The forgotten successes and sacrifices of Charles Kellaway, director of the Walter and Eliza Hall Institute, 1923–1944

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ersonal courage is most memorable when an individual shines in a time of crisis, but the quiet sacrifices of a lifetime devoted to duty are too often lost to posterity. Such seems to have been the fate of Charles Halliley Kellaway (1889–1952), who pioneered the path of independent medical research in Australia during the difficult decades after World War I.

The close of 2007 provides good reason to reflect on Kellaway's successes, especially as we recall the 80th anniversary of two pivotal events in Australian medical research. In 1927, the first Commonwealth grant for medical research was approved, while in 1928, a royal commission into the iatrogenic "Bundaberg tragedy" significantly heightened public appreciation of medical science. Kellaway was the central figure in both of these events, yet they formed only a small part of his contribution to Australian medical history (Box 1). ¹⁻¹⁴

Fortuitous wartime links

Much of Kellaway's character can be traced to his origins. Born in Melbourne into the family of a country clergyman, Kellaway was instilled with evangelical zeal and a lingering Victorian faith in duty and progress. While consistently topping his university courses via hard-won scholarships, Kellaway set his sights on becoming a medical missionary in India. Although he was clearly ambitious, the most enduring memory of Kellaway—recalled by all who met him—was his affability and willingness to assist others. ^{1,15,16} These qualities were all to be tested during World War I.

Despite the prevailing imperial fervour, Kellaway's decision to enlist was not taken lightly. He completed his postgraduate Master of Surgery and Doctor of Medicine degrees before signing up in late 1915, arriving in the Middle East just after the evacuation of Gallipoli. Here, he worked as a pathologist alongside the director of the Lister Institute, Charles Martin, who had undertaken pioneering research in physiology, including snake venom studies, in Australia at the turn of the century.

In 1917, Kellaway joined the Australian Imperial Force in France as regimental medical officer for the 13th Battalion. After a battle at Zonnebeke on 26 September, he earned the Military Cross, his commanding officer noting: "During the 24 hours following the attack he worked without a moment's respite, dealing with the wounded of five battalions in addition to his own, and at the same time controlling the work of his Stretcher Bearers. He established what must be a record by passing 400 cases through his R.A.P. [regimental aid post] in 24 hours. I cannot praise too highly his untiring devotion to duty". ¹⁷ Posted to London in 1918, Kellaway found himself working for the Royal Flying Corps and its Australian counterpart. His investigations into the physiology of anoxaemia—then a problem for military aviators—led to Kellaway's first serious scientific research and a fortuitous association with Henry Dale, Britain's leading pharmacologist. ^{1,8}

Although his experiences at the front converted Kellaway to agnosticism, his wartime work with Martin and Dale redirected his energies to a new calling—the betterment of humanity through medical research. After the war, these two mentors saw Kellaway appointed as a Foulerton scholar of the Royal Society. From 1920 to

ABSTRACT

- Charles Halliley Kellaway (1889–1952) was one of the first Australians to make a full-time career of medical research.
- He built his scientific reputation on studies of snake venoms and anaphylaxis.
- Under Kellaway's directorship, the Walter and Eliza Hall Institute gained worldwide acclaim, and he played a critical role in its success between the world wars.
- His administrative and financial strategies in the era before the National Health and Medical Research Council (NHMRC) helped local medical research weather the Depression and gain a strong foothold by World War II.

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1923, he undertook a tour of duty through many of the major English laboratories, mastering experimental techniques in physiology, pharmacology, immunology, biochemistry and pathology.¹

The second director of the Walter and Eliza Hall Institute (WEHI)

In 1923, the directorship of Melbourne's nascent Walter and Eliza Hall Institute of Research in Pathology and Medicine (as it was then known) became vacant. The WEHI at this point was the only independent centre for medical research in Australia, comprising fewer than a dozen staff and a paltry annual budget of £2500. ¹⁵ Both Martin and Dale proposed Kellaway for the post, noting his superior research qualifications over those of the other candidate. ^{15,18}

Kellaway, then aged 34, was well placed to accept the post. In addition to his scientific credentials, he had a vision for the institute and the tenacity over the following decades to see it realised. His outstanding academic and military records made Kellaway known to



Frank Macfarlane Burnet and Charles Kellaway (on the right), March 1944. Reproduced with permission from the WEHI.

