Baron Florey of Adelaide and Marston

Philatelic heritage of a great Australian

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The Florey Fellow, The Royal Society, 1970-1974

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A Nation portrays on its postage stamps images of which the country is most proud.

Apart from the Monarch's portrait, it is rare for any individual to be portrayed on two or more Australian postage stamps. Both Captain James Cook and Lieutenant Matthew Flinders have been honoured in this way. It is rarer still for an Australian to be so acknowledged. It is not surprising therefore, that perhaps the greatest Australian, Lord Florey, is honoured in this way. This philatelic heritage complements the scores of his other accolades, both national and international, which symbolise the unique contributions of his life.

When the question is asked, "Who is the greatest Australian?", there are perhaps as many answers as there are respondents.

There are those who have served their nation in countless ways. There are those who have exhibited unimaginable courage, both in peace and in war — many unrecognised or unknown. There are others who have enriched the lives of thousands through their philanthropy. There are countless others, both known and unknown, who deserve the accolade of a "famous Australian", whether such an accolade has been bestowed or not.

If one asks the question "Which Australian's life and work has saved the lives of countless millions — both in the past and in the future", one name stands out — Howard Florey. Lord Florey gave to the world the clinical use of antibiotics. His struggle to do so was immense and included his resolve to work on an enigmatic project — simply, in the first instance, to advance knowledge; to work with meticulous and inspirational bench-top detail in his chosen domain of experimental pathology; to overcome almost insuperable problems of lack of funding support to continue his work; to press on in the face of initial apathy in his chosen field of antibiosis; and ultimately to give to the world, freely and without personal financial gain, the clinical domain of antibiotics. Sir Robert Menzies, on hearing of Lord Florey's death in 1968, echoed what many had long thought:

> *"In terms of world well-being, Florey was the most important man ever born in Australia".*

Lord Florey was elected President of The Royal Society in November 1960;[1] and decorated with the Order of Merit in 1965;[2] will and It was said:

> *"In the history of medicine, the world honours Jenner, Pasteur, Lister and Florey".*[3]…[and] *the logical sequence which spans over 150 years, the gulf between almost total therapeutic helplessness and the virtual defeat most of the important bacterial diseases".*[4]

Following his award of the Nobel Prize in 1945, scores of accolades were bestowed upon Howard Florey throughout the world. In Australia, a suburb in Canberra and the Florey Lecture Theatre at the John Curtin School of Medical Research were named after him; the Florey Building at the University of Melbourne, and the Howard Florey Institute of Experimental Physiology and Medicine (in 1997, renamed "The Florey") honour his memory in Melbourne. The Florey Lecture Theatre in the Faculty of Medicine at Adelaide University, and a statue (a bronze bust) in North Terrace record his birthplace in Adelaide. In October 1973, the Commonwealth issued the Florey $50 banknote, a high denomination note which

remained in circulation until 1994. In 1998, the Royal Australian Mint struck the Howard Florey one-dollar cupro-nickel coin, of which 332,000 were minted as special issues. The Royal Australian Mint also struck a one-dollar (fine silver) proof coin in a limited edition of 20,000 pieces, specifically for collectors and investors. In 2006, the Federal Government of Australia renamed the national Australian Student Prize, "The Lord Florey Student Prize" in his honour.

Lord Florey is one of the few Australians to have been depicted on both an Australian banknote and an Australian coin; and one of a tiny and select group who has been featured on two separate postage stamps.

These, together with the Florey Medals, are the most enduring physical memorials to Lord Florey, this greatest Australian.

Lord Florey of Adelaide and Marston

Howard Florey (1898-1968) was born in Adelaide and educated at St Peter's College where he was School Captain and Dux of the Sixth Form. He entered medicine at Adelaide University in March 1916. Although he excelled in the pre-clinical science subjects, his *persona* did not sit well with the dogma of clinical teaching of his era and he graduated, "not with the expected honours", in December 1921. [5]

At the end of his fifth year of medical studies, on 8 December 1920, Howard Florey was named the Rhodes Scholar for South Australia.[6] After graduation, he entered Magdalen College at Oxford University and undertook postgraduate studies in experimental pathology, under Sir Charles Sherrington who became his lifelong mentor and "guide and friend."[7]

Dr Florey worked meticulously in the field of experimental pathology over the ensuring 15 years. Unrelated to his later work on penicillin, he contributed much to knowledge in the fields of neuroscience, lymphatic structure and function, and blood circulation. He worked sequentially in six experimental pathology units in Oxford, Cambridge, Chicago, London, Cambridge and Sheffield. In 1935, Florey was appointed Professor of Pathology and the Head of the Sir William Dunn School of Pathology in Oxford.

