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ESSAY REVIEW

BROAD-MINDED BIOLOGIST

by

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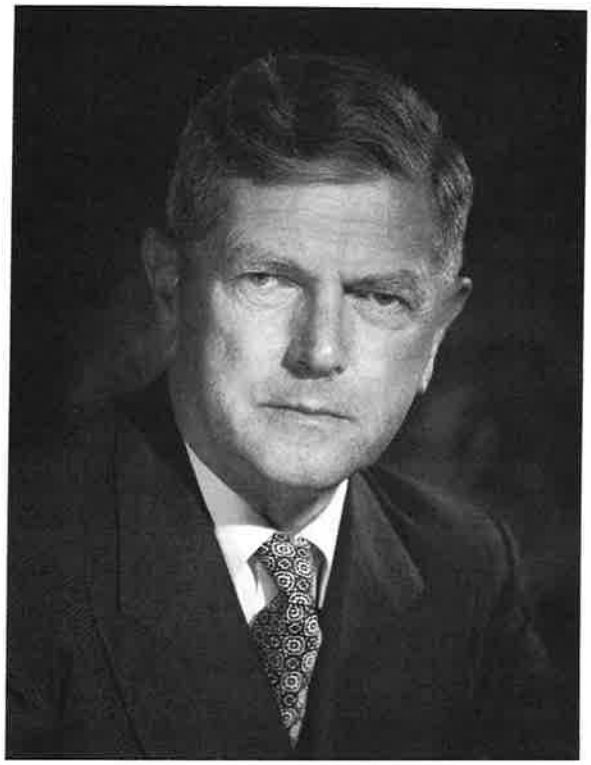
Christopher Sexton, *The Seeds of Time: the Life of Sir Macfarlane Burnet.* Oxford University Press, 1991. Pp. 301, £19.95. ISBN 019 5532740

Those who knew Burnet only after he had become a successful and widely respected scientist will be surprised to learn from this biography that, when younger, he had been shy and diffident. There is, however, no room for doubt about this. Sexton quotes illustrative comments by others, passages from diaries, and the autobiography published in 1968. Shyness and diffidence were not familial traits: there are 15 Burnet(t)s in the *DNB,* and F.M. Burnet claims five Fellows of the Royal Society as collaterals. The shyness may have arisen from his mother's preoccupation with the care of his mentally-retarded elder sister and the failure to make close contact with his father, a banker who had emigrated from Scotland to Australia in 1880. The young Burnet became an assiduous reader, with a keen interest in natural history and a special interest in beetles.

In the first 40 pages, Sexton deals with these family matters and with Burnet's school and medical education. He has here a leaning towards flowery language; instead of eating, people 'partake of bland fare'. Luckily, this tendency does not persist. A clear description of Burnet's adolescence describes his recognition of the hypocrisy of many devout and regular church-goers and, after reading Shaw and Wells, his consequent atheism. But he was not, at first, dogmatic. After unproductively attending meetings of the Student Christian Movement, he went to some alternative religious services but concluded (in 1918) that all faiths were 'almost pitiful'. Parts of his diary, written when he was 19 and when there was a war in Europe in which Australia was involved, are revealing. He foresaw that after the war there would be '. . . intolerance towards those who have not enlisted . . .'. For what he recognized as 'selfish reasons', he decided to enlist, but the Armistice resolved his ethical dilemma.



Sir Frank Macfarlane Burnet.

When 23, in a self-assessment in his diary, he wrote '. . . I believe strongly in my suitability for laboratory and research work and there are bound to be further opportunities for a well trained research pathologist who has done something new as I hope to do.' The authorities of the Walter and Eliza Hall Institute in Melbourne agreed with this assessment and he started research on typhoid fever. This was a change of direction. He had written a theoretical neurological paper on the difference between epicritic and protopathic sensations; it was rejected. His work on typhoid involved agglutinating bacterial cultures with antiserum. Two diary comments on this work illustrate aspects of Burnet's personality. He had a serum which prevented agglutination and noted that this could revolutionize vaccine therapy and make him famous. His diary in 1965 recalls that, in 1923, when cultivating bacteria on the surface of a solid medium, he had noticed some large clear plaques in the uniform lawn. Having just read D'Herelle's book on bacteriophage, he assumed that a phage caused the plaques. Self-critically, 42 years later, he wonders whether, had he noticed the plaques before reading the book, would he have realized, as Twort and D'Herelle did, that he had discovered a new phenomenon. There are several other

such self-critical comments in his diary. He felt he should have noticed hemagglutination by influenza virus; this later became a useful method of assay. In 1940, he found that polio was orally transmitted. Being wise after the event, he thought he should have realized that the virus was therefore multiplying in cell culture; in 1949, that was the basis of an anti-polio vaccine. And he observed, but did not correctly interpret inhibition of the growth of one strain of influenza virus by the presence of another strain; interferon was identified later in another lab.

