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Tribute to Michael O'Rourke (1937–2024): A Collective Tribute to a Colleague, Friend and Mentor

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Abstract

A collective tribute to a colleague, friend, and mentor from those that have known him through his journey of the meanderings of the arterial pulse in health and disease; a journey that extended beyond borders and confines, with far-reaching personal and global impact. The Editorial Board of the Artery Research Journal and the Executive Committee of the Artery Society extend their due respects to Prof. Michael O'Rourke.

Keywords Michael O'Rourke, Central haemodynamics, Arterial function, Cardiovascular disease

Michael O'Rourke

28 July 1937 – 5 February 2024

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disease; a journey that extended beyond borders and confines, with far-reaching personal and global impact.

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1 Alberto Avolio

1.1 A Fantastic Voyage

On the occasion of the funeral of Michael O'Rourke, my life-long colleague, friend, and mentor, I was asked by the family to deliver a eulogy on his international legacy, relationships, influence and achievements. I closed the eulogy with the following passage:

In late 1972, during the first year of my PhD, I was speaking to Professor John Hickie in his office at St Vincent's Hospital. I was wanting to enquire about potential cardiovascular projects. On the way out, he said I could also check with Dr Michael O'Rourke, whose office was a few doors down the corridor. The door looked shut and so I kept on walking. But as I walked past the door, I noticed it was slightly ajar. I knocked and walked in.

Sometimes I wonder what life might have been like if that door had not been left ajar, and whether I would have been a passenger on the same ship on this fantastic voyage across the vast oceans over the past 50 years, and come ashore here today to tell the story with great affection.

In this collective tribute, the story of Michael's intellectual, professional and personal journey along the many streams and tributaries of the arterial pulse and its intriguing biophysical and clinical manifestations is told with great affection and admiration by a group of individuals whose lives formed an integral and intimate part of the many phases of that journey. Each narrative is a personal reflection of how the various levels of interaction with Michael have resulted in an indelible effect on the life-course of professional careers and personal endeavours. In assembling this collection, I have attempted to arrange the tributes, as best as possible, in the chronological order in which individuals interacted with Michael, to give expression to the formation and development of his concepts and ideas that formed the great corpus of his extensive contributions to arterial haemodynamics and the arterial pulse in health and disease, to which we all humbly and respectfully pay great homage.

Michael Francis O'Rourke was born in Sydney on 28 July 1937. His father had a business that made equipment for automobiles. His memories of post-war survival and family challenges laid the basic groundwork of the sheer determination and persistence that remained with him throughout his life. The manner in which he lost his mother at the age of twelve due to cancer made him acutely aware that she might have survived if the doctor "had done things better". This was one of the main driving forces to study medicine and formed the basis of his lifelong aim to always strive to do things better to advance knowledge and improve the welfare of patients.

Following his medical degree (MBBS, 1960), he was a resident and registrar in anaesthesia at St. Vincent's Hospital, Sydney. From 1963 to 1966, he undertook postgraduate research in the Department of Physiology at the University of Sydney where he obtained his Doctor of Medicine (MD) under the supervision of Professor Michael Taylor. It was during this critical and formative period that he was inspired by the work of Taylor in Sydney and Donald McDonald (clinician and physiologist) and John Womersley (mathematician), in Britain. Their work on the biophysical relationship of blood pressure and flow in arteries presented novel ways of interpreting the information in the arterial pulse.

Michael was captivated by the rewarding engagement in interdisciplinary science and by the novel concepts of arterial impedance and wave propagation, which were investigated in experimental animals and then applied to humans; concepts that were able to explain the influence of the stiffness of large arteries on blood pressure, and which formed the basis of most of his published work throughout his lifetime. This approach promoted

the effects of wave reflection, such that pulse pressure could be reduced by decreasing the magnitude or delaying refection to occur during diastole. (This biophysical concept enabled him to be the first to introduce the intra-aortic balloon counterpulsation technique in Australia in the mid-1970s).

The basic and novel concepts in haemodynamics learned in his early years of research were expanded during his post-doctoral studies with Bill Milnor at Johns Hopkins University in Baltimore, USA in 1966–1968, where he first became acquainted with Wilmer Nichols, then a student of McDonald at Birmingham, Alabama. This friendship lasted a lifetime, and Nichols and O'Rourke have been the editors of five of the seven editions of the seminal textbook on haemodynamics "McDonald's Blood Flow in Arteries" [1], with the last edition published in 2022, some 60 years after McDonald's original monograph.

Michael's enthusiastic approach to make use of the "experiments of nature" to understand cardiovascular physiology led to experiments in diverse animals of different body size and shape to quantify the relationships of arterial pressure an flow. Many of our joint publications include experiments in guinea pigs, rabbits, sheep, dogs, wombats, snakes and kangaroos. The kangaroo waveforms are sometimes used in physiology classes to illustrate how high-intensity wave reflection can result in peak pressure in the cardiac cycle to occur in diastole (as can occur in counterpulsation).

