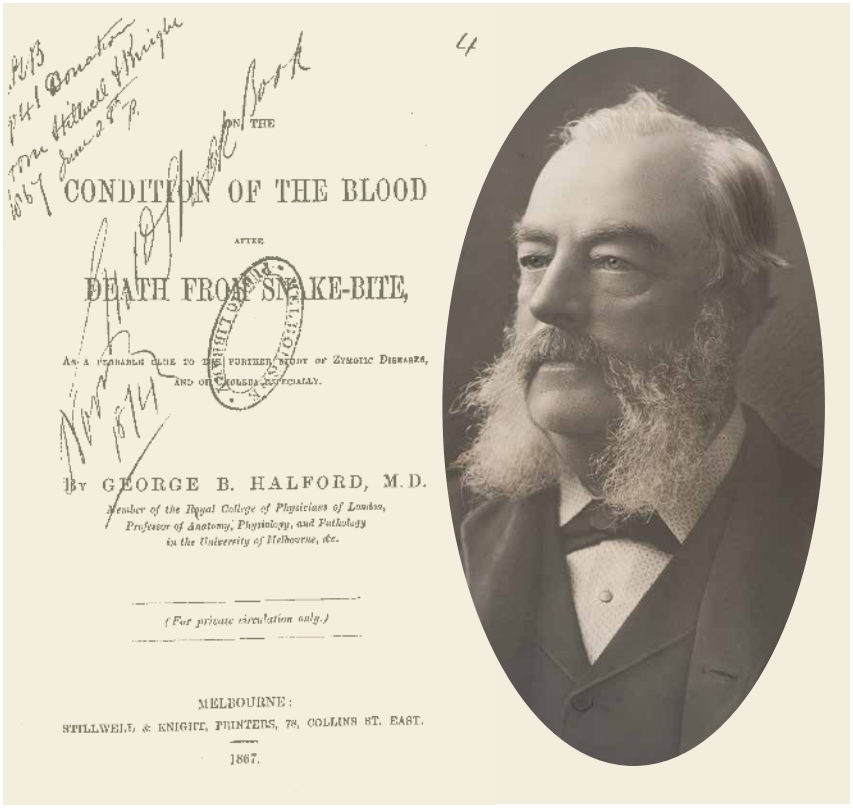
Venomous collections

Kenneth D. Winkel and Jacqueline Healy

> In many countries now, research in Universities is under severe financial restraint. This is a short-sighted policy. Ways have to be found to maintain University research untrammelled by requirements of forecasting application or usefulness. Those who wish to study the sex-life of butterflies, or the activities associated with snake venom or seminal fluid should be encouraged to do so. It is such improbable beginnings that lead by convoluted pathways to new concepts and then, perhaps some 20 years later, to new types of drugs.
>
> —John R. Vane, 1982[1]

More than 30 years after Nobel Prize-winner John Vane's invocation concerning the value of curiosity-driven research, including allusion to the role snake venom played in his pathway to pharmacological discovery, this sentiment remains just as relevant. Indeed, at least two subsequent Nobel Prizes involved the use of venoms or toxins as key sources of bioactive compounds or critical molecular probes of structure-function relationships: the 1986 physiology or medicine prize for Rita Levi-Montalcini's and Stanley Cohen's discovery of growth factors, and the 2003 chemistry prize for Roderick MacKinnon's structural and mechanistic studies of ion channels.[2] Moreover, venoms contributed, from 'improbable beginnings' through 'convoluted pathways', to early Nobel Prizes such as Charles Richet's 1913 physiology or medicine prize in recognition of his work on anaphylaxis.[3] Richet's work commenced with the study of the effects of jellyfish venom and led to a new understanding of allergy. Although the scientific utility and societal fascination with venoms, and venomous creatures, predates the University of Melbourne, this ancient theme finds expression through many of its collections.



ON THE

CONDITION OF THE BLOOD

AFTER

DEATH FROM SNAKE-BITE,

AS A PROBABLE CLUE TO THE FURTHER STUDY OF ZYMOTIC DISEASES, AND OF CHOLERA ESPECIALLY.

