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Alexander Fleming

A spore that drifted into his lab and took root on a culture dish started a chain of events that altered forever the treatment of bacterial infections

By DR. DAVID HO

The improbable chain of events that led Alexander Fleming to discover penicillin in 1928 is the stuff of which scientific myths are made. Fleming, a young Scottish research scientist with a profitable side practice treating the syphilis infections of prominent London artists, was pursuing his pet theory — that his own nasal mucus had antibacterial effects — when he left a culture plate smeared with *Staphylococcus* bacteria on his lab bench while he went on a two-week holiday.

When he returned, he noticed a clear halo surrounding the yellow-green growth of a mold that had accidentally contaminated the plate. Unknown to him, a spore of a rare variant called *Penicillium notatum* had drifted in from a mycology lab one floor below. Luck would have it that Fleming had decided not to store his culture in a warm incubator, and that London was then hit by a cold spell, giving the mold a chance to grow. Later, as the temperature rose, the *Staphylococcus* bacteria grew like a lawn, covering the entire plate — except for the area surrounding the moldy contaminant. Seeing that halo was Fleming's "Eureka" moment, an instant of great personal insight and deductive reasoning. He correctly deduced that the mold must have released a substance that inhibited the growth of the bacteria.

It was a discovery that would change the course of history. The active ingredient in that mold, which Fleming named penicillin, turned out to be an infection-fighting agent of enormous potency. When it was finally recognized for what it was — the most efficacious life-saving drug in the world — penicillin would alter forever the treatment of bacterial infections. By the middle of the century, Fleming's discovery had spawned a huge pharmaceutical industry, churning out synthetic penicillins that would conquer some of mankind's most ancient scourges, including syphilis, gangrene and tuberculosis.

Fleming was born to a Scottish sheep-farming family in 1881. He excelled in school and entered St. Mary's Hospital in London to study medicine. He was a short man, usually clad in a bow tie, who even in his celebrity never mastered the conventions of polite society. Fleming probably would have remained a quiet bacteriologist had serendipity not come calling that fateful September in 1928.

In fact, Fleming was not even the first to describe the antibacterial properties of *Penicillium*. John Tyndall had done so in 1875 and, likewise, D.A. Gratia in 1925. However, unlike his predecessors, Fleming recognized the importance of his findings. He would later say, "My only merit is that I did not neglect the observation and that I pursued the subject as a

bacteriologist." Although he went on to perform additional experiments, he never conducted the one that would have been key: injecting penicillin into infected mice. Fleming's initial work was reported in 1929 in the *British Journal of Experimental Pathology*, but it would remain in relative obscurity for a decade.

By 1932, Fleming had abandoned his work on penicillin. He would have no further role in the subsequent development of this or any other antibiotic, aside from happily providing other researchers with samples of his mold. It is said that he lacked both the chemical expertise to purify penicillin and the conviction that drugs could cure serious infections. However, he did safeguard his unusual strain of *Penicillium notatum* for posterity. The baton of antibiotic development was passed to others.

In 1939 a specimen of Fleming's mold made its way into the hands of a team of scientists at Oxford University led by Howard Florey, an Australian-born physiologist. This team had technical talent, especially in a chemist named Ernst Boris Chain, who had fled Nazi Germany. Armed with funding from the Rockefeller Foundation, these scientists made it their objective to identify and isolate substances from molds that could kill bacteria. The mission was inspired by the earlier work of Gerhard Domagk, who in 1935 showed that the injection of a simple compound, Prontosil, cured systemic streptococcal infections. This breakthrough demonstrated that invading bacteria could be killed with a drug and led to a fevered search in the late 1930s for similar compounds. Fleming's *Penicillium notatum* became the convenient starting point for Florey's team at Oxford.

In a scientific tour de force, Florey, Chain and their colleagues rapidly purified penicillin in sufficient quantity to perform the experiment that Fleming could not: successfully treating mice that had been given lethal doses of bacteria. Within a year, their results were published in a seminal paper in the *Lancet*. As the world took notice, they swiftly demonstrated that injections of penicillin caused miraculous recoveries in patients with a variety of infections.

The Oxford team did not stop there. Rushing to meet the needs of World War II, they helped the government set up a network of "minifactories" for penicillin production. Florey also played a crucial role in galvanizing the large-scale production of penicillin by U.S. pharmaceutical companies in the early 1940s. By D-day there was enough penicillin on hand to treat every soldier who needed it. By the end of World War II, it had saved millions of lives.

Pneumonia, syphilis, gonorrhea, diphtheria, scarlet fever and many wound and childbirth infections that

once killed indiscriminately suddenly became treatable. As deaths caused by bacterial infections plummeted, a grateful world needed a hero. Fleming alone became such an object of public adulation, probably for two reasons. First, Florey shunned the press, while Fleming seemed to revel in the publicity. Second, and perhaps more important, it was easier for the admiring public to comprehend the deductive insight of a single individual than the technical feats of a team of scientists.

Awards and accolades came to Fleming in rapid succession, including a knighthood (with Florey) in 1944 and the Nobel Prize for Medicine (with Florey and Chain) in 1945. By this time, even Fleming was aware that penicillin had an Achilles' heel. He wrote in 1946 that "the administration of too small doses ... leads to the production of resistant strains of bacteria." It's a problem that plagues us to this day.

When he died of a heart attack in 1955, he was mourned by the world and buried as a national hero in the crypt of St. Paul's Cathedral in London. Although Fleming's scientific work in and of itself may not have reached greatness, his singular contribution changed the practice of medicine. He deserves our utmost recognition. At the same time, we must bear in mind that the "Fleming Myth," as he called it, embodies the accomplishments of many giants of antibiotic development. Fleming is but a chosen representative for the likes of Florey, Chain, Domagk, Selman Waksman and Rene Dubos, many of whom remain, sadly, virtual unknowns. Their achievements have made the world a better, healthier place. In commemorating Fleming, we commemorate them all.

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