Howard Walter Florey—Production of Penicillin

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While Alexander Fleming is often credited with discovering penicillin in 1928, Howard Walter Florey oversaw initial clinical trials and led the team that first produced large quantities of this antibiotic, which played an important role in the Allied victory in World War II. But the antibacterial activity of penicillin was first discovered decades before Fleming’s work. Ernest A.C. Duchesne, a young military physician in Lyons, France, discovered penicillin in 1897 during a thesis project investigating antagonism between bacteria and fungi. On the advice of his mentor, Professor Gabriel Roux, Duchesne inoculated guinea pigs with various bacteria and then injected them with either the broth of a *Penicillium glaucum* culture or saline. Most of the animals injected with the culture broth survived, while those given saline died. Duchesne’s thesis was not noticed by the Institut Pasteur, and he entered the French Army and was unable to continue his research.

Penicillin remained unknown until Fleming left several bacterial culture plates on a laboratory bench, allegedly before leaving for his 1928 summer holiday. Fleming claimed that upon his return, he examined the culture plates and noted, “Around a large colony of a contaminating mold, the staphylococcus colonies became transparent and had obviously undergone lysis.” He subsequently carried out experiments with animals and then human conjunctivae, but had difficulty extracting adequate amounts of penicillin from culture and abandoned this work. Large-scale production of penicillin was developed by Florey and German-born British biochemist Ernst B. Chain more than a decade later.

Florey was born in Adelaide, South Australia, on September 26, 1898, the youngest of five children. His father was a manager for a shoe manufacturing company. Following education at St. Peters Collegiate School and the University of Adelaide, where he obtained his MBBS degree in 1921, Florey was selected as a Rhodes Scholar to Magdalen College at Oxford in 1922. In Oxford, he developed a close friendship with John Fulton, an American Rhodes Scholar. This friendship played an important role in the development of penicillin decades later.

Florey initially studied inflammation, including work on lysozyme and gastrointestinal secretion of mucus. He married a fellow medical student from Adelaide, Mary Ethel Reed, in 1926. Their daughter, Paquita, was so named because of his time in Spain studying nerve staining in the laboratory of Ramon y Cajal. An appointment in the Department of Pathology at Cambridge resulted in obtaining his PhD in 1927, with a dissertation on the physiology and pathology of the circulation of blood and lymph. He was appointed Chair of Pathology at the University of Sheffield in 1932 and two years later accepted the position of Chair of Pathology at Oxford.

Florey wanted to pursue biochemical work in his laboratory and hired Chain upon the recommendation of Frederick Gowland Hopkins, the Cambridge biochemist who was awarded a Nobel Prize in 1929 for co-discovery of vitamins. At Florey’s suggestion, Chain began studying lysozyme and in 1938 became aware of Fleming’s work on penicillin. After reproducing Duchesne’s experiments in animals, Florey and Chain began making penicillin in porcelain vessels. The first patient treated with penicillin in January 1941 was an Oxford policeman with cellulitis, abscesses, and osteomyelitis due to a scratch from a rose thorn, who improved with drug therapy but relapsed when the supply of penicillin was exhausted. Five additional patients were treated over the next three months and the impressive results were reported by Florey in the *Lancet* in August 1941. Florey approached a British pharmaceutical firm to make more penicillin but this was not possible during wartime in England.

Although Fleming had abandoned his work on penicillin years earlier, he heard via the grapevine that Florey was working on penicillin at Oxford so he visited his laboratory. He was graciously received by Florey and returned to London, but did not participate in further
studies. Whereas Florey was abrasive or avoided the media, Fleming was always available to talk to the press, which almost led to Fleming receiving the Nobel Prize for penicillin alone.

Since it was not possible to produce enough penicillin for a clinical trial in England, Florey and a young English biochemist, Norman Heatley, traveled to the United States in June 1941. They visited Florey’s old friend Fulton, who by then was a professor of physiology at Yale University. Since large fermentation tanks would be needed, Fulton made the connections necessary for Florey and Heatley to visit the Northern Regional Research Laboratory of the US Department of Agriculture in Peoria, Illinois. Utilizing a new fungal source from a spoiled cantaloupe in a Peoria market, new culture media and fermentation in large tanks resulted in the production of larger amounts of penicillin. The first patient to be treated with penicillin in the United States was Anne Sheafe Miller, wife of the Athletic Director at Yale. Her severe streptococcal sepsis was treated in March 1942, which resulted in a complete recovery. She lived until the age of 90.

Florey and his wife Ethel then conducted a successful clinical trial utilizing penicillin, and subsequently the drug became widely used in both civilian and military hospitals. Chain strongly advised obtaining a patent, but Florey emphasized that they should not be concerned with monetary awards and should make penicillin available for patients. He was knighted in 1944 and received the Nobel Prize in Physiology or Medicine with Fleming and Chain in 1945.

Subsequently, Florey became Provost of Queen’s College (Oxford) and relinquished his position as Chair of Pathology. He became President of the Royal Society in 1960 and was responsible for obtaining new quarters for the Society at Carleton House Terrace. He established the John Curtin School of Medical Research in the Australian National University in Canberra in 1965, the same year he was created Baron of Adelaide in Australia and Marston in England. He never lost his Australian accent and retained his emotional ties with his native country, despite living in England for more than four decades. Florey was known as a man of vision, energy, and persistence who also was modest and realistic about his abilities and honors. He said, “We had a bit of luck with penicillin—a great deal of luck.” He worked seven days weekly, and technicians were not anxious to work in his laboratory. He struggled against administrative duties and always wished to devote more time to laboratory research. To young investigators, he often seemed a remote and formidable figure.

His wife Ethel died in 1966, and the following year he married Margaret Jennings, who had worked in his laboratory for over 40 years. He became a heavy cigarette smoker during World War II and developed progressive angina during the last 18 years of his life. He died suddenly in Oxford on February 21, 1968, and was honored by a stamp issued by Australia in 1995 (Scott #1461D). Florey’s portrait also appeared on the Australian $50 banknote from 1973-95.