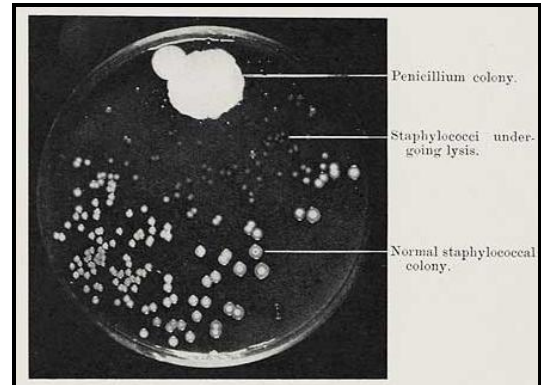


Fact Sheet: The Challenge of Mass Production

Discovery

Sir Alexander Fleming discovered the bacteria-killing properties of penicillin while conducting research at St. Mary's Hospital in London in 1928. Upon returning to his disorganized lab from a weekend vacation, Fleming noticed that one of the Petri dishes was uncovered and a blue-green mold was growing inside. Rather than tossing the contaminated dish into the trash, he looked carefully and observed that the mold had killed bacteria growing nearby. Quite by accident Fleming had discovered penicillin, the antibiotic released by the mold of the genus *Penicillium*.



Alexander Fleming's original photograph of the contaminated dish.

Alexander Fleming was well acquainted with the treatment of bacterial infections after spending World War I as a captain in the British Medical Corps. He witnessed firsthand the lack of medicine to treat infections, with disease causing approximately one third of military deaths during the Great War. Despite its historical significance, Fleming's discovery of penicillin in 1928 brought little attention. The technology and funding needed to isolate and produce the antibiotic was lacking at the time. Fleming, however, continued to grow the *Penicillium notatum* strain in his lab for twelve years, distributing it to scientists and saving the specimen for someone willing and able to transform the "mold juice" into a medicine suitable for human use.

Purification and Trials

Meanwhile, Australian scientist Howard Florey hired Ernst Chain to help with his microbiology research at Oxford University. Florey and Chain were interested in Alexander Fleming's work and in 1938, began studying the antibacterial properties of mold. Chain began by purifying and concentrating the penicillin "juice" through a complex and tiring process of freeze drying the product repeatedly. This slow and relatively inefficient process was improved upon by another researcher, Norman Heatley, who purified the penicillin by adjusting the acidity, or pH.

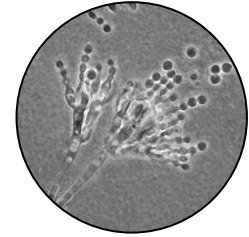


Norman Heatley culturing bacteria. The Petri dish provides bacteria with the food, moisture, and space necessary for bacteria to reproduce and grow in the lab.

On May 25, 1940 Florey's team successfully cured infected mice with penicillin, to their great excitement. Heatley oversaw the trials and recorded in his diary, "After supper with some friends, I returned to the lab and met the professor to give a final dose of penicillin to two of the mice. The 'controls' were looking very sick, but the two treated mice seemed very well. I stayed at the lab until 3:45am, by which time all four control animals were dead." Delirious with excitement, Heatley returned home early that morning, surprised to find that he had put his underpants on backwards in the dark. The usually mild-mannered Heatley noted in his journal, "It really looks as if penicillin may be of practical importance."

Mass Production

Florey and Chain's report about the mouse trials drew great interest from both scientific and military communities. World War II was well underway in Europe and the ability to combat disease and infection could mean the difference between victory and defeat. Because British facilities were manufacturing other drugs needed for the war effort in Europe, Florey and Heatley travelled to the U.S. in July of 1941 to continue research and seek help from the American pharmaceutical industry. They convinced four drug companies, Merck, E. R. Squibb & Sons, Charles Pfizer & Co., and Lederle Laboratories, to aid in the production of penicillin.



Penicillium notatum viewed with a microscope, 400x.



Penicillin production at pharmaceutical company, Eli Lilly.

Florey and Heatley ended up in Peoria, Illinois to work with researchers who had perfected the fermentation process necessary for growing penicillin. The researchers in Peoria used corn instead of glucose, or simple sugar, as the nutrient source, and the penicillin grew approximately 500 times more than it had in England! The team searched for more productive strains of *Penicillium notatum*, finding the best specimen growing on an over-ripe cantaloupe in a Peoria grocery store.

Meanwhile, penicillin was used to cure the first human bacterial infection, proving to researchers the vital importance of the drug to save lives. But, that one cure used up the entire supply of penicillin in the entire U.S! Following Japan's attack on Pearl Harbor on December 7, 1941, it was clear to scientists and military strategists that a combined effort was needed to produce the large amounts of penicillin needed to win the war. A total of 21 U.S. companies joined together, producing 2.3 million doses of penicillin in preparation of the D-Day invasion of Normandy. Penicillin quickly became known as the war's "miracle drug," curing infectious disease and saving millions of lives.

In 1945, Sir Alexander Fleming, Ernst Chain, Sir Howard Florey were awarded the Nobel Prize in Physiology or Medicine "for the discovery of penicillin and its curative effect in various infectious diseases." We have modern antibiotics today because scientists and drug companies worked together to solve a problem.



Medics using penicillin to combat infections in soldiers.