Florey's team worked initially on a range of experimental projects including the role of the lymphatic system in the mammalian body, the action of lymphocytes, and how spermicides acted. A spermicide was developed by his team and given the tradename, "*Volpar*", derived from "Voluntary Parenthood". In 1936, Florey began his work on lysozyme, an enzyme contained in various body fluids including mucus and tears, which Florey showed conferred immunity from infection. In that same year, the sulphonamides were discovered as the first chemotherapeutic agents. Sulfa drugs did not act when applied locally and had unpleasant and dangerous side effects including vomiting, rashes, liver and kidney damage and the risk of fatal aplastic anaemia.[8]

Florey believed that to be effective, an antibacterial agent had to be non-toxic and effective both locally and systemically.

The Miracle of Penicillin

In 1933, Ernest Boris Chain, a "warm-hearted, excitable and always volatile" Jewish refugee from Nazi -controlled Berlin, arrived in London. He joined Professor Florey in 1936 as a brilliant young biochemist. Florey's interest was in substances , produced by living things, which inhibited the growth of bacteria. In 1938 Chain and Florey started work on penicillin . Chain noted Fleming's 1926 paper on *Penicillium* mould which had contaminated a culture plate – and whose implications had never been followed up by Fleming. In September 1939, Florey applied for funds to study the enzymes produced by the two bacteria, *Bacillus subtilis* and *Bacillus pyocyaneus* and the fungal mould, *Penicillium*. The research team comprised Professor Florey himself, Dr Ernest Chain, Dr Norman Heatley, Dr Margaret Jennings (later, the second Lady Florey), Professor Gardner, Miss Jean Orr-Ewing and Dr Gordon Sandars.

Over the ensuring four years, Florey, Chain, Heatley and Jennings laboured mightily in growing the *Penicillium* mould, in trying to extract the active principle from the liquid culture medium, in defining its structure, and in attempting to purify the active agent, penicillin. Until relatively pure penicillin could be isolated, the team could not begin the experiments to determine its potential toxicity (if any), its safety in mammals, and ultimately its potential to kill bacteria.

The work on penicillin progressed rapidly in early 1940. Florey encountered enormous difficulties in undertaking his experimental work, particularly in the period from 1936 to 1941, when:

> *"He had to engage in the unpleasant task of grant-begging from all likely sources, with endless applications, descriptions of projects, reports, estimates, letters, interviews, and the final frustration of waiting — perhaps for months for the decision of those who dispensed funds. Often, after this tedium, the applications for funding were refused".* [9]

In 1939, the Nuffield Trust turned down ("in contemptuous terms") Florey's request for funds for his research; and Oxford University also wrote that they were contemplating cutting his research grant. [10]

Dr Heatley and the team established an entire room of fermentation flasks to grow the *Penicillium* mould; and it was shown that the precious penicillin was astonishingly potent in its effects of killing bacteria — a solution of one part in one million had bacteriostatic effects.

At 11 AM on 25 May 1940, Florey and Heatley injected eight mice with a minimum lethal dose of Streptococci bacteria. Four mice were used as untreated controls and four received an injection of penicillin, one hour later. All four control mice were dead by 3:30 AM the next morning.[11] Three of the four mice protected by penicillin survived and remained well – one who had received a smaller dose of only 5 mg of penicillin initially survived, but died two days later. Dr Margaret Jennings (later, Lady Florey), said " It looks like a miracle". They all realised it was a momentous occasion.[12]

Subsequent experiments showed that the dose of penicillin was crucial. Dr Heatley commenced a massive fermentation program using trays, pie dishes, petrol cans, lacquered biscuit tins, hospital bedpans and male urinals:

> *"The standard sort of bedpan with its protruding sprout, proved to be the most practical. It formed the model for the final specially- made containers which became available at the end of 1940".*[13]

After completing graded-dose experiments in June 1940, Florey injected 50 mice with a threefold (lethal) concentrate of staphylococci and streptococci, 25 mice serving as controls. The other 25 mice were given penicillin injections every three hours for the next two days and nights. All 25 controls were dead within 16 hours. All but one of the treated mice were alive and well 10 days later.[14] On 24 August 1940, the *Lancet* published one of the most significant milestone papers in the entire history of medicine, titled "Penicillin as a chemotherapeutic agent". [15] It was typical of Florey that the author list of this famous paper was arranged in alphabetical order, not by status or rank in the experimental team.

