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Medicine in Stamps

Robert Koch (1843-1910): father of microbiology and Nobel laureate

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"If now consider the academic subjects which influenced my scientific development and especially my relationship to bacteriology, I must first indicate that I received from the University no direct influence for my scientific direction, because bacteriology did not exist in the University." – Robert Koch

On an April morning in 1876, a small group of academics from the University of Breslau in Germany witnessed the proof that anthrax was an infection by an identifiable, living organism. Finally, a microorganism has been definitively linked to the cause—and spread—of a specific disease. The discoverer was Robert Koch, and in that historic moment, he provided the final vindication of the germ theory of disease.

EARLY YEARS Born in Clausthal, Germany on December 11, 1843, Robert Koch was the third of 13 children. A mediocre but industrious student, he undertook medical studies at Gottingen, and upon graduation, bounced from job to job, seeking financial stability. At age 24, he had married his childhood sweetheart Emma Fraatz and fathered a daughter. He initially practised in Hamburg and Langenhagen, and later in the German town of Rakwitz, now part of Poland. His wife Emma was unhappy and complained to her father, a prominent Evangelical Church official: *"It's going awful here. We have to skimp and save every penny and I'm still not sure we'll make it. I keep telling Robert we have to leave here. . ."* Koch eventually became *Kreisphysikus* (District Medical Officer) for the rural community of Wollstein. His patients loved him, but he found that his true passion was in research. Indeed, he would deliberately avoid the sickest patients in order to spend time in his homemade laboratory, which was equipped with an expensive microscope, purchased with money meant for a carriage to make house calls.

ANTHRAX AND BEYOND Koch's work did not begin in a void. By the time of his momentous demonstration in 1876, both Joseph Lister and Louis Pasteur had made a name for themselves in antisepsis and bacteriology, respectively. Koch's own study of anthrax was in part a response to an outbreak of the disease, which had devastated sheep and cattle populations and even occasionally affected humans. Koch soon proved that bacteria grown in fortified culture media could cause anthrax in inoculated animals. However, he was initially unable to explain how anthrax was directly acquired through soil contact, and this became a major stumbling block in pinpointing the aetiological agent. Later, Koch observed refractile objects in his culture material under the microscope, and correctly deduced that these were resting spores that could mature into infectious bacilli.

Koch initially doubted his own results. Fortuitously, Ferdinand Cohn, a leading bacteriologist, worked at the nearby University of Breslau. In April 1876, Koch requested a meeting with Cohn, writing: *"After many futile attempts I have finally succeeded in discovering the complete life cycle of* Bacillus anthracis*. . . However, before I publish my work, I would like to request, honored professor, that you, as the best expert on bacteria, examine my results and give me your judgment on their validity."* Cohn quickly recognised the importance of Koch's findings and became an enthusiastic advocate. He offered to publish the anthrax paper in his own journal, and introduced Koch to many prominent doctors including Joseph Lister, who became a steadfast colleague.

In 1880, Koch moved to Berlin and took a position on the newly-formed Amt, part of the Imperial Health Office. During this time, Koch developed his "plate technique," a revolutionary approach to culturing bacteria *in vitro*. Bacteria were previously grown in a liquid medium and serially transferred to fresh media to obtain purity. However, the process was tedious and yielded inconsistent results. Koch observed that pure cultures could best be achieved using a solid medium like a potato, but recognised at the same time that most solid media would not support the growth of pathogenic organisms. In solving this dilemma, Koch simply added gelatin to the liquid culture medium, which solidified when poured into shallow Petri dishes, forming agar plates on which the bacteria grew.

TUBERCULOSIS Images of Neolithic hunchbacks suggesting tuberculosis of the spine (Pott's disease) were evident as far back as 5,000 BC. Hippocrates himself described the disease, then known as pthisis, around 400 BC. But the cause of tuberculosis had remained elusive over the millennia, therefore attracting treatment modalities as improbable as fresh air, horseback riding, and iatrogenic pneumothorax. In Koch's days, the term "contagion" was used to imply the direct transmission of a disease from one person to another. Although others had raised the theory that *"invisible germs carried the contagion"*, it was left to Koch to discover the tubercle bacillus as the causative agent, which won him the Nobel Prize in 1905.

Koch's use of the plate technique provided the impetus for his eventual discovery of the tubercle bacillus. He first set out to stain the microorganism, but experienced difficulties. An accident led him to use methylene blue dye that had adsorbed a small amount of ammonia, and this batch of dye very nicely stained the bacteria. However, a fresh batch of methylene blue, free of ammonia, failed to reproduce the results. Koch soon realised that the presence of ammonia, which altered the pH, was responsible for the initial staining success, which quickly led to the determination of the optimal alkali concentration and the best staining procedure.

Having identified and cultured the tubercle bacillus, Koch took the next logical step – proving that the organism indeed caused tuberculosis. He inoculated guinea pigs with cultured specimens, and observed that the experimental animals reacted identically to those inoculated with extracts of infected human tissue. It was the definitive proof that he sought, the crowning piece in the now famous *"Koch's postulates,"* which stipulate the following criteria: (1) the organism must continually be present in the diseased tissue; (2) the organism must be isolated and grown in a pure culture; and (3) the pure culture must be shown to induce the disease when injected into an experimental animal. He presented this groundbreaking work before the Physiological Society in Berlin on March 24, 1882, and subsequently published his findings in the German literature. His seminal article was later translated into English in 1932.

In 1890, five years after he became the head of the newly-created Institute of Hygiene, Koch unveiled what he believed to be a cure: tuberculin. Through trials in guinea pigs, Koch discovered that a miniscule amount of modified culture extract, which he called tuberculin, caused infected animals to develop fever, malaise and swelling in the joints around the injection site. Although we now know that these symptoms were caused by delayed-type hypersensitivity, at the time Koch believed them to signal a cure. Many congratulated Koch on his discovery of tuberculin, including Louis Pasteur, a heretofore critic. However, it soon became clear that neither tuberculin nor a later version was effective. It was a crushing blow, and came at an inopportune time in mid-life, when Koch became increasingly estranged from his wife Emma, then falling in love with and subsequently marrying a young art student named Hedwig Freiberg, 30 years his junior.

KOCH'S LEGACY Koch's work on infectious diseases met with powerful opposition from the likes of Rudolf Virchow, and competing claims from French bacteriologist Louis Pasteur, but he triumphed. In addition to his pioneering work on anthrax and tuberculosis, he played a key role in an earlier German expedition that isolated cholera and showed its spread through contaminated drinking water. Along with his colleagues at the Imperial Health Office, he also studied the efficacy of hot air versus steam sterilisation. Distinguishing between killing and inhibiting bacterial growth, he systematically showed that chemicals then used as disinfectants were largely ineffective. In 1896, Koch began studying tropical diseases, spending the majority of his final years in Africa and New Guinea, where he helped to determine that typhoid fever was not spread by contaminated water or sewage, but rather by seemingly healthy human carriers.

In Berlin, three different institutions honoured this great man of science: the Hygiene Institute, the Institute for Infectious Diseases, and the Robert Koch Institute for Infectious Diseases. His achievements were capped with the Nobel Prize in 1905. On May 27, 1910, Robert Koch died of a heart attack. He was 67.

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