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1 The key achievements of Charles Halliley Kellaway (1889-1952)

Established the Australian Flying Corps Medical Board (1918–1919)

In 1918, Kellaway was seconded to the Medical Board of the Royal Flying Corps in London to assess trainee and invalid Australian aircrew. He was promoted to Major and established an independent Australian Flying Corps board, later credited with laying the foundations of the medical branch of the Royal Australian Air Force.²

Director, Walter and Eliza Hall Institute of Research in Pathology and Medicine (WEHI) (1923–1944)

Through diligence and personal charisma, Kellaway "made influential friends" and effectively lobbied the medical profession, government and the business community to expand the funding base for Australian biomedical research. This included the first direct funding for medical research from the Commonwealth Department of Health, stimulating the development of the National Health and Medical Research Council (NHMRC) grants system and the redirection of private philanthropy towards research needs. He expanded the staff, facilities and reputation of the WEHI as he "set in motion a tradition of full-time research in the biomedical sciences" in Australia. Under his directorship, the WEHI commenced pioneering programs such as Frank Macfarlane Burnet's virological studies and the blood bank service established by Lucy Bryce and Ian Wood. 3.4

Chairman, Royal Commission of Inquiry into Fatalities at Bundaberg (1928)

Kellaway's commission impressed the significance of medical research "more sharply than ever before on the Australian public". His commission vindicated the general safety of immunisation, while enhancing quality control for biological products, and helped save the careers of several prominent figures, including the Minister for Health (Neville Howse), the Director-General of the Department of Health (John Cumpston) and the Director of the Commonwealth Serum Laboratories (CSL) (Frederic Morgan). 5-7

(Assistant) Director of Hygiene (1923–1931), Director of Pathology (1939–1942), and then Honorary Scientific Liaison Officer (1942–1944) for the Australian Army Medical Corps

Kellaway organised effective responses to the "wide range of new and practical problems of pathology, physiology and medicine, entailed by the extension of the war into the tropics, and the rapid development in Australia of a principal base for the medical aspects of the operations of the Allied Powers in the Pacific". This went far beyond the major challenges of infectious diseases — especially viruses and rickettsiae — to tank and aircrew physiology and chemical defence.

Pioneer Australian pharmacologist and physiologist (1916–1944)

Military health research (1916–1944). This career-long commitment by Kellaway began (under Martin) with studying dysentery in the Middle East during 1916, and reached its peak during World War II. He was particularly noted for his investigations into the physiological effects of hypoxaemia, and especially hyperglycaemia.⁸

Defining the immunological basis of anaphylaxis (1920–1923). With Dale, Kellaway established the immunological basis of anaphylaxis, focusing on the critical role of histamine.¹

Hydatid disease (1924–1928). Together with Fairley and Harold Dew, he contributed to definitive studies of this pressing agricultural problem.^{4,9}

Antivenom development (1928–1938). With Fairley and Morgan, Kellaway developed the first commercially produced antivenom in Australia, made from tiger snake venom. This was released in October 1930 and transformed the management of snakebite in Australia. ¹⁰ Kellaway also worked on death adder and copperhead antivenoms, although they were not commercially released at that time ¹¹

Pharmacology of Australian animal toxins (1928–1939). Kellaway contributed over 50 papers relating to snake venoms, and many remain citation classics in Australian toxinology. 11-14 This work led in large part to his 1940 Fellowship of the Royal Society of London. He also investigated bee, platypus, redback and funnel-web spider venoms, plus Staphylococcus and mussel toxins.

Demonstrated the "slow-reacting substance of anaphylaxis" (1938). Largely in collaboration with Wilhelm Feldberg and Everton Trethewie, Kellaway provided the nascent definition of what are now known as the leukotrienes, through the study of cobra venom action. This later led Bengt Samuelsson and others to the 1982 Nobel Prize for their work on leukotrienes and prostaglandins.

Scientific Director, Wellcome Research Institution (1944–1952)

Kellaway reorganised the "many-sided research enterprise, from highly specialized and urgently demanded war-time activities to a programme of normal range and freedom", remaining at his post almost until his death from lung cancer. 1

many local clinicians, and behind the scenes he was a consummate gentleman networker. ¹⁵ These qualities benefited the fledgling WEHI as well as the careers of many of its staff, especially the young Frank Macfarlane Burnet. Indeed, what became apparent over time was Kellaway's keen ability to identify and nurture talented researchers. ^{18,19} Burnet himself said later: "I am only guessing, but I think it is a reasonable guess, when I say that the influence of Charles Kellaway in shaping the Hall institute from 1923 onward set Australia on a new path to achievement in medicine".

