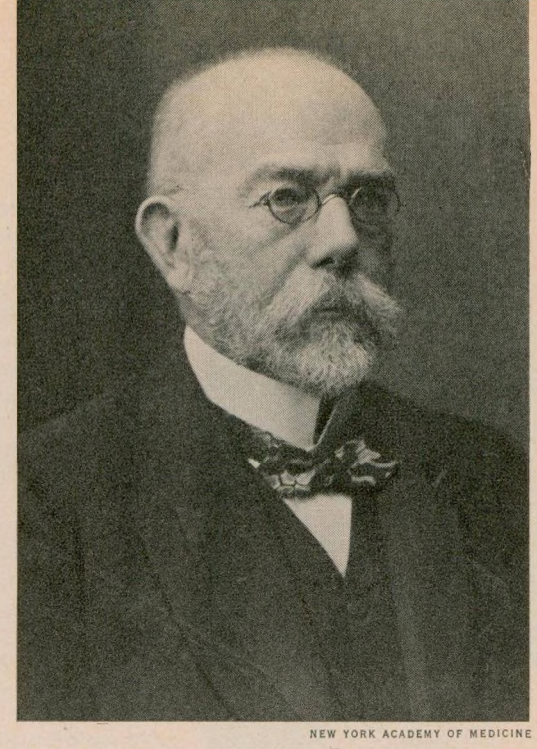


NEW YORK ACADEMY OF MEDICINE

Bacterial Detective

DEAD 50 years ago was a tireless medical sleuth who devoted a lifetime to the discovery of microbes, a man known today as the father of bacteriology, Robert Hermann Heinrich Koch.

He was born on December 11, 1843 in the Harz Mountain mining village of Clausthal, the third of eleven boys and two girls. His father was a mine official from whom he derived a love of nature and an insatiable *Wanderlust;* from his plump, mild-mannered mother he acquired an inexhaustible good nature and unflagging diligence.

Robert roamed in the mountains to collect plants, insects and animals: he made himself an aquarium and a herbarium, captured singing birds, dissected animals and strung their skeletons.

FRAU GERTRUD PFUHL

Mrs. Emmy Fraatz Koch with daughter Gertrud, 1870.

In the local school he was a good scholar, played the piano and zither, became school chess champion. His father wanted him to become a shoemaker; the school director thought he was better suited to a career in mathematics, the natural sciences or in medicine; the boy himself toyed with the idea of becoming a traveling salesman.

He enrolled at the University of Göttingen in 1862 where he studied mathematics and natural science for two semesters, changed to medicine with the aim of satisfying his lust for travel as a ship or army surgeon.

At Göttingen he came under the influence of anatomist Jacob Henle, clinician Karl Hasse and physiologist Georg Meissner who encouraged his interest in science. Henle was the author of a book on infectious diseases; he taught that conclusive proof of the germ theory of disease awaited the isolation of microbes from the diseased tissue and the establishment of their pathogenicity.

While a student Koch won a first prize of 80 thalers (about $60) for a study that proved there were no ganglionic cells in the nerves of the uterus. Wrote the boy proudly to his father: "When I was home the last time, you did not show much appreciation for my knowledge in the field of medicine. But sometimes it happens that even a blind hen finds a kernel of corn." At age 22, he wrote his doctorate thesis on the origin of succinic acid in the body, graduated *eximia cum laude.*

Koch launched his medical career as assistant in a Hamburg hospital; he may have been lured there by the city's location on the sea. He still envisioned himself a ship's doctor, often strolled longingly along the docks when off duty.

In 1867 he married childhood sweetheart Emmy Fraatz, the daughter of a Clausthal Lutheran minister*; she opposed his nautical notions, prodded him into accepting a resident physician's post at an East Prussian insane asylum. There he eked out a living for two years, then started a private practice at Niemegk (near Potsdam), settled eventually at Rackwitz in Posen (now Poznan).

Continued small earnings depressed his spirits: he considered emigrating to America; two student brothers seeking a loan supposedly found him with a dollar in his pocket. Later his practice thrived, earned him about $1100 in one year.

Exempted from military service because of myopia, Koch volunteered at the outset of the Franco-Prussian War, served five months as a field surgeon, then treated typhoid patients at a Neufchâteau hospital. In 1872 he was named district physician at 900 marks (about $215) yearly at Wollstein (now Wolsztyn), a town of 4000 inhabitants near the Polish border. Here he also built up a considerable private practice worth about $5 on a good day.

