

## MEDICAL INNOVATION: PENICILLIN (PHARMACEUTICAL: SMALL MOLECULE)

**Physician: Dr. Alexander Fleming**

**Academic: Oxford University**

**Industry: Merck & Co., Inc., Abbott Laboratories, Lederle Laboratories, Pfizer & Co. Inc. E.R. Squibb & Sons**

### Situation

***Millions of deaths a year worldwide***

Less than a century ago, bacterial infections and diseases such as pneumonia, syphilis, gonorrhea, diphtheria, scarlet fever and many wound and childbirth infections resulted in millions of deaths a year worldwide, and the world knew of no cure for these conditions. Hospitals were full of people with blood poisoning contracted from a cut or a scratch, and doctors could do little for them but wait and hope.

### Physician-Industry Collaboration

***An unusual mold***

It was not until 1928 that penicillin, the first true antibiotic, was discovered by Alexander Fleming, Professor of Bacteriology at St. Mary's Hospital in London. Returning from a holiday in September of that year, Fleming began to sort through petri dishes containing colonies of *Staphylococcus*, bacteria that cause boils, sore throats, and abscesses. He noticed something unusual on one dish. It was dotted with colonies, except for one area where a blob of mold was growing. The zone immediately around the mold was clear, as if the mold had secreted something that inhibited bacterial growth. Fleming concluded that the mold was releasing a substance that was inhibiting bacterial growth. He grew a pure culture of the mold and discovered that it was *Penicillium notatum*.

With help from a chemist, he isolated what he later named "penicillin." During the next twelve years, he grew and distributed the original mold, unsuccessfully trying to get help from any chemist that had enough skill to make a stable form of it for mass production. It was Howard Florey, Ernst Chain, and their colleagues at Oxford University who turned Fleming's original penicillin from a laboratory curiosity into a life-saving drug. Their work on the purification and chemistry of his penicillin began in earnest in 1939, just when wartime conditions were beginning to make research especially difficult, and substantial amounts of penicillin would be needed for the extensive clinical trials required to confirm the promise of the early results.

Florey recognized that large-scale production of penicillin was probably out of the question in Britain, where the chemical industry was fully absorbed in the war effort. With the support of the Rockefeller Foundation, Florey and his colleague Norman Heatley traveled to the U.S. in the summer of 1941 to see if they could interest the American pharmaceutical industry in the effort to produce penicillin on a large scale.

In December 1941, right after the Pearl Harbor attack, Florey and Heatley were able to convince the leaders of several U.S. pharmaceutical companies – including Merck, Squibb, Pfizer, Lederle and Abbott – to make a commitment to pursuing mass production of penicillin building on research carried out in the U.S. Department of Agriculture. After several unsuccessful starts, the increasingly obvious value of penicillin to the war effort led the U.S. War Production Board

(WPB) to take responsibility for increased production of the drug in 1943. The WPB selected 21 drug companies to participate in a penicillin large-scale production program, and the firms received top priority on construction materials and other supplies necessary to meet the production goals.

Penicillin production began to increase dramatically by early 1944. U.S. production of the drug jumped from 21 billion units in 1943, to 1,663 billion units in 1944, to more than 6.8 trillion units in 1945, and manufacturing techniques had changed in scale and sophistication from one-liter flasks with less than 1% yield to 10,000-gallon tanks at 80-90% yield. The U.S. government was eventually able to remove all restrictions on its availability, and as of March 15, 1945, penicillin was distributed through the usual channels and was available to the consumer in his or her corner pharmacy. By 1949, the annual production of penicillin in the United States was 133,229 billion units, and the price had dropped from twenty dollars per 100,000 units in 1943 to less than ten cents.

## Innovation Benefits

### *The beginning of the antibiotic age*

Penicillin heralded the beginning of the antibiotic age, and 60 years after its first use, it remains one of the most widely used of the drugs of this type. Penicillin-related antibiotics save millions of lives each year worldwide by enabling the treatment of bacterial infections such as pneumonia, syphilis, gonorrhea, and many wound and childbirth infections. In the U.S., deaths by infectious bacterial diseases are one-twentieth of what they were a century ago.

The global economic benefits resulting from the availability of penicillin are incalculable – easily in the trillions of dollars over the past fifty years. Longer life spans, increased productivity, and decreased hospitalizations and complications have all resulted from the availability of penicillin and related antibiotics. It is rightly named “the world’s miracle drug.”

## Patient Benefits

### *A rapid recovery from a coma*

Examples of Penicillin’s miracles occur every day. According to the World Health Organization, in May 2009, Anna Fairley was finishing an internship in Copenhagen, and began feeling sick so she went home to rest. Once home, she became increasingly ill, and was taken to the hospital with a suspected appendicitis. The doctors operated on her, but she did not get better – in fact her condition got much worse.

Anna was suspected of having an antibiotic-resistant infection, and was put into a medically induced coma, placed in isolation and under constant supervision by two nurses. She remained in a coma for six days, and three days in to it, she was not expected to recover. Fortunately it turned out she suffered from a bacterial infection of Group A Streptococcus, which proved not to be resistant. Anna was given two penicillin-related antibiotics and they began to work. Her recovery was very quick, taking just a couple of weeks, and the infection left no lasting effects.

Anna’s mother Iris will never forget her daughter’s recovery: “Antibiotics are a treasure to us. They saved my daughter’s life!”