let’s see how much blood the liver actually needs to make.” It is astounding that nobody actually thought to address this obvious question before. By looking at the heart of animals, he estimated that each time the heart beats, it squeezes two ounces of blood during systole (not a bad estimate). Because the heart beats on average 72 times per minute, he calculated that 8,640 ounces (or 540 pounds) of blood should be pumped per hour, which was four times the weight of an average human being at Harvey’s time (though
only ~3 times, alas, in the current epidemic of obesity). Obviously, it was impossible for the liver to make that much blood in one hour. These calculations led Harvey to refute the theory that blood is continuously produced in the liver. He also showed that in the veins, the blood travels centripetally. This is another thing that now seems so obvious that you wonder: why it took 1500 years to figure out that the blood in the veins flows toward the heart, not away from it as Galen had said. Harvey’s teacher, Fabricius, had described the presence of valves in the veins but had no idea what they were for. So Harvey did the obvious experiment (Figure 2). He put a tourniquet around the arm and tried to empty the veins with his finger. He noticed that the veins would always fill from the distal to the proximal part of the arm—not vice versa, indicating that blood flows from the hand towards the shoulder. When he did the same experiment in the neck, he noticed the opposite: the blood never went from the chest to the head but, rather, from the head to the chest. He thus concluded that the blood in the veins always went toward the heart.

(To be continued in the next issue.)

Roberto Bolli, M.D.
President, ISHR
peptides and angiotensin system, renowned speakers discussed a number of new and promising compounds, including cystatin C, ST2, myeloperoxidase, chromogranin, desmin and adrenomedullin. Far beyond the scope of general reviews, the scientific evidence was discussed from several perspectives: major clinical outcomes, metabolic components, pathogenesis, clinical criteria for diagnosis, and tailoring treatment to individuals.

Also discussed at the meeting were several significant developments on targeting new regulatory systems in clinical settings. In a session dedicated to potential new drugs, Markku Nieminen (Helsinki, Finland) showed nice examples in his notable talk that new drugs, such as selective cardiac myosin activators and soluble guanylate cyclase activators, truly deserve clinical attention. Also, we learned from Marco Metra’s (Brescia, Italy) talk that adenosine type 1 receptor antagonists could be another potential target for heart failure therapy. However, iron was clearly the most popular molecule at this meeting. Bringing together a multidisciplinary panel of experts, satellite and main sessions showed iron therapy as a new path to treat heart failure and related anaemia, and these observations were greeted with heightened interest in the packed auditoriums. For those who followed the clinical sessions, a whole track was dedicated to the important issue of end-of-life care and nursing management with case-based presentations. We also gained insights into an unfinished debate on the proper use and indications of implantable devices, such as CRT, ICD, and LVAD, from an excellent talk by Panos Vardas (Heraklion, Greece).

This year Yassine Sassi (Paris, France) and Robin Weir (Glasgow, Scotland) won the Young Investigators Award for the basic and clinical science sections, respectively, for their presentations. We also heard great talks from the runner-ups: Sara McSweeney (Edinburgh, UK) and Saskia Schlossarek (Hamburg, Germany) on basic science and Richard Steinacher (Salzburg, Austria) and Pilar Merlos (Valencia, Spain) on the clinical side. The ISHR European Section/SERVIER Research Fellowship winner was Carlo Tocchetti (Naples, Italy). Finally, the prestigious Outstanding Investigator Award was presented to Mathias Gautel (London, UK), for his seminal work on the analysis of striated muscle proteins involved in cytoskeletal assembly and signalling, and their involvement in heart disease.

