



EXPERIMENT ELEVEN

*Dark Secrets Behind
the Discovery of a
Wonder Drug*

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By the Same Author

Copyright

*To the researchers in science
who did the hard work, and never
reaped the glory.*

Complete honesty is of course imperative in scientific work.

—W. I. B. Beveridge, *The Art of Scientific Investigation*, 1957

PART I • The Discovery



1 • Zones of Antagonism



EVERY DAY AT DAWN IN THE summer of 1943, a young graduate student could be seen striding briskly across the peaceful campus of the College of Agriculture. He was short, wiry, and handsome, his sharp features focused intensely on his important mission. Even his clothes seemed an afterthought, a wrinkled white shirt and loose gray pants, worn and reworn like those of any devoted researcher surviving on a meager stipend and the excitement of his work. He came from the direction of the Plant Pathology greenhouse, where students were breeding new varieties for President Franklin Roosevelt's Victory Gardens. He hurried past the dairy, with its herd of experimental Holsteins, past the poultry house, where Rhode Island Reds competed with white Leghorns for egg-laying prowess, and finally arrived at the Georgian-style Administration Building, which celebrated the proud colonial history of Rutgers University.

Albert Schatz, the harried student, was the first to arrive each day at the Department of Soil Microbiology. He let himself into the empty building and descended quickly into the basement laboratory. He pulled on his long white lab coat made of heavy cotton, worn haphazardly like his clothes and with a tear down one side. Then he began work on his experiments, searching for new antibiotics among the microbes he had found in the farmyard soil.

On that morning of August 23, he sat at his workbench and [opened his notebook](#). On page 32, in his meticulous cursive, he entered the date and the title of his new experiment, "Exp. 11 Antagonists of Actinomycetes." Then underneath, with the precision of a ledger clerk, he wrote, "Control soils No. 2, 7A, 18A, leaf compost, straw compost and stable manure plated out on egg albumin agar. Transfers made from colonies of actinomycetes selected at random ... by casual macroscopic observation." And he added, for accuracy, "Some actinomycetes obtained from plates of swabs of chickens' throats from Miss Doris Jones."

It was the fourth summer of the world war and, although the New Jersey college farm was thousands of miles from the front lines, almost everything, even the plants in the greenhouse and the microbes in the soil, had some link to the war effort. Schatz had come to the college because he wanted to be a farmer, but now, aged twenty-three and at the start of his doctorate career, he found himself engaged in a special war-driven mission. Instead of hunting for microbes that could break down soil to make it more fertile, Schatz was part of a scientific race to find microbes capable of producing new and more powerful antibiotics. His Experiment 11 was a routine test, one of hundreds being made by other graduate students working on this nationwide project, but it would be much more than that.

By 1943, Eleven U.S. drug companies were producing penicillin, the first antibiotic, discovered by Alexander Fleming in 1928. The first vials of penicillin were being rushed to the front to treat common infections from battle wounds. But in this war, a new threat had emerged: biological weapons. Allied intelligence reported that Germany and Japan would not hesitate to use bombs and shells filled with deadly germs like anthrax, cholera, typhoid, and even the plague. Penicillin had no effect on such diseases.

The researchers best suited to the task of finding new antibiotics were not at medical schools, but at the agricultural colleges. "Aggies" like Albert Schatz were quite familiar with microbes from the soil that were capable of producing a chemical toxin that killed off the harmful bacteria that might be used

in biological weapons. Each time they grew these microbes in a petri dish, they saw the telltale clear zones, or “zones of antagonism,” as they were known, killing fields measured in millimeters where one microbe battled another for space or food. If they dropped penicillin into a petri dish of typhoid bacteria or cholera or the plague, no clear zones would develop. For this job, a stronger antibiotic was needed, the kind that Albert Schatz was hoping to find.

The basement laboratory where Schatz worked was primitive and sparsely equipped, grim even by the utilitarian standards of the times. But to this determined young man it was a hideaway, a place where he could work uninterrupted. And he had volunteered for this isolation. His ambitious Ph.D. had two parts: One was to find antibiotics against cholera and typhoid; a second was to find a cure for the deadliest of all infectious diseases, tuberculosis. Over the previous two centuries, two billion people had died from tuberculosis, caused by a slow-growing, pickle-shaped microbe, *Mycobacterium tuberculosis*. It was highly contagious, spreading easily from a victim’s sneeze or spit. Known as the “Great White Plague,” TB cut down rich and poor alike, although in the Industrial Revolution it spread more easily in the crowded slums and factories. In wartime it spread quickly in bombed-out cities and crowded refugee camps. There was no effective cure. Doctors had tried everything from prolonged rest to fortify the body’s resistance, to drastic collapsed-lung surgery, to a range of alchemies and the new so-called sulfa drugs discovered by German researchers from industrial dyes. Albert Schatz’s professor, Dr. Selman Waksman, had warned of the risks. Waksman insisted that when Schatz handled the deadly TB microbe, he must work alone in the basement and never bring the germ to the labs on the third floor.

