

Vale Professor Lawrie Powell AC 1934- 2022

Lawrie William Powell passed away on September 23, 2022 at the age of 87 years, bringing to an end a long and highly distinguished career as a clinician, researcher, academic, administrator and mentor. To excel in so many areas requires an exceptional intellect, unwavering commitment and determination, a passion for one's chosen field of endeavour, and a good dose of empathy and respect for others. Lawrie had all of these qualities. He might tell you that his career was founded upon a series of happy accidents that led him to a number of influential mentors, and there is a degree of truth in this, but the underlying raw material that those mentors moulded was of the highest quality.

After graduation from The University of Queensland (1958) Lawrie spent his intern year at the Royal Brisbane Hospital (RBH) (now the Royal Brisbane and Women's Hospital, RBWH), and it was at this hospital that he went on to spend most of his professional life. While at the RBH, Lawrie came under the guidance of Professor John Tyrer, head of The University of Queensland Department of Medicine. Tyrer had created a series of temporary positions that enabled young medical graduates to combine their clinical duties with some research work. It was during this time that Lawrie first became interested in the iron loading disease hereditary haemochromatosis. That interest was to be sustained for the next 60 years! Lawrie went on to become one of the world's foremost authorities on the disease, and how hemochromatosis is managed clinically today, as well as our understanding of the basic mechanisms underlying the condition, are in no small part the result of his efforts.

A pivotal time in Lawrie's career was the year he spent at the Royal Free Hospital in London in 1965/66 under the guidance of Professor (and later Dame) Sheila Sherlock. Sherlock was a legendary hepatologist and mentor, and much of Lawrie's own mentoring success had its foundations in that time at the Royal Free. It was also during this time that Lawrie's devotion to hepatology became firmly established, and the young clinician became familiar with a broad range of hepatic diseases as well as the best hepatologists Europe had to offer.

Lawrie returned to Australia in 1966 and was appointed Senior Lecturer in the Department of Medicine at The University of Queensland. It was around this time that June Halliday was also appointed to the Department, and the highly productive partnership that Lawrie and June established was to last almost 30 years, ending only when June retired at the end of 1995. June oversaw the laboratory side of the operations while Lawrie concentrated on clinical matters, but this was a true collaboration, and Lawrie was involved in the laboratory work as much as June was involved in clinical studies. Their research program was very much iron-based, and haemochromatosis was always at centre stage, but other areas of hepatology were not neglected and a broad range of topics were covered at this time. One of the most significant of these topics was viral hepatitis. This work was spearheaded by another hepatologist in the Department, Graham Cooksley, but Lawrie and June played an important role in the success of the work. Together, Lawrie, June and Graham formed a formidable team that was to endure for most of the rest of the century. In 1982 they were awarded a prestigious NHMRC Program Grant which was reviewed successfully several times before being incorporated into an NHMRC Block Grant to the Queensland Institute of Medical Research in 1998.

Through the 1970s and the 1980s, Lawrie (along with June and Graham) built a hepatology research group of international significance in Brisbane. Lawrie's personal reputation continued to grow and he not only became the top academic hepatologist in Australia, but was also recognised as a global leader in the field. His laboratory grew in size and reputation and was responsible for producing a great deal of important research on haemochromatosis and basic aspects of iron homeostasis. During

this period Lawrie trained numerous clinicians and (along with June in particular) basic researchers, and many of these have gone on to distinguished careers in their own right.

Lawrie was appointed Director of the Queensland Institute of Medical Research in 1989. June, Graham and the rest of their large research group also translocated to QIMR. Lawrie's time at QIMR was marked by considerable growth of the Institute and the strengthening of its clinical ties. He was responsible for bringing a large amount of philanthropic funding to the Institute, and with leveraged financial support from the State and Federal governments, the Institute gained a new building, the 10 storey Clive Berghofer Cancer Research Centre which opened in 2001. Lawrie retired as QIMR Director in 2002, to be succeeded by immunologist and infectious diseases expert Michael Good, another clinician-scientist who had benefitted from Lawrie's mentorship in the 1980s. The association Lawrie formed with QIMR was maintained for a further 20 years and he continued to carry out a great deal of productive research with two of his former mentees, Greg Anderson and Grant Ramm, and newly appointed group leader Nathan Subramaniam. He also remained active clinically, and indeed was seeing haemochromatosis patients up until 2021. In 2002 he also took on the new role of Director of Research at the RBWH, with the goal of stimulating research in a bustling clinical environment.