On 12 February 1941, a 43-year-old policeman, Albert Alexander, was dying in the Radcliffe Infirmary in Oxford, from staphylococcal and streptococcal infection. The maximum dose of the precious penicillin — all that was available from the entire stock that Heatley had laboured mightily to extract — produced dramatic clinical improvement.

Tragically, because there was none of the precious penicillin powder left, the patient died on 15 March 1941, five weeks after the first injection.

At considerable personal risk during the War, in 1941, Florey flew to the United States, and successfully was the catalyst for major fermentation firms to manufacture penicillin in practical quantities. The first doses of the precious antibiotic were used to save the lives and limbs of injured soldiers. By 1945, the first doses of penicillin were available for civilian use. Thus was the world changed.

Aftermath

Florey was a man of deep reserve. He had few, if any, close friends and to none other than his two wives did he reveal personal feelings of any depth. His authorised biographer. Professor Gwyn Macfarlane, wrote in 1979

> *"Florey was a rough, tough Australian, completely uncompromising, rather prickly, very energetic and tense as a coiled spring. And he brought to his work this extraordinary dedication, which was very infectious, in such a way that he really could collect a team of people who became almost as dedicated and enthusiastic as himself."*

Florey's style was to understate – describing a brilliant co-worker as "No slouch"; [16] and in describing the sequential successes of the penicillin experiments as "We have achieved some advance". It was said:

> *"Most working scientists of calibre shun limelight and avoid appearing on the stage of public affairs. Publicity is not their business and publicity is regarded as distracting, or even destructive of their work".*[17]

Florey's principal biographer, Professor Gwyn Macfarlane, wrote of Florey:

> *"Florey's approach was straightforward, logical exploration with none of the emotional misdirection of pet theories or preconceived ideas, but always with that underlying, infectious excitement of true discovery".*[18]

Florey, Chain and Fleming were awarded the Nobel Prize for Medicine or Physiology in 1945. Fleming, narcissistic, self- promoting and publicity-seeking, was believed by many to not be worthy of the award. Florey had refused to patent the discovery of the miraculous therapeutic effects of penicillin, believing that it was to be for the benefit of all mankind. Chain disagreed with this view and their relationships were never warm thereafter. All three were featured on postage stamps in several countries and on the many tribute medals which were commissioned and struck in subsequent years.

The Medal of the Nobel Prize for Medicine or Physiology.

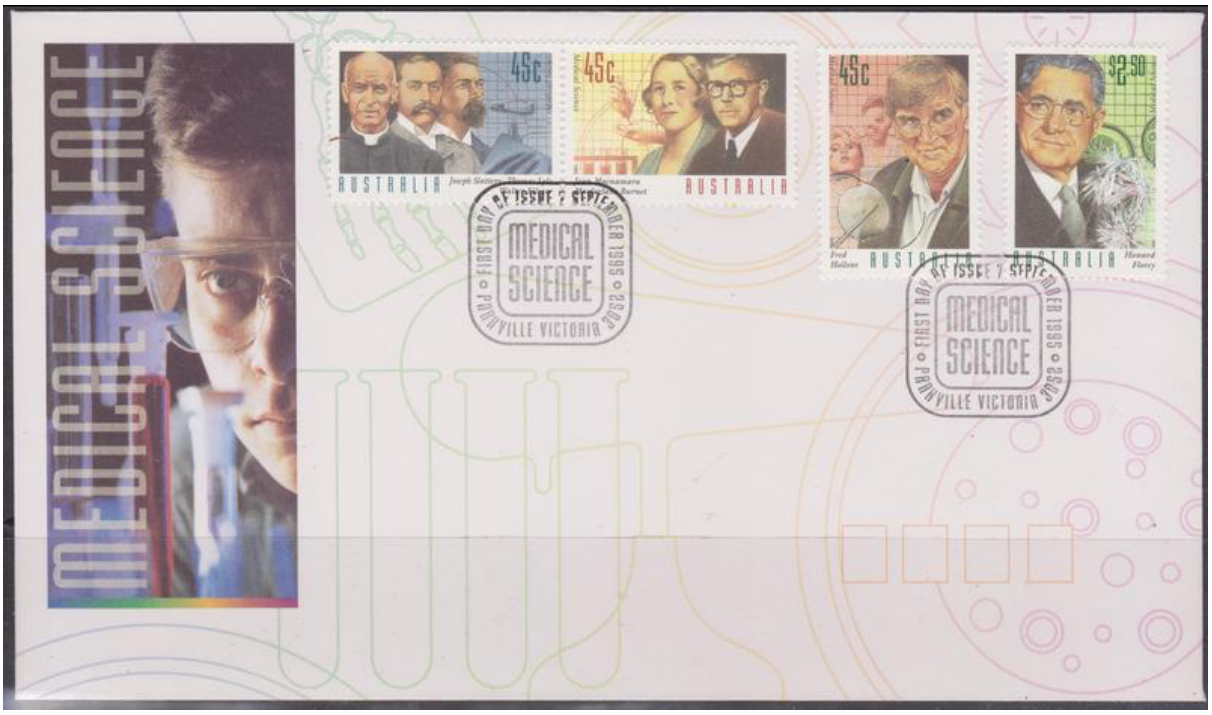
The Medal is of 23 karat gold. The obverse features the profile bust of Alfred Nobel. The Reverse features the goddess Isis receiving healing water from a healing spring, whilst supporting a female patient. At lower right is the Asklepian serpent, the metaphor of Asklepios, the Greek God of curative medicine. The Latin surround is translated as: " They who bettered life on earth by their newly found mastery".