Anthrax. Hotly debated in those days were the new discoveries in microbiology: Louis Pasteur had demolished the theory of spontaneous generation, proved that microbes caused organic decomposition, acidic fermentation, silkworm disease; Scottish surgeon Joseph Lister had demonstrated

*Their only child, Gertrud, was born a year later.

that carbolic acid and heat sterilization could appreciably reduce postoperative infection.

On his rounds through the Prussian countryside Koch frequently saw the decaying carcasses of sheep and cattle lying in the fields, listened to his farmer patients lament their losses from splenic fever.

He improvised a laboratory in a curtained-off part of his private office; it contained a microtome, a homemade incubator and a microscope given him by his wife on his birthday.

He noted that blood from an anthrax victim swarmed with tiny rods and threads; discovered also was that inoculation with the diseased blood killed mice. These observations were not new: Aloys Pollender had previously seen the rodlike forms in the blood of anthrax victims; Casimir Davaine had shown that healthy animals contracted the disease when inoculated with the diseased blood. That these rods and threads were live pathogenic organisms had been suspected by some, but proved by none before Koch.

He isolated the microbes by dropping a tiny piece of diseased mouse tissue into a hanging drop of ox-eye liquid, cultivated the organisms for eight generations.

Koch also showed that the microbes formed spores to withstand extremes of temperature: he noted beadlike dots within the threads, poured warm ox-eye fluid over the culture, saw the beads effloresce into the deadly bacilli. This explained how the organisms were able to survive the freezing Prussian winter, return each spring to plague sheep and cattle.

Before a gathering of scientists and professors at Breslau on April 30, 1876, Koch meticulously reconstructed in three days the months of labor, proved that a specific organism (*Bacillus anthracis*) caused the specific disease of anthrax. Exclaimed pathologist Julius Cohnheim: "I consider this is the greatest discovery in the field of microorganisms."

In 1877 Koch detailed his improved methods for examining and photographing bacteria, told how he had used Weigert's aniline dyes to stain flagellae, borrowed an idea from Ehrlich to photograph bacteria on coverslips. A year later his *Investigations into the Etiology of Traumatic Infective Diseases* elaborated on Lister's work, proved that infectious wounds are caused by specific organisms having a definite size, form and growth.

By showing that a particular organism could establish itself in one animal and not in another, Koch foreshadowed later work in immunology. Microscopy benefited greatly from his introduction of both the Abbe condenser and the oil immersion lens.

He was appointed to the Imperial Health Board in Berlin in 1880, where he worked in a well-equipped laboratory with two eager young assistants, Georg Gaffky and Friedrich Löffler.

Considered by some as the greatest of Koch's bacteriologic contributions is the poured-plate method of obtaining pure cultures, discovered in 1881. Until then, two media were used to get pure cultures: a fluid one containing a mixture of microbes difficult to separate, and a solid opaque one in which the germs were invisible beneath the microscope.

Koch obtained pure cultures on transparent solid media by heating gelatin and beef broth until liquefied, inoculating the microbes and allowing the mixture to solidify. One story credits the idea to his observation of the different colored specks on a boiled potato; another version is that Emmy called his attention to the different colonies of moulds on bread. Koch also pioneered the use of steam sterilization to kill spores resistant to dry heat, introduced bichloride of mercury as an antiseptic.

Constantly at odds were Koch and Pasteur, their rivalry exacerbated antagonisms already roused by the Franco-Prussian War. The two were temperamental opposites: Koch cold and methodical, Pasteur impulsive and given to sudden flashes of inspiration.

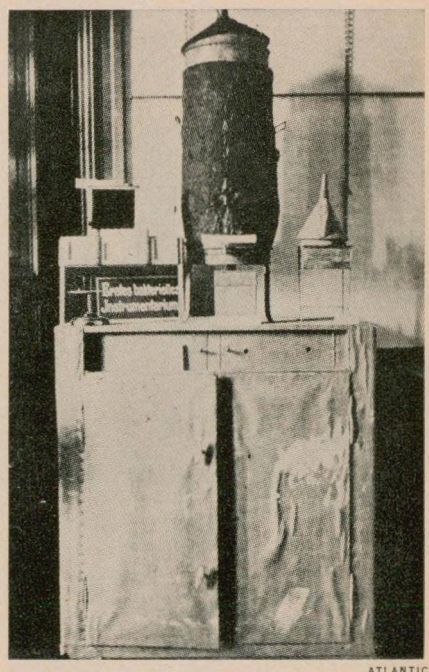
In his typically thorough fashion, Koch tested Pasteur's anthrax vaccine, found it only sporadically effective. He also ridiculed Pasteur's contention that earthworms caused anthrax, stated the disease could be controlled by burning the bodies of victims or burying them deep in cold earth where the spores could not survive. Said he: "Pasteur's teaching of the etiology of anthrax is only a little new, and this new rests on error."