It is hard to do justice in a short space to a research career that produced more than 500 publications over 60 years. Of course, Lawrie's desire to improve the diagnosis and treatment of haemochromatosis was a constant through his research career. In the face of some scepticism, Lawrie confirmed that haemochromatosis was a real clinical entity and not a manifestation of alcoholic liver disease as many believed at the time. He either led or made major contributions to several important studies to define the prevalence of haemochromatosis using populations in Queensland, Western Australia and Victoria. The true clinical penetrance of haemochromatosis remained a controversial topic in the field for many years, but a study led by Katie Allen and Martin Delatycki in Melbourne, to which Lawrie made major contributions in study design and interpretation, provides the best data currently available on the penetrance of this disease. Many contributions to understanding the biology of ferritin and its value as a biochemical marker of iron overload were made by Lawrie and June. Genetic mapping studies in his lab provided key information which assisted others in ultimately identifying *HFE* as the gene mutated in haemochromatosis. After *HFE* was identified, Lawrie's group very rapidly verified the findings in an independent population. Lawrie always believed that the basic pathophysiological defect in haemochromatosis was in the liver. He played a key role in studies of patients with haemochromatosis which showed that the disease was cured by liver transplantation. In 2001 the liver-derived peptide hepcidin was identified as the master regulator of body iron homeostasis and it was widely considered that hepcidin acted on *HFE* to regulate dietary iron absorption. However, in a major insight, our group showed the opposite to be true, and that it was *HFE* that modulated the activity of hepcidin. This is arguably the most important development in the understanding of haemochromatosis since the *HFE* gene was identified as it explained why affected individuals accumulated iron and provided the foundation for the development of therapeutics targeting the hepcidin regulatory pathway for the treatment of iron overload. Other research of note to come out of his group included key studies on the benefits of phlebotomy therapy for haemochromatosis, the ferritin receptor, the regulation of intestinal iron absorption, the pathogenesis of fatty liver disease, bilirubin metabolism, haemolysis in liver disease, and desialylated transferrin as a marker of excessive alcohol consumption. There are many more.

Lawrie's relationship with his patients was always a very important one for both parties. His patients benefitted from a treating physician at the forefront of haemochromatosis and hepatology research, while in turn those patients provided the basis for a great deal of that research. Over many years, Lawrie built up one of the world's largest haemochromatosis resources (patient data and tissue samples) and this was used for many clinical and laboratory studies. He enjoyed a strong personal

connection to his patients, and treated many of them, including many families, for extended periods of time. Indeed, he was still treating haemochromatosis patients until he was well into his 80s. One of Lawrie's long-term patients was Margaret Rankin, and it was through discussions with Margaret that the patient support group now known as Haemochromatosis Australia (HA) was born in 1991, with Margaret as its first president. Lawrie was enthusiastic about forming an organisation which could disseminate information about haemochromatosis and act as a focal point for affected individuals to meet each other and exchange stories of their experiences. HA has been an extremely effective organisation in achieving that goal and in advocacy for patients with haemochromatosis, and it continues to thrive today. Lawrie was a member of the group's advisory board from its inception and, at the time of his passing, was a patron of the society, along with founding president Margaret.

While Lawrie's clinical work and research have been extensive and globally influential, he has never neglected the discipline that provided him with the career he loved, and his influence on the hepatology and gastroenterology professions in Australia and internationally is profound. Early in his professional career he was a Director of the Australian Society for Medical Research (1968-70) and he went on to hold key leadership positions in a range of medical and scientific societies. He served as the inaugural President of the Asian Pacific Association for the Study of the Liver (APASL)(1978), the President of the Gastroenterological Society of Australia (1979-81) and the President of the International Association for the Study of the Liver (1986-88). He was also a Director of the International Bioiron Society when it first formed in 1999. Lawrie was particularly proud of the formation the APASL, a society he conceived with prominent Japanese hepatologist Kunio Okuda in the late 1970s. Not only did he serve as the Society's first President, he also was a founding editor of its flagship publication, the *Journal of Gastroenterology and Hepatology*. Both the society and the journal are still going strong after many years. Add to these achievements his extensive involvement in high level committees and boards at the university, state, national and international levels, and it is clear that he served his discipline with the highest distinction.

