

In Memoriam:

Lionel H. Opie, MD

(1933–2020)

The world's cardiovascular community lost one of its best when Lionel H. Opie, MD, DPhil, DSc, died in Cape Town, South Africa, on 20 February 2020 at the age of 86. The cause of his death was pneumonia.

Although frail for the last few years of his life, for more than 5 decades Lionel was a strong champion for the unity of cardiovascular physiology, metabolism, and pharmacology, the 3 disciplines in which he excelled as an exemplary physician-scientist treating patients into his 80s. Lionel was known and respected among his many colleagues around the world for his remarkable intellect and perfect manners.

He was born on 6 May 1933 in Hanover in the Karoo region of South Africa, where his father practiced as a district surgeon. He was educated at Bishops Diocesan College, an all-boys high school in Rondebosch, Cape Town. He studied medicine at the University of Cape Town (UCT), graduating in 1955 with first class honors and receiving the university's gold medal. Lionel was a Rhodes Scholar at Oxford University from 1956 to 1959, where he earned his Doctor of Philosophy degree with a thesis entitled *On the Physiology of Artificial Respiration*. His Oxford years were followed by 2 years of research on cardiac metabolism at Harvard Medical School in Boston before returning to England. While in England, he was mentored by 2 Nobel Prize winners: Sir Hans Krebs (who discovered the 2 most important metabolic cycles) and Sir Ernst Chain (who shared the Nobel Prize with Fleming and Florey for the discovery of penicillin).

In 1971, Lionel returned to Groote Schuur Hospital at UCT, nearly 4 years after Christiaan Barnard had performed the first successful transplant of a human heart there. At the time, the eyes of the world were on UCT and its pioneering medical research. As a committed physician-scientist, Lionel expanded his basic science knowledge of cardiac metabolism by developing a research program with a focus on the pathophysiology of myocardial ischemia. He complemented his interests in basic science with a strong inclination toward clinical research. He founded the Hypertension Clinic at Groote Schuur Hospital in the 1980s and worked there every week until he was 80. In addition, he led sessions in the hospital's Cardiac Clinic for many years and saw patients privately in the UCT Academic Hospital until he gave up all clinical work, also at age 80.

In 1997, Lionel partnered with Professor Derek Yellon from University College London and founded the Hatter Institute for Cardiovascular Research at UCT, which evolved into a model for cardiovascular research exchanges between Africa and Europe. He organized its acclaimed annual conference series, *Cardiology at the Limits*, and directed the institute until 2010.

Dr. Opie's contributions to the cardiovascular sciences mirror the advances in cardiology and biochemistry during his lifetime. Lionel distinguished himself in the



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“golden age” of metabolism when biochemistry was strictly quantitative and deeply rooted in organic chemistry. This golden age ended in the late 1960s with the general acceptance of future Nobel Prize winner Peter Mitchell’s chemiosmotic theory—that the mechanism responsible for adenosine triphosphate (ATP) production is oxidative phosphorylation of adenosine diphosphate (ADP) and that this forms the backbone of energy transfer in the heart with its enormous need for energy. Lionel’s work focused on the heart’s responses to a lack of oxygen, the basis of ischemic heart disease; on the cellular metabolism of calcium ions; and on the role of cyclic adenosine monophosphate (cAMP) in cardiac electrical instability and arrhythmias. All 3 areas of research are inextricably linked in their clinical relevance.

In his first major paper, and following in the footsteps of Richard Bing (1909–2011), Lionel hypothesized that the heart is a metabolic omnivore that oxidizes glucose when stressed and converts glucose to lactate when deprived of oxygen. This was also the content of a lecture Lionel presented in 1975 at the Peter Bent Brigham Hospital in Boston (now Brigham and Women’s Hospital), when I first met him while I was a cardiology fellow in my second year. On 29 May 1975, I wrote in my lecture notes, “Glycolytic ATP production can increase 5-fold with ischemia,” and I listed 8 different possible modes of action of glucose, insulin, and potassium presented by Lionel. To this day, 45 years later, I remember my first impressions of the lanky young scientist: hair down to his shoulders and stunningly eloquent. Today, we would call such a person a rock star. And a rock star of medical science he remained throughout his life—his hair eventually trimmed shorter, his writings even more elegant, and his speech even more eloquent, peppered with a good sense of humor.

Our paths crossed many more times over the years as we engaged in sometimes heated, but always amicable, discussions. Perhaps Lionel’s most important discovery, with his colleague Wieland Gevers at UCT, was the origin of protons (H^+) from the hydrolysis of ATP to ADP + inorganic phosphate (P_i). I got to know Lionel better in 1996 when we were both on sabbatical in the same laboratory at Oxford—Lionel writing (and in frequent contact with his office in Cape Town) and I teaching students how to perfuse isolated working hearts. We both cherished the bright students in the laboratory, and we both tried our best to get them “hooked” on cardiac metabolism. This was a challenge in the midst of the molecular revolution in cardiovascular research. Time has told, however, that we may have succeeded, at least in some small measure.

Lionel represented South Africa, perhaps even the whole African continent, in the world. Most notable were his stints as a visiting professor at Stanford University

(1984–1998) and as a visiting research fellow at Merton College in Oxford (1997). In 2005, he was awarded the Order of Mapungubwe, the highest presidential award in South Africa. Lionel also received honorary doctorates from Stellenbosch University (one of South Africa’s premier universities) and the University of Copenhagen.

Despite a long list of original publications, Lionel’s most lasting contributions to cardiology are undoubtedly his masterful reviews and his textbooks. Perhaps most popular is the book *Drugs for the Heart*, which many have dubbed the “Bible of Cardiovascular Pharmacology” and is now in its 8th edition. Also highly regarded is his book *Heart Physiology: From Cell to Circulation*, which, through 4 editions, continues to provide fundamental knowledge with emphasis on the cellular basis of cardiac function in a clearly written text enhanced by nearly 600 of Lionel’s own line drawings. Students and fellows call it the “Opie Book.” To be quoted by Dr. Opie elevated the work of many an investigator to “textbook level”—an immeasurable honor in a budding career.

It was Lionel’s genius to bring people together—early in his career as a founding editor of the *Journal of Molecular and Cellular Cardiology* in 1970 and then 3 decades later, in 2000, as a founder of the Society of Heart and Vascular Metabolism, together with Margie Chandler, Gary Lopaschuk, and the late Bill Stanley.

I am not certain whether Lionel ever visited the Texas Medical Center in Houston, but he did send one of his most talented trainees, Faadiel Essop. Faadiel spent a year in my laboratory as a Fulbright Scholar and is now Director of the Centre for Cardio-Metabolic Research in Africa (CARMA) at Stellenbosch University.

Lionel is survived by his wife of more than 50 years, Carol Opie (Sancroft-Baker); their 2 daughters, Jessica and Amelia; and 2 grandchildren, Liam and Eva. He had such an enduring personality (despite physical incapacitation in his later years) that we thought Lionel would be around forever, cheering us on in our academic journeys to excel as physician-scientists. Now he is gone. We shall miss him dearly, asking ourselves who will pick up Lionel’s mantle?

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*Heinrich Taegtmeyer, MD, DPhil,
Professor of Medicine, McGovern Medical School,
The University of Texas Health Science Center;
Houston*