By GEORGE B. HALFORD, M.D.

Member of the Royal College of Physicians of London, Professor of Anatomy, Physiology, and Pathology in the University of Melbourne, &c.

(For private circulation only.)

MELBOURNE:
STILLWELL & KNIGHT, PRINTERS, 78, COLLINS ST. EAST.
1867.

Previous page: Professor George Britton Halford, c. 1880, photograph, 17.8 × 12.7 cm. MHM00874, Medical History Museum, University of Melbourne. Shown against title page from George B. Halford, *On the condition of the blood after death from snake-bite*, Melbourne: Stillwell & Knight, 1867. 10381/11430, State Library of Victoria.

Right: Snakebite kit arranged by Dr Richard Rendle, with instructions from Dr Augustus Mueller for his antidote of strychnia, 1892; wood, metal, cardboard and glass; 2.7 × 11.2 × 8.2 cm. MHM02691, gift of Dr Robert G. Sim, Medical History Museum, University of Melbourne.

Recognising the local resonance of this topic, and inspired by its many and varied aspects, last year we curated a 'venomous' exhibition at the Medical History Museum (*Venom: Fear, fascination and discovery*, 25 March – 24 August 2013). The exhibition, and the associated catalogue,[4] featured items from the Medical History Museum, the Australian Venom Research Unit Collection, the Australian Medical Association Archives of the Brownless Biomedical Library, Baillieu Library Special Collections, the Walter and Eliza Hall Institute Archives, and the Donald Thomson Collection at Museum Victoria (not to forget external collections such as those of the National Gallery of Victoria, State Library of Victoria, Museum Victoria, Commonwealth Serum Laboratories (now CSL Limited) and the National Philatelic Collection of Australia Post, among others). The exhibition foregrounded the contribution of the University of Melbourne and associated Australian institutions to world toxinology.[5] This article highlights a variety of items, drawn from the university's cultural collections, which contributed to the rich narrative of past physical, and forthcoming virtual, 'venomous' exhibitions.

The University of Melbourne's venom story was galvanised, in April 1867, by the unfortunate fate of a Victorian manure merchant, latterly returned from Ceylon, and his exotic pet cobra.[6] It is ironic that a case of snakebite by a non-Australian snake, examined by an English doctor, led to international medical interest in Australian snake venoms, and precipitated local snakebite research that continues to this day. Specifically, the fatal bite inflicted by the cobra on his merchant owner stimulated George Britton Halford (pictured on p.15), professor of anatomy, physiology and pathology, as well as dean of the emergent medical school, to develop his radical 'germ theory' of snakebite poisoning.[7] This concept stemmed from Halford's observation, at the post-mortem examination of the cobra bite victim and in subsequent experiments, of what he thought was 'germinal matter' injected by the snake, which Halford presumed multiplied rapidly, and which he held responsible for 'the ultimate extinction of combustion' observed in snakebite patients.[8] This idea was obviously influenced by the contemporary excitement around the putative causative role of germs in the pathogenesis of infectious disease and led Halford to propose a new treatment for snakebite, using intravenously injected ammonia.

Another local and similarly incendiary character was the Prussian-born Dr Augustus Mueller of Yackandandah. Mueller promoted injections of strychnine, arguing that this poison, used as a stimulant, was an appropriate pharmacological antagonist of the venom's inhibiting effect on the nervous system (illustrated above).[9] Such was the power of his advocacy that even Queen Victoria demanded a trial of this new treatment. Fortunately the use of this product diminished as news emerged of a more scientifically based antidote, known as *serum antivenimeux* and produced by the Pasteur Institute in France.