The pursuit to understand the impact of large arteries on the development of elevated blood pressure with age led to population studies in China, showing the effects of age-related changes in arterial stiffness on the prevalence of hypertension. These studies, which have been critical to my own professional career, established the relevance of arterial stiffness and vascular ageing as significant factors that have been shown by many other investigators to be independent predictors of cardiovascular risk. The relevance of large arteries in hypertension was extensively promoted by Michel Safar and many of his students in Paris, who made seminal global contributions as part of the "Paris Vascular School". (Both Michael and Michel left the journey within a week of each other).

Michael held unwavering respect for insightful work done by others and at other times. He wrote profusely on the work done at Guy's Hospital in London around the 1870s by Frederick Akbar Mahomed who promoted the use of the sphygmograph for registration of the atrial pulse, (making the pulse the first parameter in medicine to be ever graphically recorded). This was used to diagnose disturbances in cardiovascular physiology, including hypertension, long before blood pressure could be measured with the Riva Rocci and Korotkoff techniques using the brachial cuff sphygmomanometer. Michael's ideas led to the addition of the pulse to the conventional measurement of blood pressure measurement, thus combining sphygmography with sphygmomanometry, which culminated in him being granted a US patent for the technology and in founding a company in 1994 to produce devices based on pulse wave analysis. The company's SphygmoCor system (AtCor Medical, now Cardiex) for measuring arterial stiffness and central aortic pressure noninvasively has been the global industry standard for many years.

In addition to the enthusiastic pursuit of novel ideas in haemodynamics, Michael was an academic and specialist physician. He became a specialist cardiologist with special interests in hypertension, coronary artery disease, prehospital coronary care, community defibrillation, effects of ageing on heart and arteries. He established the Coronary Care Unit at St Vincent's Hospital in the 1970s, an initiative that was used as a template for the rest of Australia. He investigated digoxin toxicity and conducted a pivotal multicentre trial of recombinant tissue plasminogen activator (rtPA) agents as therapy for heart attacks. He was the first to introduce defibrillators in aeroplanes and in the New South Wales Ambulance Service, with the first public access taken up by Qantas. In 1989 he was recognised for his contribution to medical teaching and research with a Member of the Order of Australia (AM) with the citation *"For Service to Medicine, particularly in the care of persons affected by coronary disease, and in the training of Paramedic staff."* He was made Fellow of the Royal Australasian College of Physicians, the Royal College of Physicians in Ireland (Hon), the Cardiac Society of Australia and New Zealand, the European Society of Cardiology, the American Heart Association, and the American College of Cardiology. During the period 1981–89, he was Editor-in-Chief of the *Australian & New Zealand Journal of Medicine*.

Although Michael was relatively successful in obtaining research funding early in his career, his track record does not boast many large research grants. However, he has left an unparalleled legacy of a published body of research work consisting of authoritative books, book chapters and over 500 articles, and some, at times, piercing letters to editors, fiercely defending his core ideas. He made efficacious use of some generous personal patient bequests and departmental funds that were able to provide the essential research assistant support. It was an active decision at some point in his career path not to strive for highly competitive grant funding. In his own way, he felt he could "do things better" this way.

Michael's final venture in the latter years was the application of pulsatile haemodynamic phenomena to the brain, saying the "the brain can be destroyed by the pulse". As an expressive form of closure and completion of his

intellectual journey, illustrations in his final publication in 2020 include the very same ones that appear in his first publications from his MD thesis in 1966. And in the short abstract of the article he writes that "*..principles established for function of the human systemic circulation (pulsatile flow at input and steady flow at output in capillaries) can also apply to the brain, and … such knowledge can be applied in some clinical conditions including development of dementia in older subjects*". His description of the intimate interaction of the arterial pulse and the brain was his prescient final trajectory of the journey that was abruptly truncated by acute myloid leukaemia on 5 February 2024.

It has been an immense privilege to organise and collate this collective tribute for Michael O'Rourke with whom I have had a long and continuous collaboration over the last 50 years, a voyage in which we have stood by each other's side through calm seas and roaring tempests. This collective tribute gives voice to the deep gratitude of the individuals who expressed their personal affection and to that of many others on different shores who have benefited greatly from Michael's intrinsic passion for insightful knowledge, the openness to learn from others and the strive to always try to do things better. And this has left us all with an indelible life impression.

***Professor Alberto Avolio**, Professor Emeritus, Faculty of Medicine, Health and Human Sciences, Macquarie University, Sydney, Australia*

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2 Barry Gow

2.1 Michael O'Rourke and Our Mutual Association with Other Key Players

My friendship with Michael O'Rourke began in the early 1960s in the Department of Physiology at the University of Sydney. We were both doctoral students under the supervision of Michael Taylor (MGT), an intellectually gifted medical graduate from Adelaide and a postdoctoral student of Donald McDonald in England, a pioneer and authority in the field of arterial haemodynamics. I am truly grateful to MGT for accepting me and providing many opportunities and, as well, engendering a love for mathematics and English. Unfortunately he could, at times, be pompous and aloof, insisting his postgraduate students address him as "Sir". At meetings he could be harsh in his criticism of a presentation, whereas later in America I found that one could be critical without being unkind. Nonetheless, I enjoyed a friendly relationship with MGT and gladly appreciated his intellect, wit and many skills which included music and art. On day one, when MGT showed me around his various labs, I met Ted Cleary, later to become an expert in elastin, and also Brian Learoyd who published the well-cited study of elasticity of human arteries. Learoyd's apparatus for measuring arterial diameter was modelled on that of Derek Bergel, another student of Donald McDonald. Observing the large size and structure of the apparatus, I naively suggested that it might be possible to make a small device to attach to an exposed artery to measure diameter in a living animal; and so my PhD project was born.