Other people were less critical. Burnet accepted an invitation to be curator of the National Collection of Type Cultures at the Lister Institute in London. This allowed only part-time research. After a few months he got a Beit Fellowship for full-time research at the Institute into factors influencing bacterial susceptibility to phage attack. This work, and his general knowledge of phage research, led to an invitation to write the phage chapter in the eight-volume *System of Microbiology* which was being organized by the Medical Research Council. His diary records that, while in Melbourne, he had had success in another direction: 'My education proceeds apace. Today I came very near to making friends with a girl'. On his return from London he married Linda Druce, to whom he had been writing at length. Consequently, Sexton can, by quoting from 15 of these letters, describe Burnet's life in the lab, visits to museums and art galleries, and excursions to historically interesting places near London and on the continent.

While a student, Burnet commented in his diary that 'I should like to see an organized, efficient, hygienic world but I do not want to come under the dictatorship of the proletariat in the process.' While in London he tried to clarify his political position and described the process in these long letters. He analysed in some detail lectures by Bertrand Russell, characterized as 'an irritating little blighter', and Ramsay Macdonald, characterized as a 'puzzled idealist'. Like many others, he drifted to the right as he aged. The drift was intermittent: he was one of the signers of a letter supporting the Australian Labour party in the 1972 election.

For six months, Burnet hesitated between returning to Australia to be Assistant Director of the Hall Institute, and staying in London where it seemed likely that he would get a professorial chair which was soon to become vacant. The combined pull of Druce and certainty prevailed. Soon after he returned to Melbourne, 12 out of 21 children, who had been prophylactically inoculated against diphtheria with a standard toxin-antitoxin mixture, died. When interviewed in 1985 he said that this was probably an example of what is now called the 'toxic shock syndrome' sometimes caused by intravaginal tampons. Staphylococcal toxins were his main research subject for the next year, then he got back to phage. He helped to clarify lysogeny – the ability of some bacteria, while not themselves showing obvious signs of phage infection, to release phage and lyse other bacteria. He later found a similar phenomenon with psittacosis. Parrots which seemed healthy, nevertheless became infective

as a result of stress in bird-dealer's cages. He suggested that some aspects of the epidemiology of human polio and yellow fever could be explained in the same way.

Many scientists thought of phage as a single entity. Burnet collected faeces from all the animals on his brother's farm and started a system of classification of the 50 phage strains in them. It was based on their immunological characteristics and on their ability to find receptive sites on the surfaces of different bacteria. Unlike many scientists, Burnet did not yearn to be the Linneaus of virology. He saw that an attempt to introduce a system of binomial 'classification' would, at that time, have been mere arbitrary labelling. By 1953, he felt that enough was known about the size, shape and intrinsic properties of some viruses for a classification to be possible, and he joined subcommittees, set up after a meeting of the International Congress of Microbiology, to classify some groups.

During a two-year Fellowship at the National Institute for Medical Research in London, he concluded his work on phage and published his last paper on it in 1937. Although offered a permanent job in the NIMR, he returned to Melbourne, taking with him several viruses (e.g. vaccinia, cowpox and fowlpox) on which he had begun working in London. He also brought an enthusiasm for their cultivation on the membrane which surrounds the chick embryo. On this membrane, dilute suspensions of several viruses formed countable pocks, similar to the plaques formed by phage on bacterial lawns. This made quantitative assay possible with viruses, such as those causing influenza and herpes, and with the related organisms causing psittacosis and Q fever. Sexton tells the story of the last name. Q stood initially for Queensland because the disease was first noticed among abattoir workers in that state. When there were objections to the state being thus pilloried, objectors were reassured by being told that Q stood for 'query' because the agent did not seem to be a virus in the strict sense of that term.