From these beginnings, the University of Melbourne has continued to contribute to the global debate on the nature of venom and the treatment of its effects. Specifically, a succession of internationally significant venom researchers, notably C.J. Martin (Department of Physiology), Neil Hamilton Fairley and Charles Kellaway (Walter and Eliza Hall Institute) accompanied by William Feldberg (Walter and Eliza Hall Institute) and E.R. Trethewie (Walter and Eliza Hall Institute and later the Department of Physiology). Then Saul Wiener and Struan Sutherland documented their respective

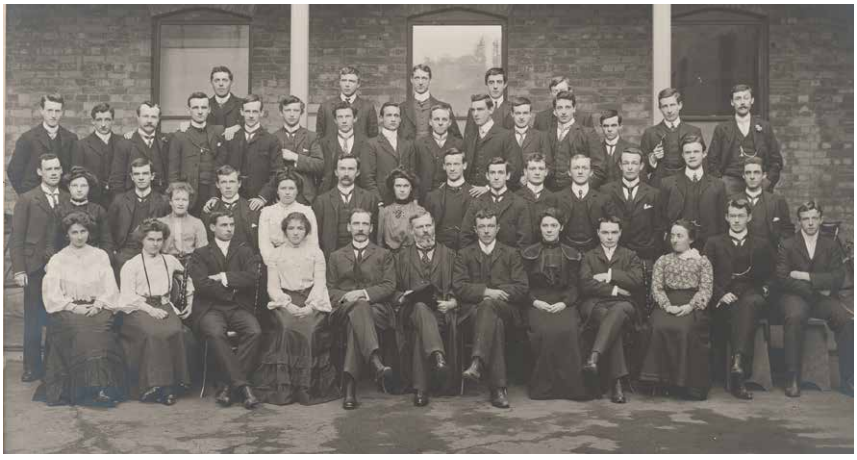
Right: Andor Meszaros, *Charles H. Kellaway F.R.S.*, 1941, bronze, 9.5 × 9.8 × 1.0 cm. MHM03203, Medical History Museum, University of Melbourne.

Below: Sears Studios, Third-year medical students with Professors C.J. Martin and Harry Brookes Allen, 1903, photograph, 24.3 × 34.1 cm. MHM00303, Medical History Museum, University of Melbourne.

pioneering venom and antivenom research as Melbourne MD candidates working at CSL.

Charles James Martin was educated at King's College and St Thomas's Hospital in London, then worked as an apprentice to Leipzig physiologist Carl Ludwig. He was appointed as a lecturer at the University of Melbourne in 1897 and eventually succeeded Halford as professor of physiology (pictured below).[10] Acutely aware of international developments in venom research, Martin saw an opportunity to make a major contribution to this emerging field. He proved the need for specific Australian antivenoms after demonstrating that the French *serum antivenimeux* was ineffective against Australian snake venoms. By 1901 Martin was awarded his Fellowship of the Royal Society, for papers that 'deal with the chemistry and physiology action of snake venom, and with the action and reaction of toxins and antitoxins'.[11]

It was the work of Fairley, Kellaway, Feldberg and Trethewie that brought Australia into the modern era of venom research. Together with Frederick Morgan, director of CSL, Kellaway (director of the Walter and Eliza Hall Institute) developed a major program of venom and antivenom research in the late 1920s and early 1930s. This work resulted in the first commercial antivenom developed for use in Australia. It was in late 1930 that the tiger snake antivenom was released.[12] This career-defining research eventually led to Kellaway's Fellowship of the Royal Society. Andor Meszaros' 1941 bronze medal of Kellaway, commissioned to celebrate that event, is pictured above. Kellaway's consistent partner in this work was the pioneering Australian medical scientist Fanny Eleanor Williams, who worked at the Walter and Eliza Hall Institute from 1920 to 1957.



The connection between the University of Melbourne and CSL continued through the post-war work of Saul Wiener and Struan Sutherland. Wiener's studies (MBBS 1947, PhD 1953, MD 1960) led to the CSL red-back spider and stonefish antivenoms, as well as beginning the study of cone snail toxins and the *Chironex fleckeri* box jellyfish venom.[13] Indeed, a particular stimulus for last year's exhibition was the donation, by Mrs Fay Wiener in late 2012, of the lifetime materials collected by her late husband, who worked at CSL from 1952 to 1958. This material now forms the Wiener Collection in the Medical History Museum (see p. 18). Wiener was a Jewish refugee from Nazi Germany; his life and career, as represented in his collection, were a victory of hope and achievement over adversity.