Michael was already measuring pulsatile blood flow with a recently acquired electromagnetic flowmeter. This instrument had only two flow probes, one for large arteries and one for small. It was obviously essential that we acquire additional probes to cater for vessel size. So we made our own probes from copper wire and dental acrylic resin, a material with which I had had some experience, from my degree and training in dentistry. It was from Michael that I learnt animal surgery when assisting him to apply the flow probes to the aortas of anaesthetised dogs. MGT had purchased an FM magnetic tape recorder, a digital-to-analogue converter and a punch paper tape machine which allowed us to digitise pressure and flow waves and later diameter waves as well. (I readily recall the rhythmic chatter of the paper punch!). The recorded waves were subjected to Fourier analysis to yield measurements of modulus and phase. This signal processing was initially done on Sydney University's first digital computer SILLIAC (one of the first computers in Australia) and later its replacement, an English Electric KDF9 for which MGT wrote a program to carry out spectral analysis of the waves. I confess I remember being somewhat envious of Michael's success at this time because his results for the relation of vascular impedance with frequency were consistent with what one might expect of a linear system. Conversely, because diameter has a nonlinear relation to pressure which was not fully appreciated then, the phase angle was seen to swing from expected lag to an unexplainable lead for higher harmonics.

Michael, it seemed to me, had a wonderful relationship with his supervisor. He finished his MD thesis, and with his wife Margaret flew off to Baltimore to study with Bill Milnor in the Department of Physiology at Johns Hopkins University. Meanwhile, I struggled with my arterial viscoelasticity and non-linearity problems, but I did have a lot of fun learning to program the KDF9 which allowed me to deal with them. For my postdoc, at MGT's suggestion I joined Donald Fry's group at NIH in Bethesda, Maryland, USA, where I collaborated with Dali Patel and Ramesh Vaishnav, all being intellectual powerhouses in arterial mechanics. Ram and I became good friends, but sadly he died of a heart attack well before his time.

I did not see too much of Michael in the ensuing years. He became a distinguished cardiologist at St. Vincent's Hospital in Sydney, where he extended the understanding

of arterial pressure/flow relationships and developed the use of intra-aortic balloon counterpulsation to improve survival rate of patients with acute myocardial infarction. Michael and I did actually collaborate when his student, Alberto Avolio, made a comparative study of impedance in rabbits and guinea pigs. If memory serves me correctly I was one of the referees for Alberto's application for a position at the Graduate School of Biomedical Engineering (GSBME). I well remember a long telephone call with Michael in this regard. Later, I met Wilmer Nichols on several occasions and acknowledge their outstanding achievement in extending Donald McDonald's classic, "Blood Flow in Arteries", which is another testament to Michael's tenacity of purpose. When in 1983 Sydney hosted the International Union of Physiological Sciences (IUPS) meeting, Michael seized the opportunity to arrange a satellite meeting on haemodynamics and gave me the task of finding a suitable venue. This turned out to be more difficult than anticipated, but Michael suggested at the last minute we might be able to hold the gathering at Bondi Leagues Club, where he had some connections. The meeting was a great success scientifically as well as being close to liquid refreshments. In the same year I recall of my attendance at the McDonald club meeting with which Michael was associated.

In conclusion, I shift my focus from Michael to his prime source of his inspiration, Donald McDonald. I recall Donald's friendliness and how much I enjoyed visiting him in Alabama where I believe was the first time I also met Wilmer Nichols. My enduring memory was of me standing in the elevator and Donald standing outside raving on about something or other while I kept my foot in the opening to prevent complete door closure. He maintained the diatribe for an eternity without seemingly taking a breath nor appreciating the fact that I had to leave. In the late 1980s I had the pleasure of taking Donald's wife, Renee for a sail on Sydney harbour. I have forgotten the reason why Michael was not among us. In 1993 I took early retirement from Sydney University's Department of Physiology to go sailing, grow grapes and make wine. Most of my cardiovascular stuff has been discarded, which consequently has affected a comprehensive recall of my association with Michael. However, the powerful impact of the early years with MGT has been indelible. Since 1993 I have held honorary visiting A/Prof appointments at GSBME, and later at the Sydney University School of Biomedical Engineering until 2022.

***Associate Professor Barry Gow**, earliest colleague (1960s), Department of Physiology, University of Sydney, Sydney, Australia*

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3 Wilmer Nichols

3.1 Those Having Torches Will Pass them on to Others—*Plato*

In the fall of 1967, with an MS degree in mathematics, physics and biology, I was accepted to pursue a PhD in Physiology and Biophysics at the University of Alabama in Birmingham (UAB) on a Special Fellowship from the National Institutes of Health. Good luck was with me because Donald McDonald had just arrived at UAB from the University of Pennsylvania, and he welcomed me as his first graduate student.

