AWESOME stories

Penicillin - "The Wonder Drug"

One day, in September of 1928, Dr. Alexander Fleming was cleaning-up his lab at St Mary's Hospital Medical School in London, England. Among the usual clutter in his work space, Professor Fleming saw something unusual in a culture plate.

He'd been investigating *Staphylococcus*, a type of bacteria. In a petri dish, containing that bacteria, some mold (also spelled "mould") was growing in the form of a ring.

Mold in a petri dish was nothing unusual, in and of itself. What caught Professor Fleming's eye, however, was something quite different.

The area around the mold ring seemed to be free of bacteria. Fleming wondered: Is there something about this particular mold which is killing off the bacteria? If so, what substance is coming from the mold?

Fleming investigated the mold a bit further. He put it in a dish so he could watch it grow. As it grew, he was able to extract some liquid from it. His additional research showed that whatever was active in the liquid, which he extracted from the mold, could also kill other types of bacteria.

Taking his research a step further, this curious bacteriologist found that he could give some of the liquid extract to small animals with no side effects. His discovery seemed to have amazing antibiotic properties.

As he continued to study the mold, Fleming realized that it was from the genus "Penicillium," which had first been described in 1809 by Johann Heinrich Friedrich Link (in *Observationes in ordines plantarum naturales*). That name - *penicillium* - was selected because the fungus, under a microscope, resembles a painter's brush. The Latin word for "painter's brush" is *penicillium*.

Busy with other things, Professor Fleming moved on to other investigations. He just couldn't squeeze-out enough of the "mould juice" to make it a major focus of his work. He did give his discovery a name, however. He called it "penicillin," and published a paper about his findings in 1929.

Then ... nine years passed. About the time Great Britain declared war on Germany, in 1939, an Oxford University Professor of Pathology - Dr Howard Florey - was examining substances capable of combating bacteria. He and his colleague, Dr. Ernst Chain, believed that penicillin was the best choice.

They faced the same difficult issue as Professor Fleming, however. What method could they use to efficiently extract the penicillin from the mold cultures? And ... how would they test the effectiveness of their samples?

Oxford University's story about penicillin tells us more:

> *With Norman Heatley, a biochemist who became Florey's research associate in 1940, the team solved both these problems. Heatley devised a new technique to measure the activity of a sample of penicillin and came up with a method called back-extraction to isolate the penicillin. He managed to automate this procedure using a set up consisting of bottles, milk churns, yards of glass and rubber tubing.*

Once Florey and his team had enough penicillin to use for testing, they worked with mice to determine whether it could effectively fight bacteria:

> *By 25 May 1940, the team had reached a point where they could carry out a new experiment that would test whether penicillin could be an important antibacterial drug. Eight mice were given lethal doses of streptococci. Four of the mice were then given injections of penicillin. By the next morning all the untreated mice were dead while those that had received penicillin survived for days to weeks.*

With the war still raging, Florey and his team believed that penicillin could be a major help for all the men who were injured in the fighting. They worked hard to produce enough penicillin for human testing:

> *He* [Florey] *turned the Dunn School* [at Oxford] *into something of a penicillin factory. Six "penicillin girls" were taken on to maintain production in 700 newly designed vessels which were continuously in use. By February 1941 Florey felt he had enough penicillin to begin trials in humans.*

The first human-subject was a police officer who was near death because of an infection. Perhaps penicillin would be able to save him:

> *With the help of Charles Fletcher, a young doctor at the Radcliffe Infirmary, on 12 February 1941, Albert Alexander, a 43-year-old policeman, became the first patient to be treated with penicillin. He had scratched his face on a rose bush, the wound had become infected and the infection had spread. Fletcher injected him with penicillin regularly over four days, and within 24 hours he was greatly improved. But supplies of the new drug ran out before his cure was complete. He relapsed at the beginning of March, and died two weeks later.*

Additional human trials, on five patients, also produced good results. To really make a difference in the war effort, however, the new drug would have to be produced in far greater amounts than the professors and their teams could concoct in a lab.

Florey did not file for a patent. He'd been asked not to do so for ethical reasons. It was thought, in Britain, that the processing of penicillin would be so significant that it should benefit all mankind.

Meanwhile, doctors at Columbia University (in New York City) wrote to Dr. Florey. Gladys Hobby and her colleagues (Karl Meyer and Martin Henry Dawson) requested a sample of the mold. They wanted to see whether they could help to produce more of the active ingredient.

As she writes in her book, *Penicillin: Meeting the Challenge*, Hobby and her team members ran out of room to store their flasks:

> *Soon hundreds of two-liter flasks ... lined every classroom laboratory bench at the Columbia University Medical School.* (Eric Lax, quoting from Dr. Hobby's book in *The Mold in Dr. Florey's Coat: The Story of the Penicillin Miracle*, at page 145.)

Even that wasn't enough room. Before long, the team members were storing their flasks underneath the seats at the University's two-story amphitheater. It turned-out to be a great incubator.

After Dr. Hobby and her colleagues published their findings, reporting that penicillin could be a very significant germ-killer, drug companies in both the UK and the US were keen to make penicillin on a large scale.

Dr. Andrew J. Moyer - an American researcher working at a U.S. Department of Agriculture lab in Peoria, Illinois - figured-out how to manufacture penicillin on an industrial scale. He applied for, and received, a patent (US 2,443,989).

By June of 1944 - when the Normandy invasion took place - there were enough penicillin supplies to make a monumental difference for the Allied forces:

> *In 1943, it was possible to treat 1500 military personnel, and only one year later, countless wounded in the D-day landings were saved by penicillin. The yield had been increased from 1% in 1 liter flasks to 80-90% in 10,000 gallon tanks...*

Fleming, who died on the 11th of March, 1955, lived long-enough to understand the widespread value of his work. He, Florey and Chain jointly won the Nobel Prize for physiology or medicine in 1945.

Norman Heatley - the "quiet, pragmatic hero in the penicillin success story" who made penicillin extraction possible - was not included in the award of 1945. In 1990, however, he received an honor even more rare than a Nobel Prize. He was given the first honorary doctorate in Oxford's 800-year history.

At the time, people called penicillin "the wonder drug." To this day, penicillin is benefitting millions of individuals throughout the world.

And ... what of the patent which was not sought by the Oxford team?

> *... Until this day the British regret that, for ethical reasons, they had asked Florey not to file for a patent on penicillin.*
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> *The University of Oxford never got its share from the fabulous profits made from penicillin in the US, and, to add insult to injury, the UK had to pay licensing fees to US companies.* (See *Biotechnology for Beginners*, by Reinhard Renneberg, at page 121.)

Credits:

Video online, courtesy Wellcome Library's channel at YouTube. The film is described as:

A government produced film about the discovery of Penicillin by Sir Alexander Fleming, and the continuing development of its use as an antibiotic by Howard Florey and Ernst Boris Chain. The film uses many modernist animations to depict the scientific research. British Industrial Film Association National Award, 1964; a First Prize, Fifth International Industrial Film Festival, London, 1964; a Diploma of Merit, Melbourne International Film Festival, 1964. 2 segments.

A Central Office of Information film. Produced by T.V.C. London Limited, written by Donald Holms, animated by Dave Rich, Gordon Harrison and Dennis Hunt, camera by John Williams, edited by Alex Rayment, music by Peter Snade and directed by Denis Rich.

See Alignments to State and Common Core standards for this story online at:
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