Although Struan Sutherland was appropriately recognised for his

Right: Struan Sutherland demonstrating the pressure immobilisation technique on volunteer CSL staff member Erin Lovering, 1979, in Struan Sutherland, *A venomous life: The autobiography of Professor Struan Sutherland*, Melbourne: Hyland House, 1998, p. 275. Australian Venom Research Unit Collection, University of Melbourne. © Copyright Struan Sutherland. Used with permission.

Below: Saul Wiener for Commonwealth Serum Laboratories, specimens used for research for the development of funnel-web and red-back spider antivenoms, c. 1955, photograph, 9.4 × 12.3 cm. MHM02013.85, Saul Wiener Collection, Medical History Museum, University of Melbourne.

success at developing the funnel-web spider antivenom, his most important legacy to the field of toxinology was the 1979 development of the pressure immobilisation bandaging technique. This first-aid technique, illustrated above, combines occlusive bandaging of medium pressure to block lymphatic transport of toxins, with limb splinting and patient immobilisation. Sutherland subsequently founded the Australian Venom Research Unit, in the Department of Pharmacology at the University of Melbourne, upon the privatisation of CSL in 1994.[14] Materials collected by Sutherland and his predecessors at CSL now form part of the Sutherland Collection and Australian Venom Research Unit Collection.

Critical contributions to the Australian story of venom were also made by others such as the naturalist Frederick McCoy (Department of Natural Sciences and National Museum), zoologist David Fleay (Department of Zoology, Melbourne Zoo and Healesville Sanctuary), herpetologist Tom 'Pambo' Eades (Melbourne Zoo, Walter and Eliza Hall Institute and CSL) as well as zoologist turned anthropologist Donald Thomson (Walter and Eliza Hall Institute and Department of Zoology).[15]

Thomson's venom research is mostly overlooked compared to his later anthropological work. But these two strands of his research came together in his work as a member of Kellaway's venom research program at the Walter and Eliza Hall Institute from 1929 onwards. Thomson explored Cape York in 1928–33, during which time he collected many animals, including 200 snakes, and wrote copious notes, which included Aboriginal knowledge of the snakes. He is pictured (opposite) undertaking field work, which included milking taipan snakes in an era of no antivenom. In contrast to his predecessors, Thomson did not embrace prevailing negative views based on social Darwinism but, rather, came to actively appreciate, value and document Indigenous perspectives.

Hence Thomson's work represents a remarkable gateway or meeting place between different forms of knowledge. One of the Health Sciences Gateway projects that the

Donald Thomson milks venom from a taipan, *Oxyuranus* sp., Cape York Peninsula, Queensland, 1928. Photograph by Donald Thomson. Courtesy of the Thomson family and Museum Victoria (TPH5383).

Faculty of Medicine, Dentistry and Health Sciences at the University of Melbourne is developing with Museum Victoria staff is an online exhibition titled *Venomous encounter*. The broader objective of this exhibition is to create a space to celebrate and explore past, present and future engagement between Indigenous knowledge, natural history and medical science. It will re-examine the currently Western-dominated historiography of an aspect of Australian natural history that has unique medical resonance: the venomous encounter. In doing so, it will seek to foster a reframing of Indigenous culture towards an enrichment of the Health Sciences Gateway's approach to the university's Grand Challenges (understanding our place and purpose, fostering health and wellbeing, and supporting sustainability and resilience) and to the university's Reconciliation Action Plan. This exhibition will follow the launch of an online version of last year's *Venom: Fear, fascination and discovery* exhibition (supported by bioCSL and a Cultural and Community Relations Advisory Group grant). Both are planned to provide a permanent site of community engagement with this fascinating topic. We hope the exhibition contributes, in a small way, to highlighting what still needs to be done in combating the fear of the power of venom.

