Howard Florey: father of the antibiotic era

The *Lancet*, 16 August 1941, in the darkest days of the Second World War, contained a paper entitled 'Further Observations on Penicillin'. Its authors were listed alphabetically as EP Abraham, E Chain, CM Fletcher, HW Florey, AD Gardner, NG Heatley and MA Jennings. There is no doubt that this paper represents one of the great landmarks in medical history and, for practical purposes, marks the birth of the antibiotic era.

The leader of this distinguished team was Professor Howard Walter Florey. This year marks the 50th anniversary of his death. Howard Florey was born in Adelaide, Australia in 1898; his father was an Oxfordshire shoe manufacturer, who had emigrated to Adelaide in 1885. Howard entered medical school in Adelaide in 1916, gained three scholarships, was good at sports and qualified in medicine in 1921. He was promptly awarded a Rhodes scholarship and worked his way to England as a ship's doctor.

Florey enrolled in the department of physiology in Oxford under Sir Charles Sherrington, who recognized Florey's qualities of hard work and a creative mind. Here, Florey studied blood flow in the brain, using a method of inserting a transparent window to make direct observation of living tissues, a technique which he later used in other parts of the body. In 1925, he obtained a Rockefeller fellowship to study mucus secretion in Philadelphia and Chicago.

In 1927, he returned to Cambridge as a lecturer in pathology. One line of research he pursued was initiated by his interest in mucus. This was to investigate an observation made in 1922 by Alexander Fleming at the Department of Bacteriology at St Mary's Hospital, London, of an enzyme which he named 'lysozyme', which was present in mucous secretions and which dissolved a variety of bacteria. Unfortunately, from the practical point of view, it acted only on relatively harmless organisms. However, Florey remained intrigued by its nature and mode of action.

In 1932, Florey was appointed Professor of Pathology in Sheffield and 2 years later moved to the University of Oxford as Professor of Pathology.

Here he recruited young research workers to investigate a number of topics – the functions of lymphocytes, the micro-circulation (using cine photography) and, importantly, work which would lead to the isolation and clinical value of penicillin.

In 1935, Florey recruited a young German Jewish refugee from Nazi Germany, Ernst Chain, to work on the action of lysozyme. Chain soon found it to be an enzyme which attacks a specific bacterial structure.

While reviewing the publications on lysozyme, Chain came across some 200 papers, going back to the mid-19th century, which recorded the inhibition of bacterial growth by micro-organisms. This included a report by Joseph Lister, of antisepsis fame, who, in 1869, found that a fungal mould, identified as *Penicillium notatum*, inhibited the growth of bacteria in urine. Lister actually tried to use the mould in the treatment of an infected ulcer on the sacrum. Louis Pasteur in 1877 noted that anthrax bacilli were inhibited in culture by unspecified bacteria. The most interesting report was that of Alexander Fleming (who had discovered lysozyme) on the inhibition of bacterial growth by the fungus *Penicillium notatum*, which he published in 1929. Further work over the next 5 years by Fleming and his biochemical colleagues failed to concentrate and purify the active substance, which he named 'penicillin'. Chain and his team set to work on the arduous task of isolating penicillin and later, with all the difficulties of wartime, of producing it in the quantities needed for clinical studies.

By May 1940, a tiny amount of crude penicillin was available for a controlled experiment. Eight mice were given a subcutaneous injection of a lethal dose of streptococci. Four were injected with the crude penicillin, the remainder acted as controls. Next morning, the four treated mice were alive and the four controls were dead – surely one of the most crucial experiments in medical history.

By the beginning of 1941, enough crude penicillin was available for the first clinical trial, the publication of which is quoted at the beginning of this article.

The next years were occupied by production of penicillin on a commercial scale, both in this country and especially in the USA, who had entered the war following the Japanese attack on Pearl Harbour in December 1941. During the war, use was almost completely confined to military cases and its value confirmed by numerous studies carried out on war wounds.

In September 1945, I had just entered my third year as a medical student at Oxford. Our course started with 10 weeks of introductory pathology, bacteriology and pharmacology. We were very impressed that every one of our pathology lectures was given by Howard Florey, even though we all knew that he was deeply involved in work of great importance.

Howard Florey was elected a Fellow of the Royal Society in 1941, was knighted in 1944 and in 1945 he received the Nobel prize for medicine, together with Ernst Chain and Alexander Fleming. In 1962, Florey was elected President of the Royal Society. Florey now relinquished his Chair of Pathology and became Provost of The Queen's College, Oxford and in 1965 became a life peer, with the title of Baron Florey of Adelaide and Marston. For some years, Florey had suffered from angina pectoris; he died suddenly in Oxford on 21 February 1968. Surely one of our greatest medical scientists. **BJHM**

Conflict of interest: none.

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