In the 1920s, snakebite was a constant threat for Australians living and working in rural areas, as well as for city dwellers living on the rapidly expanding urban fringes or close to parks, waterways and bushland reserves.

Research in other countries had established that snakebite was a medical problem with the clear potential to be solved. As early as 1894, cobra antivenom was made commercially available as a result of French research. To the disappointment of many Australians, this antivenom was not effective against common Australian snake species. The need for antidotes to the venoms of Australian snakes proved to be a uniquely Australian research problem.

Early Australian antivenom research in the 1890s was led by Charles J Martin at the University of Melbourne, and Frank Tidswell in the New South Wales Department of Health. By 1903, Tidswell had generated tiger snake antivenom, but with a lack of support and infrastructure for the project the antivenom was never moved into commercial production. It was not until 1927 that the Walter and Eliza Hall Institute (WEHI) and the Commonwealth Serum Laboratories (CSL) joined forces to continue the project. Writing in the Walter and Eliza Hall Institute’s 1927–1928 Annual Report, the institute’s director, Charles Kellaway, named Neil Hamilton Fairley as the driver behind the research.

On returning to Australia last year, Dr. N. Hamilton Fairley, who has had considerable experience with snake bite in India, drew attention to the fact that during the past two decades little work has been done on the Australian venomous snakes, and that despite serum therapy, Tidswell’s experimental work on the production of antivenine in this country had not been followed up. The low death rate has no doubt been a factor in this inertia, but many deaths could and would have been prevented had antiserum been available for general use.

To support the new program, Kellaway lobbied the Commonwealth Government to consider medical research into snakebite, as well as polio and hydatid research, to be national concerns, and received £2,500 to support the institute’s research programs. This grant was the first funding of a program of medical research by the Australian Government Department of Health, paving the way for the formation of the National Health and Medical Research Council in 1936.
Fairley and Kellaway, working with Fannie Eleanor Williams, Henry Holden and Donald Thomson from WEHI, and the director of CSL Fredrick Morgan, initiated a program of research into how Australian snake venoms act, and how the effects of snakebite could be mitigated.

The research into snakebite was initially a broad program, with Fairley conducting epidemiological studies of the frequency and outcomes of snakebite in Australians, and detailed studies of the biting mouthparts of Australian snakes. Some work on snakebite mitigation addressed the efficacy of standard first aid responses to snakebite, ligature and excision, and found them to be an inadequate treatment for snakebite. This justified the development of antivenoms, a project that had long-term and widespread benefits for Australia.

The research team’s production of antivenom required large quantities of snake venom that could be injected into experimental animals (predominantly horses) in minute, sub-lethal doses, to generate serum that had venom-neutralising, antivenom properties. Venom from significant Australian snake species was sourced from the Melbourne Zoo snake house—which was, for a time, taken over by the Walter and Eliza Hall Institute, with the reptile curator Tom Eades being an employee of the institute. The demand for venom was high, with more than 800 snakes, including tiger snakes, death adders, copperheads and black snakes, being milked in the period between 1928 and 1930. The institute’s annual reports from the period include accounts of snake-hunting trips to many locations around Australia.

By late 1930, the research team’s efforts had come to fruition, with CSL releasing tiger snake antivenom for clinical use. On 30 April 1931, soon after the first ‘official’ tiger snakebite was successfully treated with the new antivenom at the Royal Melbourne Hospital, the *Sun* newspaper summarised the work of Kellaway and his team fittingly as ‘Men who play Australia. Australia. The production of antivenoms for other toxic animals also progressed, and today Australian snakes, culminating in the production in 1962 of the ‘polyvalent snake antivenene’), stonefish (*Synanceia spp*), CSL produces antivenoms for redback spiders (*Latrodectus hasselti*), box jellyfish (*Chironex fleckeri*). These products have undoubtedly saved the lives of many people and domestic animals in Australia.

With colleagues including Fannie Eleanor Williams and Henry Holden, Kellaway identified that venoms are a complex mixture with different components having different effects: in the case of snake venoms, some components could destroy red blood cells or disable muscle cells, while others caused anaphylaxis, an extreme and life-threatening immune response.

Through work on the anaphylactic effects of snake venom, Kellaway and Wilhelm Feldberg identified the ‘slow reacting substance of anaphylaxis’ (SRS-A), a substance that causes the body’s smooth muscle cells to contract, and plays a major role in inflammatory diseases such as asthma. SRS-A remained enigmatic for many years after Kellaway’s work, finally being identified in the 1980s as a mixture of cell signaling molecules called leukotrienes. Kellaway’s work also ventured into the burgeoning field of immunology research, investigating how immunity to venom develops.

Many considered Kellaway’s venom research to be one of the highlights of his research career, with his 1940 citation for Fellowship of the Royal Society stating that his contributions ‘on the physiological actions and immunology of snake venoms has made him pre-eminent amongst investigators of this subject’.

The collaborative research into snake venoms carried out by the Walter and Eliza Hall Institute and Commonwealth Serum Laboratories scientists was an important era in Australian medical research, yielding direct therapeutic benefits for many Australians who had unfortunate encounters with venomous native fauna, as well as spawning broader fields of research. Australian venom research continues today, and Australian researchers are using components of venom to guide the development of new pharmaceuticals for a range of conditions.

The support of the Commonwealth Government in snake venom research was also a landmark in the history of Australian medical research, and may well have been used to justify the establishment of the National Health and Medical Research Council, with the landmark of receiving government funding, WEHI and CSL researchers had produced an antivenom that was saving the lives of snakebite victims. To many Australians, this exemplified the promise of medical research, and the hope that research offers the community.

**Professor Douglas Hilton**

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1 Antivenin or antivenene, the terminology originally used to describe the antitoxin developed against snake venom by Albert Calmette in 1894, was derived from the French venin, meaning venom, that itself came from the Latin venenum, meaning poison. As it was developed in France, the term antivenin was used. Later in 1981, the World Health Organization determined that the preferred English nomenclature was antivenom, although antivenin remains in common use in francophone countries.