It is difficult to find someone who knew Lawrie who would not speak fondly of his role as a mentor. So many clinicians and scientists have benefitted from his guidance over the years that it would be difficult to name them all. Some of those mentees whose names do come to mind include Geoff Farrell, Jacob George, Darrell Crawford, Barbara Leggett, Elizabeth Powell, Michael Good, Michael Burt, Grant Ramm, Greg Anderson, Nathan Subramaniam and Prue Hart, all of whom have gone on to become professors and to occupy senior academic and leadership roles in their own right. So many of us have benefited from his wise counsel, letters of support and extensive connections, and he took great pride in any successes we achieved.

Lawrie was ever passionate and enthusiastic in whatever he did. He loved ward rounds and teaching. Despite a busy clinical practice and extensive administrative commitments, he always set aside time for lab meetings, and would never miss the weekly pathology sessions when liver biopsies were reviewed. He took an interest in everyone's work and always had something insightful to say. He kept our minds focused on what we would do with our data – Where will you present this? What journal are you aiming for? He read all manuscripts that were sent to him and provided feedback far more rapidly than you would expect for someone with so many other commitments. The science of course was paramount, but so was the presentation, and no draft escaped his strong editorial hand. All members of the unit were strongly encouraged to join biomedical societies, to attend their meetings and present work, and to become involved in running the society. Being a member of the community was in his ethos. Although he was first and foremost a clinician, he and June Halliday were united in ensuring that the research that came out of their laboratory was of the highest standard. Every person new to the lab, no matter how many High Distinctions they had on their academic record, was first set to work on some routine tasks. It was only after they demonstrated that their practical work was of a

sufficiently high technical standard that they allowed to do 'real' research. We are all the better for this stringent grounding.

With his prodigious research output, his well-recognised clinical acumen, his enormous contributions to his professional field and his effectiveness as a mentor of the highest rank, it is no surprise that many accolades came his way. These have included the Eric Susman Prize for Medical Research of the Royal Australian College of Physicians (1976), the Distinguished Research Prize of the Gastroenterological Society of Australia (1988), the award of Companion of the Order of Australia (AC)(1990), the Marcel Simon Prize (1991), the Gold Medal of the Canadian Liver Foundation (1997), University of Queensland Alumnus of the Year (1999), the Queensland Premier's Millennium Award for Excellence in Health (2000), being named a 'Queensland Great' (2002), a Centenary Medal of the Commonwealth of Australia (2003) and the Distinguished Achievement Award of the American Association for the Study of Liver Diseases (2008). Lawrie is the only Australian to win this last award, and at the time he received this honour, he was only the third person outside North America to do so. He was also elected an Honorary Fellow of the Royal College of Physicians (London) and the Royal College of Physicians (Thailand), and was awarded Fellowship of the Australian Academy of Technological Sciences and Engineering.

Lawrie's passion for medicine and research was easily matched by his devotion to his family. He met his future wife Margaret while they were at university and they were married in 1958. Their marriage of over 60 years yielded 5 children and 13 grandchildren, and Lawrie was incredibly proud of everything they have achieved. The support of Margaret was a key factor underlying Lawrie's entire career. She was always there to support him and was the ever gracious host to hundreds of visitors from all corners of the globe over many years. Without the support of his family, it would have been much more difficult for Lawrie to achieve what he did.

In closing, Lawrie Powell was a remarkable clinician, scientist and person. He leaves behind an imposing legacy, and one that will continue to bear fruit for many years to come. We all have our own personal recollections of Lawrie. He affected each of us in individual ways, but instilled in all of us the passion for enquiry and the value of dedication and commitment. He was unique, and the lives of so many are better for his influence.

Greg Anderson, Grant Ramm, Nathan Subramaniam, Geoff Farrell, Darrell Crawford
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