Florey Philatelica

In 1995, Australia Post issued a Commemorative postage stamp featuring Lord Florey, as a high denomination ($2.50) postage stamp. It featured Lord Florey with a background of scientific graph paper and culture plates growing *Penicillium notatum.*

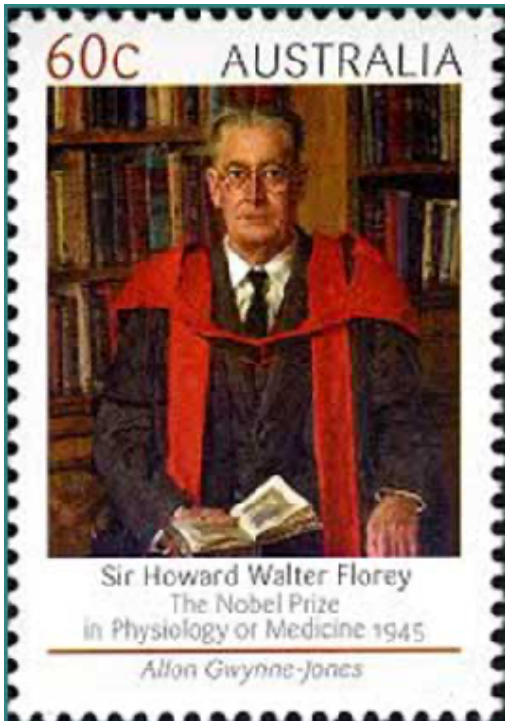
Australia Post also issued a commemorative 10 stamp sheetlet; and on 7 September 1995, issued an Australia Post postcard featuring antibiotics.

A miscellany of both Australia Post and commercial first Day covers, featuring five Nobel laureates, were also printed.



In 1995, Australia Post combined with Note Printing Australia to produce a limited edition portfolio which displayed both the $50 Australian Florey banknote and the 10-stamp Florey sheetlet. Each portfolio contained the same sheet number and banknote number as a matched pair, all with the prefix “HF”, Lord Florey’s initials. The total issue of 3500 individual portfolios was printed in two editions — a Black Edition of 2500 items, and a Red Edition of 1000 items.

On 28 August 2012, Australia Post issued a 60-cent stamp to honour Lord Florey, as one stamp of a five-stamp commemorative issue to honour Australian Nobel laureates. Sixty cents was the standard postage letter rate in that year. The Florey stamp was designed by Lynnette Traynor, an artist of the Australia Post Design Studio. She incorporated the portrait at of Lord Florey, painted by the English artist, Allan Gwynne-Jones (1892-1982).[19]



The Florey portrait was painted in 1962 from a sketch made by the artist. The Royal Society obtained the portrait in 2007. It hangs in The Royal Society's building in Carlton House Terrace, in London, in tribute to Florey's role as President of The Royal Society and of his role in changing the course of history.

Reproduction of the original sketch for the Florey portrait, courtesy of Mr Keith Moore and The Royal society, with acknowledgements.[20] The Florey stamp was produced by offset lithography,26x37 mm with perforations 14.5x14.

References

1 Note. The Presidency of the Royal Society "confers the highest honour that can be awarded to a scientist in Britain… not only in the world of science but in the wider relations of science to industry, education and government (Macfarlane, p.374). Florey, the first Australian President of The Royal Society, was diffident about accepting the post but "began his Presidency quietly and also with modesty" (p. 376). "Baron" is a rank of British nobility. "Lord" is the form of address for any member of the nobility.

