A Tribute to Franz Halberg, MD

Dr Franz Halberg, a towering figure in cardiovascular research who founded and developed the new science of modernized chronobiology, passed away a month shy of 94 years of age on June 9, 2013. The chronobiological vocabulary and ambulatory monitoring methods were his original conceptions. Dr Halberg’s international stature and contributions to hypertension research through chronobiological methods were monumental, and we pay our respects to this outstanding scientist, educator, and scientific father and his dedication to the advancement of heart attack and stroke victims, hypertension research through chronobiological methods in individual monitoring, analyses, and interpretation in variations as a function of Time.

In the early stages of his professional life, his keen observations of biological variations in living beings enabled him to find periodicities shared between biological systems and their broad environments, influenced by the sun and the cosmos, leading to chronomics (broad time structures beyond circadian rhythms). Biological time structures (clock hours) and chronomes are considered essential parameters in blood pressure monitoring, as well as in neurohormonal rhythms and other organs/systemic variations. The impact Dr Halberg had in science stemmed not only from his original findings but also from his vision of their implications that led beyond a scientific breakthrough to a new way of thinking as a truly great scientist. His lifetime of hard work after his medical education and training seeking optimal configurations of the time structure has contributed to some of the greatest advancements in the modern scientific world and standardized clinical practice, especially in hypertension. His research on timing guided by the circadian clock observed early changes in blood pressure and heart rate variability, especially large fluctuations in amplitudes and shift changes in peak hours among heart attack and stroke victims, and cancer patients. The changed rhythms can be detected during subclinical stages by ambulatory monitoring, and it is critical to detect changes at an early stage to start planning prevention and treatments for a cure before more advanced clinical stages. These include individualized timed sampling according to endogenous circadian secretion and administration of medications for the most effective time-based individual rhythm for improved efficacy with reduced adversity. Thus, appropriate circadian timed treatment makes controlled malignant hypertension manageable and reduces the risk of stroke and other adverse cardiovascular events. Although this giant step in pioneering individual chronobiological monitoring and analytical methods in cardiovascular research explored genetic and epigenetic influences in the biological system, the current individual ambulatory monitoring of cardiovascular parameters can be limited to apply on a large clinical scale. Thus, scientists are continuing to modify and improve the monitoring methodology with new advancements in circadian individual monitoring methods.

In 1959, Dr Halberg first coined the term circadian. He recognized the important role played by the cell’s RNA and DNA cycles in complementing the hypothalamic–pituitary–adrenal system as a mediator of photic inputs, and subsequently added pineal gland feedback in understanding that there are endogenous physiological networks that respond to the cosmos. Since then, the word circadian has become a standard expression in the scientific description of the daily rhythm and part of the established vocabulary of cardiovascular and hypertension researchers. He showed that rhythmic variations in time in various biological systems are partly endogenous, which influence all living beings and can be manipulated by environmental synchronizers. Circaseptan (of about 7-day rhythms), circannual (of about-yearly rhythms), and many more expressive chronobiological terms were coined, and methods in monitoring ambulatory blood pressure and heart rate were developed. His methods in ambulatory blood pressure monitoring have become the standard in experimental and clinical practice nowadays. His approach to time variations and subclinical physiological changes reset modern clinical practice.

Dr Halberg was born and raised in Bistritz, Romania. He attended the University of Cluj in Koloszvar and received his medical degree in 1943. After working as a scientific/University assistant in the Department of Anatomy at the University of Innsbruck, he came to the United States in 1948 for postgraduate fellowship, working at Harvard Medical School/the Peter Bent Brigham Hospital in Boston with a World Health Organization fellowship in clinical endocrinology. He joined the faculty at the University of Minnesota Medical School in 1949, where he spent the remainder of his career, as faculty and founding/leading the Chronobiology Laboratory in the Department of Laboratory Medicine and Pathology. He became a professor of multiple departments in the medical school system, including the Departments of Pathology, Physiology, Biology, Bioengineering, and...
Oral Medicine at the University of Minnesota, and in addition to Halberg Chronobiology Center at the University of Minnesota Medical School campus, he led multiple Halberg Chronobiology Centers, officially affiliated with (1) the René Descartes University in Paris (France); (2) the Faculty of Computer Science at the Autonomous University in Madrid (Spain); (3) the University of Krakow (Poland); (4) the University of L’Aquila (Italy); (5) the University of Ferrara (Italy); (6) the University of Szeged (Hungary); (7) Masaryk University (Brno, Czech Republic); (8) Tyumen State Medical Institute (Tyumen, Russia); (9) People’s Friendship University of Russia (Moscow, Russia); and (10) the Therapeutic Society of Moscow (Russia). Dr Halberg received medals from the University of Montpellier (France) and honorary doctorates from the University of Montpellier (France), Ferrara (Italy), Tyumen State Medical Institute (Tyumen, Russia), Masaryk University (Brno, Czech Republic), University of L’Aquila (Italy), and People’s Friendship University of Russia (Moscow, Russia).

Dr Halberg’s lifetime accomplishments are summarized in his >3600 scientific publications in cooperation with colleagues around the world, bridging disciplines to establish individualized healthcare. It is no exaggeration to call him legendary and place him among the greatest figures in the history of cardiovascular research, and his 1969 published article has become a Citation Classic.2 Dr Halberg is regarded as the father of modern chronobiology in cardiovascular biomedical research and timed therapy. Numerous scientists were trained in his laboratory >70 years of his chronobiological methods in cardiovascular research. Many professional members worldwide called him their mentor and turned to him for advice, from study design and data analysis to the interpretation of results in the time dimension. Minnesota Medicine called him Father Time, and colleagues in Russia and Azerbaijan honored him as Lord of Time. Dr Halberg served for more than 10 years as President of the International Society for the Study of Biological Rhythms. After the Society’s name was changed in 1971 to the International Society for Chronobiology (ISC), his service was continued as the President of ISC for another 15 years to shape the ISC as a permanent world stage professional society. As Editor-in-Chief of the journal Chronobiologia, which published between 1974 and 1994, later becoming the official journal of the ISC, he paid tribute to Arthur Jores4,5 and invited Kalmus6 to recount the Foundation Meeting of ISC. In 2010, Dr Halberg started a new medical journal, the World Heart Journal, dealing with various subjects in the biological clock, especially in cardiovascular research, and served as Editor-in-Chief until his passing.