It was another year when the lucky ISHR delegates could enjoy the Mediterranean summer. Nice is a sunny, glistening city with a charming old town, just minutes from the Acropolis Congress Centre. It was easy to get around, exploring the Cote d’Azur and the pebble shores of the sea. Also, one could sit in the old town at night, when it comes alive with tourists out for a good time, buskers, restaurant tables spilling out onto the cobblestone streets. After struggling with an enormous fish in the bouillabaisse at Cours Saleya, we can happily agree with the notion that French food is a privilege; and we understand the importance of dietetic management and “heart healthy foods”, which was stressed earlier by Hélène Guibert’s (Nantes, France) talk on the first day of the French section of the meeting.
The Latin American Section of the International Society for Heart Research (ISHR) held its XVII meeting together with the Congress of the Argentine Federation of Cardiology (FAC). The meeting was held at the Buenos Aires Sheraton Hotel located at the epicenter of the city. Holding the meeting jointly with FAC allowed the organizing committee to reach and surpass their goals, which were to achieve a close interaction between basic scientists and clinical cardiologists, and to provide grounds for young investigators, fellows, interns and students to interact with more senior and prestigious researchers and clinicians in the field. These aims were met not only by having invited speakers with clinical background within the symposia organized by ISHR (and vice-versa in the clinical symposia organized by FAC), but also by having a complete day for basic and clinical poster presentations, all of which were moderated by panels of expert professionals. Another objective of this meeting was to call an assembly in order to elect new officers of the Latin American Section of the ISHR (LAISHR).

The meeting was extremely busy; there were at least 150 participants at the activities organized by the ISHR who blended together with over 5000 attendants at the congress of FAC. The program included one day of symposia followed by a second day of poster presentations. Our international guests, Drs Mark Anderson (USA), Stephane Hatem (France), Ariel Escobar (USA), and Julio Copello (USA), as well as our Latin American participants, Drs Alejandro Aiello, Cecilia Mundiña-Weilenmann from Argentina, Homero Rubbo and Walter Reyes Caorsi from Uruguay, gave marvelous talks and stimulated passionate discussions among attendants. Other Latin American participants that acted as coordinators of the symposia or the conference were Drs Paulina Donoso from Chile, Drs Gustavo Perez, Elena Lascano and Alberto Crottogini from Argentina, and Dr Eduardo Migliaro, president of the LAISHR, from Uruguay. Another highlight of the meeting was the midday conference given by Dr Roger Hajjar, “Targeting calcium cycling in heart failure”, which was of great interest to both clinicians and researchers. No less important were the poster sessions, where from among the 44 abstracts presented, a panel of judges, comprised of Drs Claudia Capurro, Belisario Fernandez and Hernán Gomez LLambí, selected the winner of the ISHR International Poster award. The prize was given to the poster titled: “CaMKII-dependent sarcoplasmic reticulum phosphorylations are involved in myocardial necrosis and apoptosis pathway after ischemia/reperfusion”, by Dr M. Salas et al from the Cardiovascular Research Center, La Plata, Argentina.

During the Latin American Section’s assembly, Dr Martin Vila Petroff from La Plata, Argentina was proposed and elected president for the upcoming period. Dr Vila Petroff was honored to receive this distinction and made a summary of the future goals of the LAISHR. Among these is the goal to have the 2010 annual meeting of the LAISHR within the World Congress of the International Society in Kyoto, Japan. For this purpose, the LAISHR has joined forces with the Australasian Section of the ISHR, and has organized several symposia which have been accepted by the Congress Chair, Dr Matt Hori. Another objective expressed by Dr Vila Petroff was the commitment of the LAISHR to pursue the possibility of having the 2016 World Congress in Buenos Aires, Argentina. This would be a fantastic opportunity to be able to share Latin American science with the broader international community, to give all members of the LAISHR the opportunity to interact with international leaders in the field, as well as to provide the members of the International ISHR with a new and unique location with outstanding geography, social traditions, and touring opportunities.

During our meeting, we also had time to relax and enjoy a stupendous closing dinner with all the invited speakers and a night out in the city with Dr Mark Anderson and his father which culminated at a tango show in one of the oldest and most traditional coffee shops in Buenos Aires.

(continued on page 14)
Dear Colleagues,

It is my great honor and pleasure to host the XX World Congress of the International Society of Heart Research on May 13 – 16, 2010, in Kyoto. The preparation for the Congress is going well and registration has already started in September. As the President of the World Congress, I cordially invite you to the Congress in the most beautiful city in Japan.

The main theme of the Congress is “Paradigm Shift to Integrated Cardiology – Gene, Function and Life”, which covers discussion of a wide variety of research topics relevant to understanding the cardiovascular system in health and disease and the application of this knowledge to clinical cardiology. At the World Congress, I would like to stress the importance of discussions between basic scientists and clinicians at the same table, with an over-arching theme of “Bringing Clinicians and Basic Scientists Together Towards Integrated Cardiology”. A unique feature of the Kyoto Congress will be the incorporation of Section Meetings within the Congress Program. Each Section will have an opportunity to hold business meetings and other Section activities, including a session in their own language if desired.