Dr Kenneth D. Winkel is director of the Australian Venom Research Unit, and a senior research fellow at the University of Melbourne. He has published over 100 papers and book chapters and is a co-editor of the first book on venomous bites and stings in Papua New Guinea.

Dr Jacqueline Healy is curator of the Medical History Museum, University of Melbourne. She was the inaugural director of Bundoora Homestead Art Centre from 2002 to 2011. Previous positions include director of the Museum and Art Gallery of the Northern Territory and director of public programs at the National Gallery of Victoria.

The **Medical History Museum** is located on Level 2 of the Brownless Biomedical Library. It is open Monday to Friday from 10 am to 5 pm, Saturday from 1 pm to 4 pm and closed on Sunday.

1 John R. Vane, Nobel Banquet Speech, 10 December 1982, www.nobelprize.org/nobel_prizes/medicine/laureates/1982/vane-speech.html.
2 Rita Levi-Montalcini, 'The nerve growth factor: Thirty-five years later', Nobel Lecture, 8 December 1986, www.nobelprize.org/nobel_prizes/medicine/laureates/1986/levi-montalcini-lecture.pdf; Roderick MacKinnon, 'Potassium channels and the atomic basis of selective ion conduction', Nobel Lecture, 8 December 2003, www.nobelprize.org/nobel_prizes/chemistry/laureates/2003/mackinnon-lecture.pdf.
3 Charles Richet, 'Anaphylaxis', Nobel Lecture, 11 December 1913, www.nobelprize.org/nobel_prizes/medicine/laureates/1913/richet-lecture.html.
4 Jacqueline Healy and Kenneth D. Winkel (eds), *Venom: Fear, fascination and discovery*, Medical History Museum, University of Melbourne, 2013; see 'Venom', *University of Melbourne Collections*, issue 13, December 2013, p. 56.
5 'Venom: Fear, fascination and discovery', *Visions*, 12 July 2013, http://visions.unimelb.edu.au/episode/166.
6 Peter Hobbins, 'Snake germs and Professor Halford's webs', *UMA Bulletin: News from the University of Melbourne Archives*, no. 29, July 2011, pp. 3–5.
7 George Britton Halford, *The new treatment of snake-bite: With plain directions for injecting*, Melbourne: Stillwell and Knight, 1869. Special Collections, Baillieu Library, University of Melbourne.
8 George B. Halford, 'Experiments on the poison of the cobra-di-capella', *Argus*, 26 April 1867, p. 6.
9 See Peter Hobbins, 'Spectacular serpents: Snakebite in colonial Australia', in Healy and Winkel (eds), *Venom: Fear, fascination and discovery*, pp. 37–44.
10 Juliet Flesch, 'Snakebite and chloroform', in *Life's logic: 150 years of physiology at the University of Melbourne*, Melbourne: Australian Scholarly Publishing, 2012, p. 22.
11 Harriette Chick, 'Charles James Martin, 1866–1955', *Biographical Memoirs of the Royal Society*, 1 November 1956, vol. 2, pp. 173–208.
12 Peter G. Hobbins and Kenneth D. Winkel, 'The forgotten successes and sacrifices of Charles Kellaway, director of the Walter and Eliza Hall Institute, 1923–1944', *Medical Journal of Australia*, vol. 187, no. 11–12, 3–17 December 2007, pp. 645–8.
13 Ken Winkel, 'Saul Wiener AM, 1923–2010' (obituary), *Chiron*, 2011, p. 29.
14 J. Tibballs, 'Struan Sutherland: Doyen of envenomation in Australia', *Toxicon: Official Journal of the International Society on Toxinology*, vol. 48, no. 7, December 2006, pp. 860–71.
15 Ian Temby, 'Donald Thomson: Australia's Lawrence of Arabia', in Healy and Winkel (eds), *Venom: Fear, fascination and discovery*, p. 94.