Dr Halberg’s endeavors earned him numerous awards. He was a Fellow of the New York Academy of Science and of the American Association for the Advancement of Science and an honorary member of the Romanian Academies of Science and Medical Sciences and was elected as a Corresponding Member of the French National Academy of Medicine. He was a recipient of the prestigious Arnold-Lucius-Gesell Prize from the Theodor-Hellbrugge Foundation and an elected member of the prestigious Leibniz Society and of the International Academy of Science. He was one of the last 2 recipients of a lifetime career award from the National Institutes of Health in the United States. His achievements in the new field of chronomics earned him the O.Yu. Schmidt Medal and diploma for outstanding merits in the development of geophysics, the first such award given to a nonphysicist. Dr Halberg was the founding Fellow of the Board of Directors of the International College of Cardiology and International College of Nutrition, placing an emphasis on energy metabolism and time of eating in various population groups, which may produce benefits in the primordial prevention of cardiovascular and other chronic diseases.7–9

As our scientific father figure, Dr Halberg was hard-working and imposing but also a consummate gentleman. He was revered as a teacher, mentor, and advocate for students and young scholars, especially those coming from overseas to study under his mentorship. His many successes in completing his medical education and achieving numerous scientific accomplishments are even more meaningful in the light of the adversity he faced in war-torn Europe during World War II.

He was always there to advocate for students and young scientists, especially those coming from foreign countries. Dr Halberg and his wife Erna Halberg frequently served as a host family for students and overseas scholars for holiday celebrations, showing nothing but the best hospitality with special home-made holiday meals year after year. Even after Mrs Halberg’s passing, Dr Halberg continued the tradition well beyond his 90th birthday. We still do not know how they managed to prepare such large holiday dinners with regularity for such a large group of laboratory members. Many foreign students and visiting scholars did not drive, and Dr Halberg himself frequently drove everyone from the laboratory to his home and back to everyone’s respective homes.

The stories go on and on. Many of those he helped were far away from home, and Dr Halberg and his family provided for them and protected them as their extended family. He was always there for students facing difficulty to help encourage them. When they were hospitalized, Dr Halberg took time out of his busy schedule to visit and discussed the best treatment options with their doctors. For high school students who participated in summer research programs in Dr Halberg’s chronobiology research laboratory, they monitored their own cardiovascular profiles with great pride and analyzed their own data, publishing their summer work with Dr Halberg. Dr Halberg extended unique care and patience to reach out effectively to diverse age groups. After learning of the importance in timing of cardiovascular profiles, these students have often continued to use chronobiological methods in their practice and in writing scientific publications. They express great respect for Dr Halberg as an invaluable contributor to their learning experiences.

In Dr Halberg’s mind, nothing was impossible. His fellow scientists, including many students from high schools and colleges and scholars around the world, have worn instruments to monitor blood pressure and heart rate every 30 minutes so analyze circadian rhythms. This was the beginning of modern medicine acknowledging biological rhythm variations in all living creatures, discovered and established with
chronobiological methods for the current understanding of timing in various endogenous influences, which can be modified by the environment. He pioneered the analog computer system before the digital computer era for the application of large-scale computation in comprehensive analytical methods for data collected around the clock, as well as the individual ambulatory monitoring in cardiovascular profiles and all other biological systems. In the 1960s, computer-linked data analysis was primitive, such that the data were entered starting with punched cards to be read by computers. Many students and scholars, who never had any computer knowledge before coming to his research laboratory, became acquainted with computer-linked chronobiological data analyses from an early stage under his direction. The linear least-squares rhythmometry analytical method, adopted during his early stage of data analysis, is still used as one of the core chronobiological analytical methods.

Dr Halberg’s contributions as an educator benefitted not only his fellow scientists but also next generation scientists in supporting student education and their activities. When high school students asked him to take a break for tennis, he again accompanied them. Career development toward medicine should ideally start during high school. Dr Halberg established that example well. His devotion to science and education in his spirit and his courage captivated students, professionals, politicians, business leaders, and all who knew him. Thus, as an inspiring role model, he taught us not only science and medicine but also about life through his example of courage and endurance and dedication to the highest standards through his spoken and unspoken expressions. Dr Halberg was like a father to many young members, such that many of us do not refer to him on a first name basis. His devotion to his family and extended educational efforts also led his two lovely physician daughters into academic medicine and professional family life of Dr Halberg and his wife. Even approaching the age of 94 years, he was still active 7 days a week at the Halberg Chronobiology Center at the University of Minnesota Medical School. Until his last breath, Dr Halberg was grading student papers with his comments and working on timing for diagnosis, prognosis, treatment, and foremost prevention in clinical practice.

His work is continued at the multiple Halberg Chronobiology Centers around the world. His remarkable accomplishments and innovative approach led to many new scientific concepts in cardiovascular research and treatment. As a peerless scientific colleague and mentor, we will miss him very much but will remember him through his everlasting legacy. He will remain in our memories as a shining star of the best of humankind, who motivated, stimulated, and inspired us with his devotion to education, his warm and generous spirit, and his courage. May he rest in everlasting peace.

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References
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