2 Note. The Order of Merit was instituted in 1902, to honour a maximum of 24 living members, from throughout the Commonwealth, for distinguished service in any of the fields of human endeavour and service. It is "The pinnacle of the British honours system".

3 Macfarlane, Gwyn. *Howard Florey. The Making of a Great Scientist.* Oxford, Oxford University Press, 1979:1.

4 Ibid.:3-4.

5 Macfarlane, Gwyn. *Howard Florey. The Making of a Great Scientist.* Oxford, Oxford University Press, 1979:54.

6 Ibid.:52.

7 Fenner, Frank. "Florey, Howard Walter, Baron Florey of Adelaide and Marston (1898-1968)". In: *Australian Dictionary of Biography.* Volume 14. Melbourne, Melbourne University Press, 1996:188 - 190.

8 Note: It was subsequently found that the sulfa drugs had to be converted to sulphanilamide in the mammalian liver, and it was this chemical that was the active chemotherapeutic agent, circulating in the blood, which killed bacteria.

9 Macfarlane, Gwyn. *Howard Florey. The Making of a Great Scientist.* Oxford, Oxford University Press, 1979:272.

10 Ibid.;296.

11 Ibid.;315.

12 Ibid.;315.

13 Ibid.;36.

14 Ibid.:319.

15 Chain EB, Florey HW, Gardner A.D., Heatley NG, Jennings MA, Orr-Ewing J, Sanders AG. Penicillin as a chemotherapeutic agent. Lancet 1940; 2:226.

16 Macfarlane G. *Op cit*:294.

17 Ibid.:3.

18 Ibid.: vii.

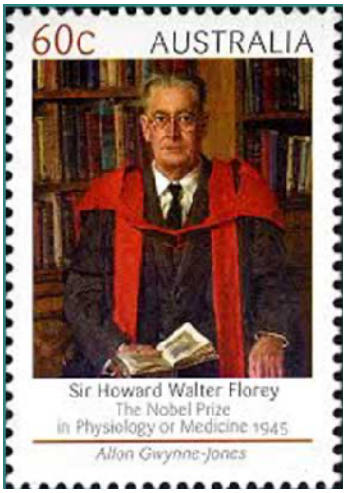
19 Note. Allan Gwynne-Jones CBE DSO RA (1892-1982) was one of Britain's leading portrait painters in the 20th century. He had graduated as a solicitor but never practised in law. He served as a soldier and was decorated for gallantry at the Battle of the Somme in 1916. Formerly the Professor of Painting (1923-1930) at the Royal College of Art in London, he re-joined the Slade School of Art where he painted the Florey portrait.

The Author

Professor John Pearn was awarded the first Florey Fellowship of The Royal Society, in 1970 for his research work in experimental pathology — initially for his contributions in the domain of platelet function in leukaemia in polycythaemia (1961); and subsequently for his work on thalidomide teratogenesis (1962-1963); and subsequently for his extensive study of the hepatotoxic and teratogenic effects of indospicine, an amino acid produced by *Indigofera spicata*, a legume about to be introduced to the Australian pastoral and agricultural scene in 1966 — as a planned program of pasture improvement, hastily abandoned after this discovery.

His research undertaken during the Florey Fellowship from 1971 to 1974, at the Institute of Child Health in London and the Muscular Dystrophy Research Unit (University of Newcastle Upon Tyne), established and defined the clinical and the genetic syndromes of the spinal muscular atrophies, a group of paralysing diseases of childhood.

Professor Pearn delivered the *Sherrington Lecture* at the University of Oxford on 30 November 1995, at Magdalene College, Oxford, where Florey had undertaken his Rhodes Scholarship under the aegis of Sir Charles Sherrington. Later, he delivered the Meryon Lecture 2001 at Worcester College, Oxford University, on 6 July 2001. Later, Professor Pearn (by then, an Honorary Research Fellow of Green- Templeton College, Oxford) was presented with one of Lord Florey's original penicillin culture flasks by the University of Oxford, for his contributions to experimental pathology, research and medical heritage.

Professor Pearn and his family became close friends with Lady Florey, Lord Florey's second wife, who, as Dr Margaret Jennings, was a co-author on the original penicillin paper published in the *Lancet* in 1940.

On 24 September 1991, Professor Pearn delivered the Address in Westminster Abbey, London, on the date of the birthday of Lord Florey, on the Occasion of the 50th Anniversary of the discovery of the clinical uses and success of penicillin; as the invited guest of the Royal Society of London, the Dean and Chapter of Westminster Abbey, and the Agent General of South Australia; and of Dr Norman Heatley, co-author of the original penicillin paper in the *Lancet*.