

# Frank Macfarlane Burnet (1899–1984): Australia's gift to immunology

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At the turn of the 20th century, the immune system was an enigma, but a boom in research would soon arrive. One of the pre-eminent pioneers of that age was an Australian physician-scientist named Frank Macfarlane Burnet. His prodigious and ingenious work in the fields of immunology, virology and bacteriology provided the foundation for a myriad of medical breakthroughs. Indeed, the life-giving field of solid organ transplantation is deeply indebted to the vision and foresight of Burnet.

**OF BEETLES, BOY SCOUTS AND FAITH** Burnet was born on 3 September 1899 in the small town of Traralgon in the state of Victoria, Australia. His father worked for Colonial Bank and his mother was a housewife. Both parents were of Scottish ancestry, having come from immigrant families that had made Australia their new home. Affectionately known as Macfarlane or 'Mac' to family and friends, Burnet was the second of seven children.

When Burnet was ten years old, his family moved to the small rural town of Terang, Victoria, which left an inefaceable impression upon the young lad. An extremely bashful child, he took to exploring the town's surrounding countryside alone, immersed in the splendor of nearby Lake Terang. These experiences instilled in Burnet a great passion for and curiosity about nature, and he became an ardent participant in the Boy Scouts. He was drawn to the study of biology and began to amass a lifelong collection of beetles, often annotating entomology texts with his own notes and illustrations. A voracious reader of books on natural sciences, he regularly wrote to libraries in Melbourne to obtain additional sources from which to learn. Notably, he developed a precocious interest in the writings of Darwin and HG Wells, which stimulated, respectively, his understanding of evolutionary concepts and the interplay of science and society, as well as influencing his perspective on religion. Although he came from a Christian home, Burnet was openly agnostic throughout his adulthood, declaring that faith in organised religion was "an effort to believe what common sense tells you isn't true".

Burnet's scholastic initiative and aptitude quickly captured the attention of the community minister, Reverend Samuel Fraser. The Reverend felt that the young man was particularly bright

and in need of academic nurturing. To this end, he encouraged Burnet's parents to send their son away for a formal university education. Burnet eventually obtained a residential scholarship to the University of Melbourne, where he selected medicine as his academic pursuit. In 1922, he earned his MBBS degree and graduated as salutatorian in a particularly illustrious class that would produce a number of future researchers. Subsequent to his MBBS, Burnet prepared himself for the MD degree certification examination and successfully completed it in 1924.

**FROM NEUROLOGY TO BENCH RESEARCH** While spending a compulsory year as a resident medical officer, Burnet studied with one of Melbourne's most respected neurologists, Dr RR Stawell. Burnet enjoyed his experience and became convinced that he wanted to be a clinical neurologist. However, the hospital superintendent, believing that Burnet possessed characteristics that were better suited to laboratory work, intervened and steered him toward research. He was denied a training position in neurology and assigned to a registrar position in the pathology lab. Although he was initially disappointed, Burnet quickly discovered a latent passion for scientific investigation. At that time, the pathology laboratories of the University of Melbourne fell under the directorial umbrella of the Walter and Eliza Hall Institute, an academic organisation of



clinical and bench research. Burnet was fortuitously exposed to a project that investigated the theoretical treatments of typhoid fever, which sparked his imagination and inspired him to formulate hypotheses of his own. In the same year, he authored a publication on the agglutination reactions of typhoid.

Burnet's potential as a researcher impressed the director of the institute, who dispatched him to the Lister Institute in London, United Kingdom, to obtain additional training in research. For the next two years, from 1925 to 1927, Burnet studied bacteriophages and obtained a PhD from the University of London. Upon his return to the Hall Institute, he became an assistant director and was given his first assignment – investigating the Bundaberg Disaster, in which 12 children died from a contaminated vaccine. At the same time, he conducted pioneering work on bacteriophages and offered an early description of lysogeny, a method of viral reproduction, that served as a platform for future Nobel laureates

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in the characterisation of viral genetics. His legacy to virology also included the development of the haemagglutination assay and the understanding of the epidemiology of the herpes simplex virus. In 1944, he became the director of the Hall Institute and ushered in a particularly prodigious period of research, now referred to as the Golden Age of Virology.

Burnet also worked on bacteria, including characterising the causative bacterial agents in both psittacosis and Q fever. During his work with the Q fever organism, he was the first person in the laboratory to directly contract the illness, a casualty of hands-on bench research. The organism responsible, *Coxiella burnetii*, was named in his honour.

**A SCIENTIFIC GIANT** Burnet was a consistent and highly productive bench researcher, authoring some 30 books and countless publications that spanned six decades, beginning with his first in 1924. His magnum opus dealt with concepts of immune tolerance and clonal selection. In 1941, he authored a monograph entitled *The Production of Antibodies*, which is now widely regarded as a classic publication in the field of immunology. In this work, he proposed notions of ‘self’ and ‘non-self’, which described how an individual’s immune system was able to differentiate between the cells and protein that make up its own body from those of foreign micro-organisms or substances. In 1959 he published another book, called *The Clonal Selection Theory of Acquired Immunity*, which dealt with how the human body developed and produced antigen-specific antibodies. His hypothesis that the body could learn to reject or accept particular antigens, a concept now known as ‘immune tolerance’, was more than a fanciful abstraction, as it exerted a powerful impact on the direction and momentum of medical immunology. In part because of Burnet’s work, patients worldwide have gained longer and better lives with transplanted hearts, livers, kidneys and other organs. For his efforts, Burnet shared the 1960 Nobel Prize in Physiology or Medicine with Peter Medawar, a rare achievement for an Australian.

**THE COUNTRYMAN** In Australia, Burnet was equally renowned for his work in public health and his role in developing the sciences. Although he was a lifelong introvert, he managed to train himself to be a cogent public speaker, delivering speeches

and spearheading campaigns dealing with public health concerns such as smoking and nuclear radiation exposure. He served on numerous scientific advisory boards, including a term as the president of the Australian Academy of Science, leaving his mark on national health attitudes and shaping future physician-scientists. He was steadfast in his loyalty to Australia, turning down an offer from the prestigious Harvard University in order to stay and work in his home country. Burnet’s sense of national pride was evident in his acceptance speech for the Nobel Prize: *“I have come to this celebration from a greater distance than any previous laureate and as the first Australian to appear on the Nobel list, I think that this occasion has a rather special significance for my own country, a middling small country a little bigger than Sweden but only now beginning to create an image of its own in the eyes of the world. Someday I hope that we will take our place along with Sweden as one of the centres where knowledge can go along with social progress to the good life we all seek.”*

The country that Burnet so loved named him Australian of the Year and appointed him Knight of the Australian Order. His image appeared on national postage stamps, and his hometown of Traralgon, Victoria, erected a statue in his likeness. Following his death from colorectal cancer in 1984, Australia held a state funeral in his honour, a rare tribute for a man outside the world of politics and government.

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