Florey & Chain—Penicillin Isolation

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Alexander Fleming published his landmark paper discussing antibacterial effect of *Penicillium Notatum* mould in 1928. However, Fleming was somehow unable to convince a true chemist to help him extract and stabilize precise antibacterial compound found in the mould broth filtrate. Had Fleming been able to do so, penicillin for medicinal use would possibly have developed a decade earlier. Domagk’s discovery of antibacterial activity of Prontosil (Sulpha) in 1939 raised the issue of chemotherapy with a new urgency. Isolation of new antibacterial stimulated matters further, when WW-II gave important military incentive to fight against infection.

Two people came forward to push Fleming’s work on penicillin further in 1940. Howard Walter Florey (1898-1968): an Australian-English pathologist and Ernst Boris Chain (1906-79) a German-English biochemist at the Oxford University revisited Alexander Fleming’s neglected work on penicillin. Howard Florey obtained his medical degree in 1921 from University of Adelaide. He travelled to England as a Rhodes Scholar studying at Oxford and Cambridge and received a PhD.

Howard Florey obtained his medical degree in 1921 from University of Adelaide. He travelled to England as a Rhodes Scholar studying at Oxford and Cambridge and received a PhD. at Cambridge (1927). Ernst Chain was educated in Germany and received his degree in Chemistry and Physiology from Wilhelm University of Berlin (1930). He immigrated to England in 1933 due to Hitler’s anti Semitic policies. Chain was working under Sir Frederick Hopkins on phospholipids, when he was invited to Oxford to join Howard Florey (1935). Florey and Chain went on to isolate the actual anti-bacterial agent from the mould and obtained a yellow powder from mouldy broth that contained the agent, rather quickly in 1940. Chain was primarily responsible for working out the chemical process in isolating and concentrating the germ killing agent in penicillin. He theorized structure of penicillin, which was later confirmed by X-ray crystallography done by Dorothy Hodgkin. He also discovered enzyme penicillinase, which destroys penicillin. The duo showed that penicillin effectively cured bacterial infection in mice and a few human subjects having life threatening infective illnesses. These experiments proved that penicillin would work effectively in humans. Huge stumbling block was that it was enormously difficult to isolate enough penicillin to treat even one person.

Due to the pressures of WW-II in 1940, the Oxford team under Howard Florey as lab supervisor and Ernst Boris Chain as a biochemist discovered how to isolate the germ-killing agent penicillin. Florey devised a method of mass production of the drug; but the yield was low. Florey travelled to the US along with his team member Norman Heatley in order to interest pharmaceutical companies in producing the drug, and informed them about the process. Florey’s team succeeded in efficient extraction of penicillin and by 1945, Penicillin production became an industrial process for the Allies in WW-II. After the war, penicillin became an important medical work horse. Unlike other antibiotics discovered later, penicillin has remarkably low toxicity save for the anaphylactic shock.

Florey was knighted in 1944 & Chain in 1969. The 1945, Nobel Prize in Physiology or Medicine was shared amongst bacteriologist Alexander Fleming, pathologist Howard Florey and biochemist Ernst Chain.