Tuberculosis. Koch turned his attention to tuberculosis in 1881 at a time when the disease was killing one in seven persons. Jean Villemin and Julius Cohnheim had already established its contagiousness; René Laënnec had boldly postulated that lupus, phthisis and scrofula were caused by the same organism, although Virchow and his followers stubbornly maintained that they were different diseases, often inherited.

After more than 200 failures, Koch stained the elusive tubercle bacillus (*Mycobacterium tuberculosis*) with an alkaline solution of methylene blue and a Bismarck brown counterstain which turned all but the bacilli brown.

When he found that the germs would not grow on the usual media, he substituted the coagulated blood serum of cattle devised by British

FRAU GERTRUD PFUHL



ATLANTIC

FRAU HEDWIG KOCH

Top to bottom: Koch (standing at right) as a student, 1861; home-made incubator used in early anthrax experiments; members of 1883 cholera expedition (left to right) Profs. Gaffky, Treskow, Koch, Fischer.

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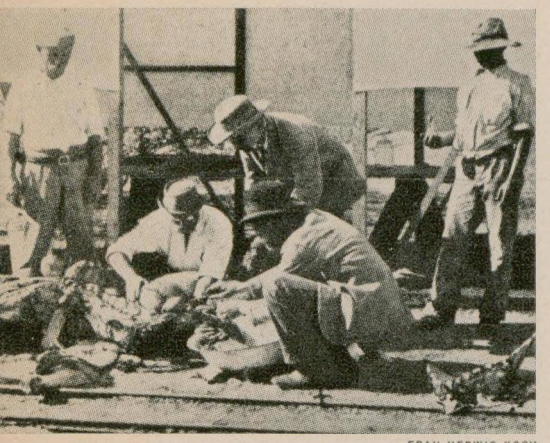


FRAU HEDWIG KOCH

FRAU HEDWIG KOCH

BETTMANN ARCHIVE

Top to bottom: Koch dissecting a cow in Kimberley, South Africa, 1896, during studies of rinderpest; on a hunt in Egypt, 1895; with assistant Friedrich Löffler.

physicist John Tyndall. He then cultivated the microbes for several generations, reproduced the disease in guinea pigs, cats, rats, rabbits and a dog, then recovered the organism from the diseased tissue in every case.

On March 24, 1882, occurred what Paul Ehrlich later called "the most majestic scientific event in which I have ever participated." The occasion was a meeting of the Berlin Physiological Society in the laboratory of Emil Du Bois-Reymond attended by some of the finest scientific minds in Germany.

Flanked by Gaffky and Löffler, Koch proceeded in clear and logical terms to recapitulate his tuberculosis experiments.* His evidence was overwhelming, it answered all questions before they were asked. When he finished there was no applause, comment or discussion for the first time in the society's history; even the hostile Virchow remained absolutely still.

Koch's lone error was a statement that the bacilli contained spores: a notable feature was the inclusion of the four postulates which were to become the fundamental basis for proving the etiology of a disease; the organism must be found in the body, isolated from it and grown in pure culture, cause the disease when inoculated into animals, be recovered from the diseased tissue.

Publication of the paper 17 days later fomented a surge of optimism in which Koch was showered with the adulation normally reserved for emperors and generals: verses were composed to the "bacillus-father"; sold were 100,000 red handkerchiefs imprinted with Koch's picture.

Ironic twist is that Koch's worst mistake related to the disease which won him his greatest fame, followed the reversal of one of his earliest tenets on tuberculosis. From the first he had felt that improved sanitary conditions and housing were the best ways in which to combat the disease; he considered sanatoria of limited value at best, ruled out almost entirely the efficacy of chemotherapy. But in 1890 at the Berlin International Congress of Medicine he announced the discovery of tuberculin† which he advised would cure lupus and early phthisis.