The Scientific Program includes:

- A total of 48 Symposia, including 23 symposia sponsored by ISHR International, 10 Section-sponsored symposia (Australasian, Chinese, European, Japanese, Latin American, North American) and 15 industry-sponsored symposia organized by the Congress Committee. Three sessions are titled as memorial sessions for Profs. Norman Alpert, Howard Morgan, and Yoshio Ito.
- A Novel Laureate Lecture by Oliver Smithies, University of North Carolina at Chapel Hill, on embryonic cell and gene targeting technology.
- A Special Lecture by Shinya Yamanaka, Kyoto University, on induced pluripotent stem (iPS) cells.
- ISHR Award Lectures, including
  1. Distinguished Lecture Awards: - Keith Reimer Distinguished Lecture - Janice Pfeffer Distinguished Lecture - President’s Distinguished Lecture.
  2. Outstanding Investigator Award
  3. Research Achievement Award
  4. Peter Harris Distinguished Scientist Award
  5. Distinguished Leader Award
- Free communications and moderated poster sessions
- The Richard J. Bing Young Investigator Award Competition
- Morning Tutorial Lectures for early career researchers
- Luncheon Seminars
- Evening Satellite Seminars

The contents of the symposia will span from basic research to translational and clinical research, from gene to function who generously shared their knowledge with the younger crowd in a fertile scientific exchange, and thus made possible the accomplishment of the major objective of the meeting: to generate a learning environment for young people. Our section continues to grow and has exciting plans for the future.

Alicia Mattiazzi, MD
President of the Organizing Committee,
La Plata, Argentina

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and life; and will cover a broad range of topics, including genome, intracellular organelles, ion channels, membrane receptors, signal transduction, cardiovascular development, angiogenesis, cellular damage and protection, cardiovascular diseases, atherosclerosis, stem cells and regeneration, regenerative therapy, clinical advances in cardiology and novel therapeutic targets.

Enjoy the Social Program
The social programs include the following events:

- A get-together on the evening of first day - Thursday, May 13
- A short excursion to enjoy the Japanese traditional “Aoi Festival.”- Saturday, May 15. This festival is one of the most graceful festivals in Japan, and it has been well preserved since the eighth century.
- Optional sight-seeing tours. Kyoto is home to nearly 2000 Buddhist temples and shrines, reflecting its long history as the cultural and religious center of Japan. More than 60 museums throughout the city offer visitors the opportunity to view priceless works of art and important cultural objects. Kyoto is also a panorama of the changing seasons, and the timing of the Congress will allow participants to enjoy the lush greenery of early summer.
- Travel Awards are available
The ISHR will provide travel awards for young investigators from all participating ISHR Sections, with the award recipients to be selected by the relevant Section executives.

Registration and Abstract Submission
Registration and hotel reservation is available on the Congress home page (www.ishr2010.com). There are plenty of hotels in Kyoto with very reasonable prices, offering a wide variety of choices.

We are expecting a total of 2000 participants from all over the world, considering that the major ISHR Sections will hold their Section meetings in conjunction with the ISHR World Congress. You are cordially invited to share in the excitement and success of the 2010 World Congress in Kyoto!

Masatsugu Hori, M.D., Ph.D.
President, the ISHR XX World Congress;
President, Osaka Medical Center for Cancer and Cardiovascular Diseases;
Professor Emeritus of Osaka University Graduate School of Medicine

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Important Dates
Deadline of abstract submission:
November 30, 2009
Deadline of advance registration:
March 31, 2010
Deadline of hotel reservation:
April 15, 2010
HEART NEWS AND VIEWS

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Visit the Web version at www.dialogues-cvm.org

The forthcoming issue, devoted to FRIENDS & FOES OF THE CARDIAC MYOCYTE will feature articles by:

R. Ferrari; F. Crea and G. A. Lanza;
N. Danchin; D. Matthews and others

For further information on Dialogues in Cardiovascular Medicine please contact:

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