Shortly after arriving in the United States from England, McDonald joined Ernst Attinger at the University of Pennsylvania and using methods outlined in McDonalds textbook "Blood Flow in Arteries", they wrote and published an article that used Fourier Series to analyse pressure and flow waves in a biological system. Since pressure and flow waves are periodic pulsatile functions, they can each be represented mathematically as the summation of sines and cosines of different frequencies (i.e. Fourier Analysis). The article showed that the use of this analysis was valid in the cardiovascular system since deviations from periodicity and linearity were found to be within the range of measurement errors. Also, these errors can be minimised if the frequency response of the instruments used to measure them is flat to at least 10 Hertz.

After finishing my coursework, I met with my graduate committee and after receiving approval of my research project, I began performing experiments and collecting data. The long-term goal of my research was to develop a method that could be used to measure pulsatile blood flow in the ascending aorta without opening the chest. If this could be done one could measure pulsatile pressure along with the flow and calculate aortic input impedance. I would begin collecting raw data in the summer of 1968 with the idea of graduating in the spring of 1970.

The experimental protocol called for measurement of pulsatile ascending aortic blood flow as a reference using the electromagnetic flowmeter. The accuracy and calibration of the flowmeter was determined using the method published by Michael O'Rourke in 1965. In 1967, Michael published three other related articles that were of interest to me. One of the articles was co-authored by Michael Taylor, who was an excellent mathematician, and had worked closely with Donald McDonald in London a few years early, but was now back in Sydney. My experiments were performed in open chest dogs and the aortic input impedance was measured and defined as the hydraulic load presented to the left ventricle during ejection by the systemic circulation.

In 1968, Michael O'Rourke left Sydney and journeyed to Baltimore, Maryland to work with Bill Milnor at Johns Hopkins University School of Medicine on pulmonary artery input impedance in humans. By 1973 McDonald and I published two articles together. In 1972, I would also travel to Baltimore to work with Milnor for two years on a new method of measuring propagation coefficients and characteristic impedance in arteries. I met Michael for the first time in 1968, when he visited McDonald in Birmingham. In the fall of 1974, I was recruited to the University of Florida School of Medicine by Richard Conti with appointments in Cardiovascular Medicine and Physiology to develop a research program in both basic science and clinical medicine. With the development and evaluation of the catheter-tip electromagnetic flowmeter by Chris Mills and Ivor Gabe in the late 1960s, instantaneous blood flow velocity could be measured. With this catheter, along with the measurement of high-fidelity pulsatile ascending aortic pressure we were able to measure the input impedance of the human systemic circulation. In the summer of 1982, Michael visited me in Gainesville, Florida and presented Cardiac Grand Rounds at the University of Florida College of Medicine. He spoke about pressure and flow waves in systemic arteries and the anatomical design of the arterial system. In this presentation he showed haemodynamic measurements in animals of different size and shape including wombat, rabbits, guinea pigs and diamond pythons. The next day after his presentation, I took him canoeing on the spring-fed Ocklawaha River and as were floating along, a huge alligator slid off the bank and swam underneath the canoe. Michael was always interested in projects that had never been attempted before, so he asked me if pressure and flow had ever been measured in alligators or crocodiles; not to my knowledge, I said. He then invited me to join him in Australia and explore the possibility of measuring pressure and flow waves in the arterial system of crocodiles. I told him, I thought it would be more fun to do the project in kangaroos and he agreed. So, in January of 1983, me, my wife and two teenage children headed out for Sydney. Alberto Avolio was working with Michael at the time, so the three of us got together and wrote the protocol for the kangaroo experiments and the rest is history. My family and I spent eight months of the most enjoyable time of our lives in Sydney and the kangaroo study was the most interesting and fun project I have ever participated in and working with Michael and Alberto was a joy. During that time, we became really close to Michael, his wife Margaret, and his wonderful children. During those eight months, we wrote and published six articles and laid the ground work for revising and updating McDonald's text book "Blood Flow in Arteries"; the seventh edition was published in 2022. From 1984 to 2022 Michael and I wrote and published 31 articles together and five editions of "Blood Flow in Arteries".

Michael O'Rourke had such a profound effect on both my academic career and my personal life, and I will always remember the joy he and his family brought to my life and the life of my family.

Professor Wilmer Nichols, *Emeritus Professor of Cardiovascular Medicine, University of Florida College of Medicine, Gainesville, FL, USA*