Koch had observed that when tuberculous guinea pigs were injected with tubercle bacilli, a violent reaction occurred at the site of inoculation followed by the formation of an ulcer which later healed (Koch phenomenon); from this he deduced that there was a substance in the bacillus valuable in the diagnosis and treatment of the disease.

*His paper was called *Ueber Tuberkulose*, later became *Die Aetiologie der Tuberkulose*.

†A boiled glycerine extract of tubercle bacilli.

Announcement of the discovery drew a horde of hopeful physicians and patients to Berlin to obtain some "Koch lymph." Wrote American physician Edward Trudeau: "A thousand dollars were freely offered for a bottle of tuberculin which contained about a teaspoonful, and the substance could not be procured at that price from those who had been fortunate enough to procure some. Crowds paraded the streets in Berlin chanting hymns in Koch's honor and shouting his name."

Subsequent overdoses and other misuses of the lymph brought disastrous results; Virchow even charged that it spread the disease. Disappointed millions vehemently censured Koch, but through it all he never lost faith in tuberculin as a genuine cure. History since showed that the lymph achieved its greatest value as a diagnostic, not a therapeutic agent.

Disputed by biographers is the extent of Koch's culpability for the fiasco. One view is that he was impelled by pressure from the German government to announce his discovery prematurely; another view is that the error was entirely his own, as proved by his subsequent introduction of new tuberculins.

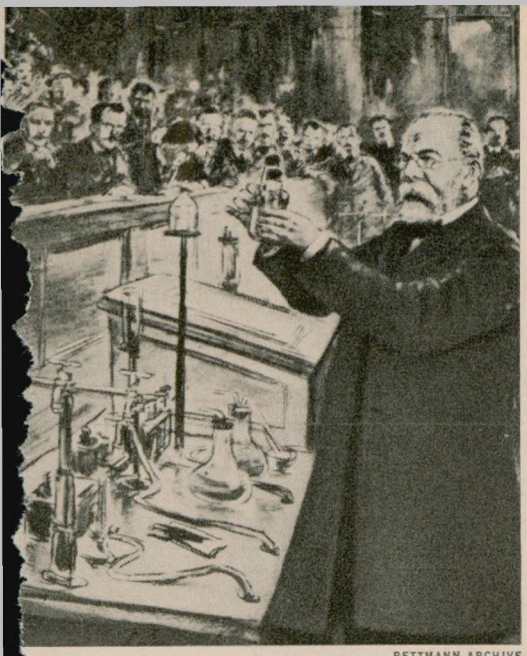
Another grievous error was his pronouncement in 1901 that bovine tuberculosis was not dangerous to humans. Originally he considered the human and tubercle bacilli the same; later he conceded that they differed, but believed the human danger from the bovine organism no greater than that from heredity. Later studies showed that children who drank the milk of tuberculous cows could fall victim to the disease.

Cholera. In 1883 Koch was named privy councillor, then posted to Egypt as head of a German commission that sought to avert a cholera epidemic before it reached Europe.* The French sent a competing commission headed by two Pasteur disciples, Emile Roux and Louis Thuilliers; when Thuilliers later died of the germ he had come to seek, Koch graciously placed wreaths on his coffin with the words: "They are simple but they are of laurel, such as are given to the brave."

When the Egyptian epidemic abated, Koch traveled to India where cholera was endemic, there proved that a comma-shaped bacillus (*Vibrio cholerae*) caused cholera.

He showed that the microbes thrived in polluted water, warned that human carriers spread the infection; his findings led to health examinations and marine quarantine of vessels returning from infected areas. In later years he pointed out the connection

*While in Egypt, he discovered the Koch-Weeks bacillus that causes infectious conjunctivitis (Egyptian ophthalmia, pink eye).



BETTMANN ARCHIVE

FRAU HEDWIG KOCH

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Left, Koch demonstrates tuberculosis findings before Berlin Physiological Society; center, Shibasaburo Kitasato; Koch (at right) dissecting a crocodile while investigating sleeping sickness, German East Africa, 1906.

between polluted water and the spread of typhoid, dysentery and malaria, urged control by water filtration. Returning as a hero to Germany, he was awarded 100,000 marks (about $23,800), decorated with the Order of the Crown, with star.

