Sir howard florey's discovery of penicillin

GENERAL INFORMATION AND EDUCATION

Sir Howard Florey was born on 24 th September 1898 in Malvern, Adelaide, Australia. From a young age he was very fond of science. He graduated as the Dux at St Peter's Collegiate School. Even though Florey was born into a wealthy family, instead of working in his father's successful shoe-making business, he decided to study medicine at Adelaide University.

Florey graduated in 1921 with a degree in MBBS and in the same year won the Rhodes scholarship for Australia to Oxford University. He travelled to England as a ship's surgeon, arriving in 1922. In Oxford, he developed a close friendship with John Fulton, an American Rhodes Scholar. Florey enrolled in the physiology department at Oxford University under Sir Charles Sherrington. Sherrington recognised Florey's creative mind and drive towards medicine. Here at Oxford University, Florey obtained a first class in the Honour School of Physiology.

In 1924, he was awarded the degrees of Bachelor of Science and Master of Arts. He moved to Cambridge as a John Lucas Walker Student (scholarship) to work as a student in the pathology department. In 1925, Florey went to the United States of America on a Rockefeller Travelling fellowship for three months in Philadelphia. While in America, he accepted an offer for a Freedom Research Fellowship at the London Hospital. He was then appointed Huddersfield lecture in Special Pathology at Cambridge in 1927. During this time he married Dr Mary Ethel Hayter. It was at Gonville and Caius College in Cambridge where he obtained his PhD for his research on blood and lymph flow.

In 1932, Florey became the Joseph Hunter Professor of Pathology at the University of Sheffield. He focussed on tetanus, gastrointestinal function and lysozyme at Sheffield University. In 1935, he then when on to become the Professor of Pathology at Oxford University. He bought his department to life by attracting young postgraduate students, expanding his lines of research and forming teams.

SCIENTIFIC BREAKTHROUGH

Florey wanted to pursue biochemical studies. With recommendation from Frederick Gowland Hopkins, a biochemist who received the Nobel Prize in 1929 for the co-discovery of vitamins, he hired Ernst Chain. Chain began studying lysozymes and in 1938 became aware of Alexander Fleming’s work on penicillin.

Penicillin remained unknown until Fleming left bacterial culture plates on his laboratory bench before going on a summer holiday in 1928. When Fleming returned from his holiday, he realised that the bacterial growth on the cultural plates had stopped growing. He then carried out several experiments with animals, but had difficulty extracting adequate amounts of penicillin and abandoned his work.

Florey and Chain were able to successfully conduct experiments with penicillin in animals. They injected 8 mice with *Streptococci* and one hour injected 4 mice with penicillin. The 4 untreated mice were dead within 16 hours whilst the 4 treated mice survived. However, Florey needed more penicillin to run human trials. To get more penicillin, Sir Howard Florey approached various British pharmaceutical firms to make more penicillin but

he was refused because World War 2 was exhausting wartime medical supplies. Instead, they began making penicillin in porcelain vessels and proceeded to human trials. In January 1941, the first patient was treated with penicillin. They treated an Oxford policeman with cellulitis, abscesses and osteomyelitis due to a rose thorn. The policeman’s condition improved with penicillin but his condition degraded when the supply of penicillin was exhausted. Florey concentrated the drug back from urine, then reinjected it, which was successful until it eventually ran out. Five other patients were treated over the next three months and had similar results. The results were published in the Lancet in August 1941.

Not being able the produce penicillin for a clinical trial was a major challenge. However, Florey and an English biochemist Norman Heatley, travelled to the United States of America in June 1941. They went to visit Florey’s old friend from Oxford University, John Fulton. Fulton was the Professor of Physiology at Yale University. John Fulton was able to set up a meeting for Florey and Heatley to visit Northern Regional Research Laboratory of the United States Department of Agriculture in Peoria, Illinois. At this laboratory there was large fermentation tanks which were necessary for the production of penicillin. This solved their problem.

Florey and his wife Mary Ethel Hayter Reed then conducted successful clinical trials using penicillin. Penicillin was then supplied to all hospitals, especially military hospitals.

Sir Howard Florey received the Nobel Prize in Physiology or Medicine along with Alexander Fleming and Ernst Chain in 1945.

SECRECY OF PENICILLIN

During the development of penicillin, World War 2 was occurring at the same time. The British government went to great lengths to prevent penicillin from falling into enemy hands. However, news leaked out about penicillin. Agents attempted to track down where *Penicillium* cultures had been distributed. However, Fleming reassumed everyone that no cultures had gone to Germany. Everyone believed him, including Florey but in the 1930's Fleming had sent a culture of Penicillium to Dr Schmidt in Germany. However, he was not able to replicate the strain. The secrecy of penicillium remained throughout the war and when the war finished the need of secrecy was ended.

LIFE AFTER THE SUCCESS OF PENICILLIN

Florey became the Provost of Queen's College in Oxford and became the President if the Royal Society in 1960. In 1965, Florey established the John Curtin School of Medical Research at the Australian National University in Canberra. In the same year, he was created the Baron of Adelaide and Marston in Britain.