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4 Dean Winter

4.1 Michael O'Rourke—A Remembrance, and the Advancement of Arterial Tonometry

I met Michael nearly 40 years ago when he visited our bioengineering laboratory at Southwest Research Institute in San Antonio, Texas. We had a major industrial client for whom we had developed a series of noninvasive blood pressure monitors (NIBP). The next project for our client was to develop a continuous NIBP monitor that could replace the traditional invasive arterial line. I was newly arrived at the Institute as the project began and was sceptical of the approach being pursued. So, naturally or unfortunately, I was soon tasked with developing a new approach. Knowing that the arterial waveform could be detected transcutaneously, my thought was that if the waveform could be calibrated it could be used to continuously and noninvasively determine arterial blood pressure. I approached Huntly Millar of Millar Instruments who I knew previously from my time at the University of Houston, and he modified one of his pressure catheters so that we could applanate a palpable artery and record the waveform. Shortly after we received the first prototype arterial tonometer, Michael visited the Institute for Surgical Research in San Antonio and made a side trip to our laboratory. He had been thinking about the concept of arterial tonometry and, in fact, had been recently scolded by Huntly for using one of Millar's rather delicate catheters as a tonometer, so he was quite excited to see our prototype. He recorded my carotid artery pulse waveform and pronounced my arteries "young." He then recorded my boss's waveform and pronounced his arteries "old." My first, but not last, embarrassing moment with Michael. But Michael told it as he saw it. That was the beginning for me of a long collaboration and friendship—he was my mentor, colleague, and supporter in difficult times.

Following that first meeting, our client who was sponsoring the tonometry development provided tonometers for Michael's research and support for my collaboration

with him. I and Institute colleagues travelled to Sydney several times over the following years, helping with data collection, and signal analysis and interpretation. On my first trip to Sydney to work with Michael, he picked me up at the airport and said to a severely jet-lagged me, "come on, let's go." I said "where are we going?" "We're going to the zoo to do a wombat," and we spent the rest of the day doing ultrasound studies. My first wombat experience.

Our formal collaboration lasted only about a couple of years as our Institute client's goals and Michael's research goals started to diverge. But our informal and amicable collaboration continued over the next several years. Michael frequently introduced me to colleagues as the person who taught him tonometry—an introduction which I found both generous and, again, embarrassing.

Over the next few years, we met in Australia, the United States, and at various conferences. During that time Michael continued to develop arterial waveform analysis and began a commercial venture, PWV Medical (later AtCor Medical, now Cardiex) based on a generalised transfer function developed in his laboratory that allowed the ascending aortic waveform and pressure to be determined from the radial arterial waveform detected by a tonometer. When the company expanded into the U.S., I took early retirement from the Institute to accept AtCor's offer to join them as Vice President for Scientific and Clinical Affairs.

Michael knew everyone around the world who was involved in the field of arterial blood pressure and pulse wave analysis. A large part of my job with AtCor was going with Michael to conferences and on visits with colleagues to absorb his extensive knowledge in blood pressure and arterial mechanics and apply that knowledge to both clinical and research applications. I also spent many hours with him at his clinical practice learning how he applied central blood pressure analysis to patient management. The applications grew as other researchers found new areas that central blood pressure and arterial waveform analysis provided both clinical insight and utility. Applications ranged from hypertension management to drug development to cardiovascular risk assessment to heart failure to preeclampsia to intracranial pressure monitoring and many, many more. It became a source of frustration to both of us that, as a small business, AtCor could not provide timely support for all of the new avenues that were opening up.

Through numerous visits, my family and I got to know Michael and Margaret and their family quite well. We spent enjoyable times with them at Hunters Hill and Palm Beach. We travelled together on post-conference trips in Greece, France, Austria, and Germany. We were honoured to know them both and will miss them.

Dr Dean Winter, *ex VP, AtCor Medical Inc. (Current address: 1713 Iowa St, Costa Mesa, CA 92626, USA*)

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5 Christopher Hayward

5.1 Eulogy Delivered at the Funeral of Michael O'Rourke: Perspective of a Fellow Cardiologist

I want to thank Michael's family for inviting me to contribute to the remembrance of this giant in cardiovascular medicine.

My first memory of Michael was as a medical student in first year physiology lectures. He described the cardiovascular system of the kangaroo. I was enthralled. I went on to complete my first research degree of Bachelor of Medical Science with Michael as supervisor. He was energetic, enthusiastic, iconoclastic, and generous with his time, warmth and friendship.

When I reflect on his legacy, as a cardiologist, in hindsight, he contributed more than one would think possible. Things that we rely on and take for granted. He was involved in establishing the Coronary Care Unit at St. Vincent's Hospital in Sydney, which was used as a model for coronary care units across the country. He brought his knowledge of cardiovascular physiology to bear on the introduction of counterpulsation balloon pumps, used in very sick patients, and still the most common device used across the world for temporary mechanical heart support. He ran a multicentre trial of "clot-buster" drugs in heart attacks, presenting the results internationally. He introduced public access defibrillators into Qantas, the New South Wales Ambulance Service, and continued to support both with regular training and teaching.

Michael's legacy as a cardiologist is twofold. His knowledge and care saved many, many lives. His other legacy is as a supervisor, mentor and colleague to generations of cardiologists, physicians and researchers around the world. His international standing, influence and legacy was greater than many realised locally. He was recognised for his contribution to medical research and teaching with a Member of the Order of Australia (AM).

I benefited immensely from meeting Michael, being sponsored and encouraged by him, and hopefully learning from him. His passing is a loss for all of us who knew him, but also those who did not have that privilege, yet benefited from his myriad contributions. On a deeply personal level, I miss his cheeky grin, his generosity and his warm friendship.