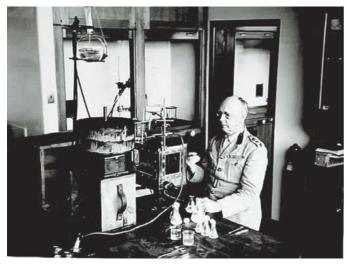
Institutional administration was probably Kellaway's strongest suit. Via the structures he set in place at the WEHI, including multiple research streams and flexible working arrangements, he encouraged many budding researchers to taste life at the bench. He also taught postgraduate medical students and was a visible contributor to the British Medical Association and the Australian Association of Physicians. In this way, Kellaway built the WEHI's profile, especially in a medical culture that largely favoured clinical observations over laboratory research. Moreover, Kellaway's austere background ensured that he understood the value of money. After he had built up a network of benefactors in the 1920s, his parsimony

almost certainly saved the WEHI from financial collapse during the Depression; ^{15,16} other local institutes did not fare nearly as well. ^{20,21}

Establishing a precedent for Commonwealth funding

Of broader significance, Kellaway also pioneered the system of Commonwealth sponsorship for medical research programs. In late 1927, he approached the Minister for Health, Neville Howse, and the powerful Director-General of the Department of Health, John Cumpston, with a proposal. Kellaway sought federal funding for a range of projects, including research into polio, hydatid disease and snake venoms. ^{22,23} Cumpston was generally equivocal about the value of funding research, ^{5,24} but enthusiastically supported Kellaway's requests, and several grants ensued. Although most federal finance trickled away during the Depression, a precedent had been set. The willingness of the Commonwealth to support medical science at the WEHI not only assisted Kellaway in establishing a new virus research department for Burnet in 1934, but helped pave the way for the National Health and Medical Research Council (NHMRC) in 1936. ^{15,22,23,25}

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Charles Kellaway in his laboratory at the Walter and Eliza Hall Institute of Research in Pathology and Medicine during World War II. Reproduced with permission from the WEHI.

Kellaway also helped raise the public profile of medical research, albeit via an iatrogenic disaster. In early 1928, the local medical officer of health in Bundaberg unwittingly inoculated 21 children with diphtheria toxin–antitoxin that had become contaminated with a staggeringly high titre of *Staphylococcus aureus*. Within hours, 18 children had become seriously ill and 12 eventually died, including three from one distraught family. The "Bundaberg tragedy" became an international media sensation and a public health disaster in Australia, where mass immunisation programs were only just gaining acceptance. ^{6,26} Kellaway, as the premier local figure in medical science, was asked to chair a royal commission into the tragedy, alongside noted pathologist Peter MacCallum and the bacteriologist Arthur Tebbutt.

The thoroughness with which Kellaway and his fellow commissioners approached the clinical, environmental and pathological aspects of this politically charged inquiry won widespread medical and lay acclaim, leading to improvements in the manufacture and administration of biological products.⁷ There were important scientific consequences too: under Kellaway's guidance, Tebbutt and the WEHI's departmental heads painstakingly laid out the potential pathogenicity of Staphylococcus, which had previously been considered relatively innocuous.^{3,7} The resultant work on staphylococcal toxins helped build Burnet's reputation as a talented bacteriological researcher,²⁷ while the immunological aspects of the tragedy are credited with sowing the seeds for his clonal selection theory.²⁸ Nevertheless, while the stigma of the Bundaberg tragedy took years to overcome, most practitioners were keen to accept the commission's findings and move on, meaning Kellaway's stewardship of this important investigation was largely forgotten.^{5,6}

An international scientific reputation built on venom

The 1920s were a halcyon decade for pharmacological and physiological research, and Kellaway's Foulerton scholarship brought him into the laboratories of Britain's leading researchers, especially Henry Dale. Kellaway and Dale collaborated on a series of elegant experiments that confirmed the immunological basis of anaphylaxis, but

determined that its physiological effects were not the result of proteinaceous "anaphylatoxins", as was generally supposed. Rather, their work led to an appreciation of the primacy in anaphylaxis of histamine, which Kellaway further explored in subsequent collaborations during his English sojourn. Tissue injury and anaphylaxis remained significant themes throughout Kellaway's career, although he did not return to a concerted study of their underlying physiological processes until the late 1930s.