Koch was named director of the new Hygienic Institute at the University of Berlin in 1885, began to assemble a distinguished group of colleagues and pupils. The influx continued when he became head of the Institute for Infectious Diseases six years later and the building on Klosterstrasse became a veritable Mecca for bacteriologists.

Also working there for varying periods were Shibasaburo Kitasato, codiscoverer of the *Pasteurella pestis* of bubonic plague; immunologist Emil von Behring, codeveloper of diphtheria and tetanus antitoxins; Gaffky, who discovered the *Micrococcus tetragenus* and was the first to cultivate the *Bacillus typhosus;* Löffler, codiscoverer of the *Bacillus diphtheriae,* and William Henry Welch, discoverer of *Staphylococcus epidermidis albus, Bacillus aerogenes capsulatus* and a founder of Johns Hopkins Medical School.

During the last 15 years of his life, Koch kept constantly on the move in quest of new microbes: he went to South Africa in 1896 at the request of the British government, there developed a method of inoculation against rinderpest (cattle plague, steppe murrain), also studied tropical malaria, blackwater fever, Texas fever and sura; he also visited Italy and Java.

In 1904 the prevalence of red water fever, horse sickness, recurrent fever and trypanosomiasis took him to tropical German East Africa. He returned there two years later as head of a Sleeping Sickness Commission which studied the habits of the tse tse fly (*Glossina palpalis*), introduced atoxyl (an arsenic compound) as a remedy for trypanosomiasis. He also described a "banana-belly" condition among native children fed excessively on stewed banana mush.

Honors piled up endlessly: he was given Royal Society membership in 1897, five years later succeeded Virchow as a member of the French and Austrian Academies of Science; 40 of his students brought out a *Festschrift,* and a marble bust was sculpted in his honor.

In 1904 he relinquished to Gaffky his post as director of the Institute, retired with a comfortable annual pension of 100,000 marks. For his work on tuberculosis he was given the Nobel prize for medicine and physiology.

Koch made his first trip to the United States in 1908 where he was reunited with his brothers, one of whom was an Iowa farmer, was named an honorary member of the New York Academy of Medicine.

Back in Germany from Japan, Koch continued to work despite recurrent

CULVER SERVICE

BETTMANN ARCHIVE

Left, Koch and second wife, Hedwig; above, with bacteriologists Mijajihma (center) and Kitasato, Tokyo, 1908.

CONTINUED

asthmatic attacks and severe cardiac pain. On an April night in 1910 he suffered an attack of angina pectoris with vomiting and asthma. He felt better the next day, but developed pulmonary edema, and a rapid and irregular pulse; a complication was his own erroneous belief that he was tuberculous.

He was stricken with a second attack a week later after addressing a meeting of the Academy of Science. His condition was diagnosed as myocarditis, was treated with digitalis, morphine, concentrated coffee and warm compresses on the heart. After some slight improvement, he journeyed for the warm weather to Baden-Baden, died there on May 27th as he sat on the balcony of his room watching a setting sun. His body was cremated and the ashes placed in the Institute.*

The Man. In private life Koch was a fond and doting parent and a reserved husband. It is said that he would sometimes absent-mindedly walk past his house, but never past his laboratory. Also reported is that sometimes on returning from work he would greet his daughter and ignore his wife.

He and Emmy drifted further apart after daughter Gertrud married a military surgeon in 1888. He took to frequenting the Lessing Theatre near his laboratory where he met an actress named Hedwig Freiburg, 29 years his junior. In 1893 he divorced Emmy and married Hedwig. This reportedly displeased the government, caused many friends to snub him; the indignant citizens of Clausthal destroyed the tablet placed on his boyhood home.

Russian biologist Ilya Mechnikov recalled that details of this romance interested professors at a Congress of Physicians far more than all the scientific papers submitted. Many years later Dr. Trudeau met the couple in America, wryly observed: "You could not blame Koch, but what on earth could this woman see in him?"

To strangers he was aloof, austere, reticent. Though an innovator himself, he was often unreceptive to the new ideas of others, but would yield if compelled by the weight of scientific evidence. He was praised for selflessly enumerating his errors in the same manner as his triumphs, criticized for adopting the work of others without crediting the source.

Summing Up. By Koch himself: "If my success has been greater than that of most . . . the reason is that I came in my wanderings through the medical field upon regions where the gold was still lying by the wayside. Fortune is necessary to be able to distinguish gold from the base metals, but that is no great merit." END

*Now the Robert Koch Institute for Infectious Diseases.