Having discouraged a tentative offer of a professorship at Harvard, Burnet started his 21-year Directorship of the Hall Institute in 1944. About 1957, the main direction of research there veered from studying the agents causing disease, to studying the host's reaction to them. This was in accord with his tendency, shown since boyhood, to be a natural historian or ecologist. He described his first book, *Biological Aspects of Infectious Disease* (1940), as written '. . . from the point of view of a biologist as much interested in how the parasite species survives as in how the host survives it', and said he aimed '. . . to present a simple account of the microorganisms which cause disease, of the processes within the body which are called into action against them, and of the way infection persists and spreads within the community'.

He was fascinated by the manner in which placental embryos learn to recognize as 'self' those antigens to which they were exposed before birth. Thus, just as a cow calf, if the twin of a bull calf with which it shares a placenta, becomes a freemartin because of prenatal exposure to male sex hormones, so *all* twin calves share antigens and so can accept grafts from each other after birth. He explained the principles of

immunological tolerance and of the need to inhibit the immune mechanism of a host before attempting an organ transplant, in *The Production of Antibodies* (2nd ed., 1949). From this he went on to formulate the clonal selection theory of antibody production.

Early explanations of the specificity of antibodies had the antigen impressing itself on the lymphocytes so that the globulin they produced later fitted the antigen. A refinement of that idea had unstimulated lymphocytes producing many different globulins; if one of them fitted the antigen, that complex was able to stimulate lymphocytes to make its type of globulin in future. Burnet liked the Darwinian aspect of this suggestion, compared to the Lamarckism of the earlier one, but he pushed the process of selection further back and suggested a varied, and frequently mutating, population of lymphocytes. Union of one lymphocyte with the antigen stimulated that cell into clonal multiplication. He compared his hypothesis to the already fairly well-established ideas about the production of adaptive enzymes. Work in the Hall Institute confirmed that lymphocytes differed initially, and that one clone, confronted with two antigens, chose between them. To an outsider, it may look as if Burnet had made a rather simple, even obvious, suggestion. However he, and most experts, look on it as his most important contribution to biology.

No one questioned Burnet's unusual scientific acumen and originality, but there was some criticism of his method of running a lab. For example: the sudden switch from virus research to immunology was thought dictatorial; his antipathy towards group research, with elaborate and expensive equipment, was thought old-fashioned and mean; statisticians resented his neglect of their skills; some colleagues complained that they were expected to be obedient and not to argue. Sexton, just after disparaging Burnet as an amateur ethologist, indulges in some amateur ethology himself. Apropos of this, he points out that Burnet's 11 closest colleagues during 40 years were women.

Scientific success brought many invitations to lecture and write articles on themes other than pure science. These did not please everyone. He argued that experimental research should not be a principal occupation in a University Medical Faculty, that literature was a very important hobby but not a University subject, and that nuclear power was an '. . . interim experiment to allow the development with all deliberate speed of the only perpetual and non-polluting source of industrial power: the energy of the sun'. He annoyed doctors in parts of Australia where child mortality had diminished, by suggesting that this was more the result of improved maternal education than of their efforts; he annoyed molecular biologists everywhere by arguing that proper distribution of known methods of preventive and curative medicine would do more to promote human welfare than would result from their discoveries. An undated note suggests that, if Nobel were alive now, prizes for eliminating conflicts, controlling population, conserving resources and maintaining human genetic health, would replace the existing ones.

Few scientists have left biographers (and book reviewers) such a rich mine of personal information as Burnet. He was an assiduous diarist, letter writer, filer of odd notes and author of 31 books, most of which included some personal information. All this was possible because, as an associate reports '. . . he rarely crossed out a word, and almost never produced a second draft; the first, neatly hand-written draft was ready for typing out as the final draft, ready for the publisher'. Sexton has quarried this abundant lode skilfully. Although more than half Burnet's books were translated and several were published in paperback as well as hardback, Sexton tells a strange story of his distress at finding some of them, in an unnamed library, apparently unread because in mint condition. To be perpetually dissatisfied with achievement is perhaps a feature of genius.

Burnet was one of the most honoured of all Australians: appendices list decorations, membership of academies, membership of committees, international lectureships, and an apparently complete list of publications. The index is adequate.