Professor Christopher Hayward, *Senior Staff Cardiologist, St. Vincent's Hospital and Victor Chang Cardiac Research Institute, Sydney, Australia*

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6 David Gallagher

6.1 Michael O'Rourke: Clinician Scientist and Gentleman Physician

I had the opportunity of working for Michael O'Rourke as a junior doctor, cardiology trainee and doctoral fellow for a decade from the early 1980s.

Michael was the original Director of the Coronary Care Unit at St. Vincent's Hospital in Sydney in the early 1970s. He stood out as an exemplar of applying basic science to clinical practice, particularly with his introduction of intra-aortic balloon counterpulsation to the Coronary Care Unit. His involvement in the management of acute coronary syndromes extended to conducting an early thrombolysis trial using recombinant tissue plasminogen activator (rTpa) at St. Vincent's Hospital, deployment of paramedic-initiated defibrillation throughout the state of New South Wales, trials of paramedic-initiated thrombolysis using automated ECG interpretation, public access defibrillation, and especially the introduction of defibrillators in airport terminals and Qantas aircraft.

Apart from this clinical body of work and busy private practice, Michael pursued active research in his chosen field of arterial haemodynamics, particularly with approaches of comparative pathophysiology using postmortem specimens from the Sydney Taronga Park zoo, population-based pulse wave velocity analysis with Alberto Avolio and subsequently population-based noninvasive (applanation tonometry) arterial waveform analysis with Ray Kelly, who was being mentored by Michael in clinical application of haemodynamics, but whose illustrious career was truncated by premature death. Ray's seminal study of "Noninvasive determination of age-related changes in the human arterial pulse" is still Michael's most highly cited publication (Kelly R, Hayward C, Avolio A, O'Rourke M, *Circulation* 1989;80(6):1652–9) [2].

Michael was extremely generous with his time and support to trainees and students in the department. His extensive reading and knowledge of the history of medicine and cardiology was freely imparted. Admittedly, this imparted knowledge often fell on fallow ground.

Michael was actively involved in the international hypertension research communities and had ongoing relationships with many international clinicians and researchers including Michel Safar, Bertrand Pitt, Douglas Weaver, Mary Roman, Richard Devereaux, Steven MacMahon and Harvey White. When these colleagues visited Australia they would often attend dinner at Michael's home, generously hosted by his wife Margaret. The dinners were large crowded and convivial affairs due to Michael also inviting a host of students and trainees. Michael was at various times on the editorial board of international cardiac journals including JACC and Hypertension. It has been said of Michael that one problem for him was finding someone to speak to at his level of expertise in Australia.

Michael represented not only the ideal of the clinician scientist but also the gentleman physician. He was humanitarian and gifted intellectual in equal measure.

Associate Professor David Gallagher, *Consultant Physician and Cardiologist, Riverina Cardiology, 20 Docker St, Wagga Wagga, NSW 2650, Australia*

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7 John Cockcroft

7.1 Michael O'Rourke: A Paradigm-Shifting Researcher

In defining the term "paradigm shift", Thomas Kuhn stated that "Scientific advancement is not evolutionary, but rather is a series of peaceful interludes punctuated by intellectually violent revolutions, and in those revolutions one conceptual world is replaced by another".

Michael O'Rourke was above all a revolutionary whose ground-breaking research led to a conceptual change in the way the circulation was perceived in terms of pulsatile haemodynamics. In order to better measure and understand circulatory haemodynamics, he developed the SphygmoCor system, modelled on Mahomed's original sphygmograph. It is a tribute to Michael's work that the SphygmoCor system is in regular use in the clinical laboratories of cardiovascular researchers worldwide.

I first met Michael in 1994 on a lecture tour in Turkey. Having read his book co-edited with Michel Safar "Vascular Dilatation: Mechanisms and Therapy", I was determined to visit his laboratory. So, in the hotel bar that evening, I plied him with many gin and tonics, made my pitch and went on later that year to spend a very enjoyable attachment in his laboratory in Sydney. The visit had a profound effect on me and set the stage for my future career. Furthermore, I met and interacted with many researchers who have become friends and collaborators to this day.

In Michael's early career he was a friend and colleague of Donald McDonald, and subsequently he became co-author of the iconic textbook "McDonald's Blood Flow in Arteries" which, in its many subsequent editions, remains the 'go to' reference for researchers in vascular haemodynamics worldwide. In 2006 the ARTERY society introduced the McDonald lecture in tribute to Donald McDonald and it was therefore an obvious choice for Michael to deliver the inaugural McDonald lecture at the ARTERY meeting in Athens in 2006. Michael went on to receive the ARTERY Lifetime Achievement Award, and it was my personal pleasure to present this to him in Vienna in 2010.

One of Michael's last reviews, "The application of arterial haemodynamics to clinical practice" was published in

our own journal *Artery Research* [3]. Fittingly, this was a synopsis of much of his seminal work. His final publication, "The Human Systemic and Cerebral Circulations: Contrasts in Structure and Function was also in *Artery Research* [4].

A strong supporter of ARTERY, Michael was intimately involved in establishing our sister society The Pulse of Asia, members of which will also be paying tribute to Michael's life and work. His legacy will live on in our hearts and minds.