His wife, Mary Ethel Hayter Reed died in 1966 and in 1967 he married Margaret Jennings. Jennings had worked in Florey's laboratory for over 40 years.

Since Word War 2, he became a heavy smoker and developed angina in the last 18 years of his life. On the 21 st February 1968, he died suddenly in Oxford.

Sir Howard Florey was honoured by appearing on the Australian $50 banknote from 1973 to 1995. He also was honoured with a stamp in Australia in 1995.

CLINICAL USES OF PENICILLIN

Penicillin is used most commonly used in respiratory-tract infections, bone and joint infections, skin and soft tissue infections, nervous system infections, urinary-tract infections, sexually transmitted diseases and many more infections.

Common infections it treats in the respiratory-tract are *Bacterial tonsilli* , *Pneumococcal pneumonia* , lung abscess, chronic bronchitis and gram-negative pneumonia. In the bone and joints, it treats *Staphylococcus aureus* , *Streptococci pyogenes* and *H. influenzae* . In skin and soft tissue, penicillin treats *Erysipelas* and *Streptococcal lymphangiti* , *Cellulitis* (caused by *Staphylococcus aureus*) and *Postoperative sepsis* . Infections in the nervous system that penicillin can treat include meningitis and brain abscess. Penicillin can treat lower-urinary-tract infection caused by sensitive bacteria. It can also treat gonorrhoea, a sexually transmitted disease.

Penicillin can also treat *E. coli, salmonella, shigella.* Penicillin is further used for infections in the middle ear, sinuses, stomach, bladder and kidneys. It is also used to treat blood infections (sepsis), meningitis, endocarditis, childbirth infections and many more infections.

THE IMPACT OF PENICILLIN

One of the major benefits of the mass production of penicillin was that it was able to be used in the D-Day landings in 1944. It was used to save the lives of many wounded soldiers.

Another major impact of penicillin was that penicillin was saving millions of lives because people were not dying of infections that are now easily treated. The global economic benefits resulting from the availability of penicillin are immense – caused longer lifespans, increased productivity and decreased hospitalisations and complications. It further decreased patient suffering and improved patient relief. It is named as ‘ the world’s miracle drug’.

From around 1950 to 1970 was called the Golden Age of antibiotic discovery, because a variety of new medicines were discovered and provided treatments for many conditions. In this error, there was a massive global effort to try to identify new antibiotics which lead to the discovery of many successful antibiotics.

SUBSEQUENT PHARMACEUTICAL INNOVATIONS

John Sheehan, an American organic chemist was able to make the first total synthesis of penicillin in 1957. This took time as the formation of the β–lactam ring was an obstacle. He also made 6-aminopenicillanic acid which the building block for the formation of synthetic penicillin.

The subsequent discovers of penicillin include Ampicillin, Amoxicillin, Methicillin, Dicloxacillin, Carbenicillin, Piperacillin, Ticarcillin, Clavulanic acid and many more. Penicillin G and Penicillin V are naturally occurring. This

means that it is formed during the process of mold fermentation. The rest of the derivatives are semi-synthetic. This means that the structure, 6-aminopenicillanic acid is altered in various ways.

Similarly, for those who are allergic to penicillin, cephalosporins such as cephalexin are used. These are β–lactam antibiotics that are structurally similar to penicillins.

- https://www. adelaide. edu. au/seek-light/stories/howard-florey. html
- https://www-nejm-org. ezproxy. library. uwa. edu. au/doi/full/10. 1056/NEJM196008182630710
- https://web-b-ebscohost-com. ezproxy. library. uwa. edu. au/ehost/detail/detail? vid= 1&sid= 9a143781-4190-44fc-b468-75e873646cf8%40pdc-v-sessmgr04&bdata= JnNpdGU9ZWhvc3QtbGl2ZQ%3d%3d#AN= 2394606&db= bth
- https://www-clinicalkey-com-au. ezproxy. library. uwa. edu. au/#!/content/playContent/1-s2. 0-S0025619615003043? returnurl= null&referrer= null
- https://www. medicinenet. com/penicillins-injection/article. htm
- https://www. healio. com/endocrinology/news/print/endocrine-today/%7B15afd2a1-2084-4ca6-a4e6-7185f5c4cfb0%7D/penicillin-an-accidental-discovery-changed-the-course-of-medicine
- http://www. cyto. purdue. edu/cdroms/cyto2/17/chmrx/penems. htm
- https://www. ndhi. org/files/2813/8990/1147/Penicillin. pdf
- https://www-ncbi-nlm-nih-gov. ezproxy. library. uwa. edu. au/pmc/articles/PMC5369031/

- https://www-sciencedirect-com. ezproxy. library. uwa. edu. au/science/article/pii/S0140673682910406
- https://www. ncbi. nlm. nih. gov/pmc/articles/PMC5403050/
- https://www. ndhi. org/files/2813/8990/1147/Penicillin. pdf