

Her Penicillin, Too: There is a necessary connection between those who discover and those who develop the discovery into practical application for public consumption.

Mold, discovered by chance in a lab petri dish by Professor Alexander Fleming in 1929, was named penicillin. After four years, unable grow enough cultures to perform research, he ended his study. Ten years later penicillin became the world's first antibiotic, often cited as the most important weapon developed (not discovered) during World War II.

But penicillin wouldn't be if it weren't for a conundrum of dedicated scientists who started where Fleming stopped. All faced the same issue as he, production of the mold. One of these dedicated scientists was Gladys Hobby.

Born in New York City in 1910, Hobby received her degree from Vassar College in 1931, then her master's in 1932 and her PhD in bacteriology in 1935, both from Columbia University. In the course of her dissertation work, she became part of a bacteriological research team at the College of Physicians and Surgeons of Columbia University.* They focused on finding human uses for penicillin. As well, Dr. Hobby had a professional patient agreement with Presbyterian Hospital.

As a microbiologist with dual access to pathological materials and research subjects at the hospital and to cutting-edge microbiology on the main Columbia campus, she commanded a unique position well suited to translational research.

Between 1934-43 Dr. Hobby, with biochemist Dr. Karl Meyer and clinician Dr. Martin Henry Dawson, carried out research on infectious diseases at the Columbia's College of Physicians and Surgeons. Dr. Hobby, just 30, was beginning what would become a high-profile career as a researcher and administrator.

In 1939, the same year Great Britain declared war on Germany, two Oxford University professors of pathology, Dr. Howard Florey and Dr. Ernst Chain became interested in the potential of penicillin and began their own study. In 1940 they made a pivotal discovery and reported their findings in "The Lancet."

Their paper didn't create much of a stir in England, but had an immediate impact on Dawson, Meyer, and Hobby. They obtained a sample of the penicillin mold from Fleming to facilitate research on how to use it in humans. After acquiring a sample of the mold, the three scientists were off and running. Hobby immediately set to work growing cultures.

We naively undertook 'to make some penicillin' Hobby recalled, and quickly learned this meant becoming a kind of brewmaster, an expert in the fermentation processes required to produce the drug. Not long after, because there were no adequately large incubators in their small laboratory, hundreds of two-liter flasks . . . lined every classroom laboratory bench at Columbia University Medical School. The flasks moved in and out of classrooms as the students moved out and in.

They eventually learned the school's two-story amphitheater was an excellent incubator. The flasks were stored under the seats eight to nine months when room temperatures were within the range suitable to grow the mold. To vent the fumes produced in the process, a still was set up on a fire escape.

Dr. Hobby later wrote that the techniques they used seemed very primitive, but provided enough concentrated and partially purified penicillin to convince the efficacy of the drug and enough to help save a few patients' lives. They initiated clinical trials of penicillin but it was clear larger amounts would be needed for clinical use.

In 1940, less than a month after their research began, Meyer tested what little penicillin they could produce on two men. Though the doses were too small to produce a therapeutic response, they confirmed the Oxford group's observation that penicillin was not toxic. The first patient treated with penicillin was at Columbia University by Dawson with Meyer and Hobby.

They presented their findings in Atlantic City at a meeting of the American Society for Clinical Investigation in 1941. Several newspapers including *The New York Times*, carried news of the team's findings on its front page.

The press coverage got researchers in academia and in pharmaceutical companies to take note. The Mayo Clinic immediately began work developing the drug as did Pfizer, Inc. Pfizer formed an informal partnership with Hobby's group that greatly increased the amount available to then be analyzed by Dawson, Meyer, and Hobby.

But, because of the mold's inability to penetrate more than one to two millimeters, it grew in stationary culture in shallow layers one inch or less in depth. The number of culture flasks, bottles or trays required was tremendous. Many believed penicillin would never be produced in amounts sufficient for general use.

Concurrently, in 1940, the Northern Regional Research Laboratory of the U.S. Dept. of Agriculture (NRRL) opened in Peoria, IL by Percy A. Wells, an expert in mold fermentation. Wells knew the ability of fermentation to increase yields of products and instantly recognized it as the solution to improving yields of penicillin. But, the brewer's yeast available at Oxford, important to the production of penicillin, was not available in the U.S.

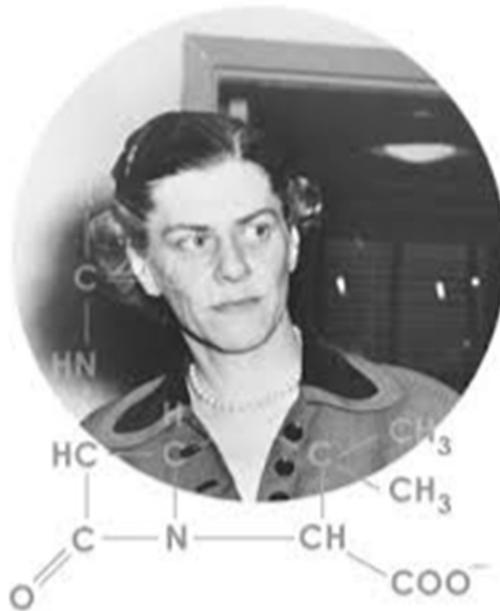
It was suggested corn steep liquor, a by-product of wet corn milling, be used in its place. It was cheap and readily available in Peoria, located in the corn belt of the United States. Development of corn steep liquor-lactose is one of the most important developments in the large-scale production of penicillin.

By August 1941, U.S. Department of Agriculture scientists in Peoria were producing a high-yielding mold, and additional pharmaceutical companies were showing interest in the drug. Pfizer alone was producing enough to replace the supply manufactured by Hobby and Meyer.

In 1944 Dr. Hobby left Columbia to continue her research at Pfizer, one of the companies leading the research on methods for production of penicillin. Her research work at Pfizer also contributed greatly to the development of the powerful anti-tuberculosis drug streptomycin.

Dr. Fleming, who died in 1955 at age 73, lived long enough to understand the widespread value of his work. Fleming, Florey and Chain jointly won the 1945 Nobel Prize in Medicine.

Dr. Gladys Hobby, who also lived long enough to see the widespread value of her work, died in 1993 at the age of eighty-two. In addition to her research, she authored a book, several hundred scientific articles, founded and edited the journal *Antimicrobial Agents and Chemotherapy*, and was a charter fellow of the American Academy of Microbiology.



Albeit no single firm or individual was responsible for the successful development of penicillin, there is a definite connection between those who discover and those who develop the discovery.

*Dr. Virginia Apgar's alma mater—see column Oct./2003 “One Woman/Every Baby.”

Sources: Hobby, Gladys. *Penicillin: Meeting the Challenge*. Connecticut: Yale University Press, 1985; Oatman, Eric: “The Drug That Changed the World” at: <http://www.cumc.columbia.edu/psjournal/archive/winter-2005/drug.html>; <http://www.nwhm.org/education-resources/biography/biographies/gladys-hobby/>.