I have many personal recollections of Michael and his kindness towards me over the years. The last time I met him was in November 2019 in Sydney when I had lunch with him and Alberto Avolio in a restaurant above a bookshop opposite his beloved St. Vincent's Hospital. I had no idea that this was the last time I was to see him. Lunch was extremely enjoyable and I remember Michael looking well and being in very good form. The conversation was, as always stimulating, and we all left afterwards with smiles on our faces. It is the way that I always want to remember him. His passing marks the end of an era. May he rest in peace.

Professor John Cockcroft, *School of Sports and Health Sciences, Cardiff Metropolitan University, Cardiff, United Kingdom*

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8 Audrey Adji

8.1 A Tribute to Michael O'Rourke: The Honour of Knowing Such a Wonderful Clinician and Scientist

I was first introduced to Michael by Alberto Avolio. Back then, in late 2000, when I was just about to complete my biomedical engineering degree with general medicine background, and looking for work, Alberto thought that I would be the most suitable person to assist Michael with his research. I began with learning how to measure blood pressure carefully, master the use of applanation tonometry and getting extremely good at detecting and recording tonometric arterial pulse waves. The rest is history, and I ended up working alongside Michael for 20 years, until his retirement from clinical practice and research.

Michael introduced me to the ebbs and flows of clinical research. Two things that he always said: "Research is 90% perspiration and 10% inspiration" (quoted from Edison and adapted by Shaw), and "Make yourself indispensable". Those two things stayed with me as I navigate my research career.

Michael's fascination with the arterial pulse remained throughout his research career, sometimes stubbornly fixated to a certain extent. Michael put all his thoughts down by using the old-fashioned pen and paper. On many occasions, I would find him surrounded by handwritten papers all over his office. His distinctive handwriting could be read only by a few people, including myself. I started writing when submission of research papers was still done with snail mail, printing copies of typed manuscripts, and hand-drawn figures. As everything moved to digital, I had to digitise Michael's hand-drawn figures to perfection, down to every line and shape. Similarly, with his presentation slides, they had to be perfect, including every text font size and placement. At times I had to remind him not to forget his poster or USB stick containing his slides. As it happened a few times, Michael would forget his poster, and I had to arrange for the poster to be printed close to where he was at the time, sometimes overseas. Another time, he would forget or lose the USB stick which contained his presentation slides, so I had to email these to the meeting organisers. Then the manuscripts—many of them in hard copies—sometimes forgotten somewhere and nowhere to be seen anymore—and had to be rewritten or retyped. Many papers we wrote had been accepted and published, but many others had been rejected and sat on the backburner.

When I decided to start my PhD journey with two small children in tow, Michael agreed to be my supervisor alongside Alberto, without hesitation, allowing me to split my time between continuing with clinical research work and actually working towards my PhD. He would reach out to his network across the world to help me throughout my PhD, for which I will be forever grateful. He taught me the importance of establishing and maintaining collaborative networks worldwide.

After completing my PhD, and with Michael approaching retirement age, he would let me take chances in establishing my own career, some successfully and some unsuccessfully. Michael was there to support me when things did not work out for me, but would be the first to celebrate if things did work. Not long after I finished my PhD, in 2016, we started revising the 7th edition of McDonald's Blood Flow in Arteries, aiming for publication on the 60th anniversary of the original monograph (1960–2020). I spent countless hours with Michael editing the text, altering figures, adding and updating references. It reflected his obsession with perfecting the book, somehow knowing that this 7th edition would be his last. Unfortunately, the pandemic hit just before the book could be published. This somewhat gave Michael an opportunity to re-revise the book, and I lost count of the number of revisions I went through with him. I am grateful that we were able to complete the task at the end, and Michael had the opportunity to see his ultimate work in the hands of the greater scientific community. Although, up to his last moments, Michael was still thinking about the imperfection and wishing to start another revision of the book!

His captivation with the rewarding engagement in interdisciplinary science and by the novel concepts of arterial impedance and wave propagation was something that I learnt greatly from Michael. Michael was able to break the "silo" of traditional cardiology in describing "systolic and diastolic" blood pressure, and instead harnessing the information contained in arterial pulse waveform to explain age-related arterial stiffness and its associated ill effects pertaining to hypertension and cognitive function. Michael was able to introduce and apply this concept to other disciplines and was convinced that blood pressure control is the key to delaying the damage to arteries and end-organs, and to minimise cardiovascular risk. He was a firm believer in the natural phenomenon of arterial pulsatility, and this has now become my research vision to apply haemodynamic principles across the broad spectrum of cardiovascular disease. Michael's openness to always learn new things and improve medicine will remain in my cherished memory.

Michael has been my great inspiration in research. Personally, Michael is also a life-long teacher and colleague with great passion and eagerness to always contribute immensely to research and clinical medicine. Throughout my working years with Michael, I have seen colleagues get along well with him, but not everyone. His approach to research and his fierce stubbornness may have cost him a little, but Michael was always generous with his time and knowledge to all who wished to learn from him. He continuously strived to do things better and always looked for new avenues to advance knowledge. Michael has taught me so much, in academic research and real life, and I will always admire him. At the end, I have the honour of knowing such a wonderful clinician and scientist. Vale Michael O'Rourke, and rest in peace.