In the first years after his return to Australia, Kellaway's scientific work lacked focus, although a partnership with Harold Dew at the WEHI produced valuable work on hydatid disease. Then, in 1927, Neil Hamilton Fairley suggested that he and Kellaway should collaborate on a program to study local snake venoms. This project, which Kellaway pursued for over a decade, became the foundation of his international scientific reputation. Working first with Fairley and then a series of talented fellow investigators, Kellaway's team laid out the clinical aspects of envenomation, including what was then considered optimal first aid. They also characterised the pharmacological activity of the major Australian snake venoms, with additional studies on their immunology and biochemistry.

While this work involved few technical innovations, it highlighted Kellaway's strengths as an investigator, namely his intellectual rigour, his mastery of experimental technique, and his deep understanding of human and animal physiology. He focused particularly on the neurotoxicity of local snake venoms, suggesting at first that they acted primarily via myolytic damage, before incorporating the emerging concept of chemical neurotransmission into his schema. 12-14 The venom program was also of immediate clinical benefit as it involved a collaboration with the Commonwealth Serum Laboratories (CSL) to manufacture tiger snake (*Notechis scutatus*) antivenom. 5 Kellaway supervised its first use in 1931, and then became a recipient himself after a bite from a snake that he was milking. While the treatment was successful, Kellaway subsequently developed serum sickness and thus became intimately acquainted with his two main fields of study: envenomation and anaphylaxis! 1,4

As the 1930s wore on, Kellaway's international stature as a venom researcher grew. His studies encompassed spider, mussel and even platypus toxins but lacked the clear direction of the early work. However, by the end of the decade, a new series of collaborations with Wilhelm Feldberg and then Everton Trethewie encouraged Kellaway to use venoms as research tools, particularly to further his interest in tissue damage. These investigations identified two phases in the tissue response to anaphylaxis or injury, the first an immediate circulatory consequence of histamine release, and the second a prolonged contraction of smooth muscle, which was attributed to the liberation of a slow-reacting substance of anaphylaxis (SRS-A). This phenomenon intrigued pharmacologists for decades, particularly as SRS-A is released only in minute quantities and is intrinsically unstable. In fact, it was not until the 1980s that SRS-A was characterised as the leukotrienes, leading ultimately to the development of leukotriene receptor antagonists for the treatment of asthma. Therefore, Kellaway's pioneering work on SRS-A has been considered his most profound contribution to experimental physiology. 16

Final years in London

When World War II broke out, Kellaway's personal research career effectively ended, but not before his work in venoms was recognised internationally, including by a coveted Royal Society of London fellowship and an invited series of Dohme lectures at Johns Hopkins

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University in 1936.¹²⁻¹⁴ During the war, Kellaway rejoined the Australian Army, first as Director of Pathology and later as Honorary Scientific Liaison Officer, where his experience and contacts helped with coordination of local and international military research programs.

With the tide of war turning, in 1943 he accepted Dale's invitation to become head of the international Wellcome Research Laboratories in London. In this capacity, he was responsible for steering a vast array of research programs away from pressing military needs toward a postwar commercial focus. As with his time at the helm of the WEHI, Kellaway's tenure as director of the Wellcome Laboratories was "bedevilled by difficulties, foreseen and unforeseen", including dealing with the Wellcome Foundation's grave financial crisis of 1946–1948.^{29,30} Therefore, in undertaking this extremely challenging administrative role, Kellaway not only sacrificed any possibility of a return to the bench but, once again, demonstrated his "untiring devotion to duty". By shouldering the burden of leadership at Wellcome, Kellaway contributed crucially to the survival of what has ultimately become the world's second-richest medical charity—the Wellcome Trust—and one of the foremost medical libraries.29

An inveterate smoker, Kellaway was quietly consumed by lung cancer but persisted at his post until physically unable to work, dying on 13 December 1952.

All who met Kellaway commented on his generous, friendly nature and his ease in forming enduring professional and personal relationships. He displayed a genuine interest in other people and sustained a happy marriage through what must have been trying times. Kellaway also excelled at his hobbies, including bird photography and fly fishing, reflecting his fascination with technical apparatus and his deep love of nature.

As his early war service proved, Charles Kellaway was both courageous and indefatigable. In sacrificing to some extent his own research career for the mundanities of administration, finance and infrastructure, Kellaway laid a path for others, such as Burnet, to travel. As a different sort of "medical missionary", his efforts during the fraught interwar years ensured that Australia could truly stand on the world's stage through the postwar golden age of medical research.

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Competing interests

None identified

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