Dr. Audrey Adji, Senior Postdoctoral Scientist, *Victor Chang Cardiac Research Institute, Sydney, Australia*

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9 Junichiro Hashimoto

9.1 To the Memory of Professor Michael O'Rourke: A Heartfelt Goodbye from Woolwich Wharf

It was 2004 in New Orleans that I met Professor Michael O'Rourke for the first time at the American Heart Association scientific sessions. After my first presentation experience at an international conference, a gentleman came up to me to shake my hand. His smile made me feel greatly relieved. At that time, I was not aware that he was the same doctor who wrote McDonald's Blood Flow in Arteries, which I had read through with enthusiasm since long before.

Repeated reading of his book gradually made me eager to learn directly from him. I sent him my application for study abroad in Sydney, and fortunately, he was kind enough to accept it. Our collaboration thus started from 2005. Besides daily training for applanation tonometry in clinical practice, literature reviews on arterial haemodynamics were made through our mutual discussions to publish several articles (O'Rourke MF, Hashimoto J [5, 6]). His views were always clear from our clinical experiences, even when we discussed mathematical or biophysical aspects of pulse waves. His mentorship helped me to deeply immerse myself in understanding fundamental mechanisms. On holidays, I often visited various beaches in the Eastern suburbs of Sydney (including Clovelly, Coogee and Maroubra) to look out at sea waves which demonstrate transmission and reflection phenomena, as he probably used to do himself. When I left Sydney in 2006, he and his wife Margaret kindly drove me and my family from home to Kingsford Smith airport.

Even after my return to Sendai in Japan, our collaboration continued. Inspired by his theoretical perspectives, my research focus was directed to arterial pulsatile pressure-flow relationship and its pathophysiological impact on hypertensive damage in various organs including the heart, kidney, and brain. Through these series of clinical research, his hypothetical views were proved to be practically valid. In subsequent studies, his original focus on systole for pulse waveform analysis has been extended effectively to diastole.

He visited Sendai in 2009 to give a lecture at Tohoku University. We also sometimes got together overseas at international conferences of Artery and Pulse of Asia as well as American Heart Association and International/European Society of Hypertension. He introduced me to many of his close colleagues from all over the world. He always encouraged me to proceed further even in challenging situations. He was an enthusiastic researcher, a genuine scientist, and an empathic clinician.

Sydney harbour reminds me of the very first day in Spring 2005 when I visited his office in St. Vincent's Clinic for my 1-year overseas study. He took me for a drive to show me the beautiful scenery around Sydney and his home suburb of Hunters Hill. On the way back, he kindly saw me off at Woolwich wharf where I got on a ferry to Circular Quay. From on board, I saw him waving goodbye with a gentle smile. Our collaboration began from there. Twenty years later, at his funeral, I was saying goodbye to him from the same place. Thank you Michael, I will never forget your kindness. You were, and always will be, the only mentor for me. May you rest in peace, with your beloved Margaret.

Professor Junichiro Hashimoto, *Miyagi University of Education/Tohoku University Graduate School of Medicine, Sendai, Japan*

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10 Charalambos Vlachopoulos

10.1 Do Not be Afraid to be Wrong; The Foundation to Ultimately be Right

I gathered all my courage and asked him with a trembling voice: "Maybe I am missing something here, but what you are now defending is in sheer contrast with what you supported in that older publication. Either now or then, there is something wrong". With a reassuring smile, Michael O'Rourke instantly replied: "We were wrong at the time. Having done everything *lege artis*, this is what we found then and we thus supported it. Now we have more evidence and we believe otherwise".

It was like a revelation. A young aspiring researcher would never have thought that the world-renowned Professor, the epitome of the scientific pioneer, could be wrong, least so admit it. But in the end, this is a hallmark of great minds; to admit that they were occasionally wrong. And this is so important for many reasons. Firstly, it captures the very nature of things. As Heraclitus, the Greek philosopher, said, "τα πάντα ρει" ("everything is in a state of flux"), meaning that everything is in constant motion, in a process of change and transformation. Secondly, it is not only a token that one has grasped this particular principle of life, but it is also proof that they lead a virtuous life. Only when you are genuine, honest and value-abiding you can embrace and accommodate failure. "Fail again, fail better", said Samuel Becket. "… and then you will succeed"; and this could well pertain to Michael with the life example he has set.

Maybe this can explain why Michael was so passionate about his views and why his passion was so transmissive. In a virtual debate with Peter Higgs, Richard Dawkins said: "The true scientist, however passionately he may 'believe' in his theory, knows exactly what would change his mind: evidence". And Michael was in search for evidence all of his life.

The wisdom implicit in this episode I have recounted is only one of the many things that people fortunate enough to work and live with Michael could gain.

A lot can be said about Michael's scientific legacy. Uniquely, he brought two worlds together; biophysics and clinical medicine. "Translational" is a fashionable word these days. Michael was one of the very few that long before it almost lost its meaning had already embodied it.

It is not only a matter of transferring knowledge. It is also a matter of living and acting in a way that you become an example. By safeguarding and raising circulatory science, his own Telemachus, Michael was a true Mentor.

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