In recent days, Schatz’s laboratory had taken on the appearance of an ancient dispensary. In one corner an aging autoclave, a kind of pressure cooker used for sterilizing glassware, hissed away. Conical glass flasks contained rich dark brews of meat extract similar to gravy, a concoction Schatz used to feed his microbes. On his bench were rows of petri dishes with microbe food in agar, the jellied extract of algae that microbiologists use for growing their molds. The microbes Schatz was cultivating came from the multicolored and somewhat mysterious group known as the actinomycetes or “ray fungi.” These are strange, thread-like creatures that first appeared more than four hundred million years ago. They have wispy hyphae like the tentacles of a jellyfish, half bacteria and half fungus, a sort of evolutionary link between the two. They were favorites of Dr. Waksman, and common in the farmyard soil, and they had already shown promise in producing antibiotics. They form strikingly beautiful colonies of blues, reds, and grayish greens, and in the soil they are responsible for the pleasant odor of earth after a light rain.

Albert knew where to look for them. His favorite hunting grounds included the compost heaps of moldering leaves and twigs outside Plant Pathology, and the college stables, where he filled pots with fresh horse manure. The richest for his experiments, he knew, was the freshest—less than twelve hours old. Each gram of soil or compost Schatz collected was teeming with millions of different microbes, but always some actinomycetes. He diluted the soil with tap water and let drops of the mixture fall onto petri dishes containing microbial food in the jellied agar. Then he incubated the dishes and watched the actinomycetes grow. Within a few days, he had good colonies of mold in his petri dishes. Some of them were surrounded by the telltale clear zones, indicating that they might be antibiotic producers. He chose his likely candidates for their robust look and their widest zones of antagonism, like a gardener spotting a sturdy shoot, or a farmer selecting a high-yielding crop for breeding. Then he tested them for their action against known disease-producing bacteria from the same group as the typhoid and cholera germs.

By mid-September, he had selected two strains of a species of a gray-green actinomycete named *griseus*, Latin for “gray.” One strain had come from heavily manured farmyard soil and he named

18-16, for the sixteenth strain of the eighteenth soil sample. The other came from a colleague, Doris Jones, as he had noted in his lab notebook. He named her strain D-1, for Doris. Much quicker than he had dared to hope, Schatz had become convinced that he had discovered a new antibiotic, the first to be found in the Department of Soil Microbiology for several months, and everyone was excited, especially Dr. Waksman.

But no one could yet know whether his discovery would be useful as a medicine; if it was powerful enough to destroy typhoid and cholera it might also destroy human body cells. And it was only the first stage of Schatz's project; he still had to see if his new antibiotic would be effective against the toughest germ that causes TB. Schatz checked and rechecked Experiment 11, running the same tests over and over again until he was sure that he had not made a mistake. Each effort was carefully recorded in his lab notebook.

By the middle of October, he had confirmed that 18-16 and D-1 were indeed behaving like good producers of a new antibiotic. On October 19 at two o'clock in the afternoon, he placed a culture of *Actinomyces griseus* in a test tube and sealed it for posterity by heating the end over a Bunsen burner and twisting the glass shut. That weekend, he wrapped the tube in cotton wool, put it in his pocket, and caught the train from the Rutgers University town of New Brunswick to Newark, then the bus to Passaic, where his parents lived in a working-class section of the textile town on the Passaic River. There, he showed the test tube to his father, Julius, and his uncle Joe and presented it to his mother Rachel. She had not finished grade school and had no real idea what the test tube represented. He told her that he had found a new medicine that might eventually fight the infectious diseases, maybe even tuberculosis, that she had seen too often destroying the lives of her friends and neighbors. That she could understand.

2 • The Apprentice and His Master



The schatz family came from the peasant class in the old Russia, and their entry into America is an immigrant story of the kind often told at the turn of the twentieth century. Albert's grandfather Shlomo (Sam) Schatz, was a butcher, and his grandmother's family, the Tunicks, were known for their physical strength and much revered in the community for forming **local vigilante committees** to defend Jews during the pogroms. Sam himself was a strong man who once, legend has it, leaped on a bull that was running amok through the village and wrestled it to the ground. But Russia was a barren and hostile place, especially for Jews, and Sam left his village on the outskirts of Minsk in 1899 and immigrated to America, leaving his pregnant wife, Rose, and their five children with her father Ephraim. He arrived at Ellis Island and moved in with a cousin on Manhattan's Lower East Side. It took him five years, working as a house-painter, to save enough money to bring his family, including Albert's father, Julius, to New York.

The family lived in a walkup, and soon after their arrival one child died of a weak heart. They moved into a Brooklyn tenement, and Sam and Rose had six more children, but the man who could wrestle a bull grew weak from **heavy smoking** and living in the putrid city air. When doctors told him he should leave for a life in the country, the Jewish community had just the answer.

Baron Maurice de Hirsch, a German-born Jewish banker, gave mortgages to immigrant Jews to enable them to build their own barns and homes. He also set up the small Woodbine Agricultural College in New Jersey to produce "intelligent, practical farmers." With the help of Hirsch funds, Sam Schatz bought a dirt farm in Fitchville, Connecticut, joining other Jewish settlers in small farming communities across the state. On most of these farms the soil was poor, exhausted by Yankee farmers who had abandoned it to move west or, in some cases, for better jobs in the cities.

The Schatzes were the first Jewish family at Bird's Eye View Farm, a stone house, two wooden barns, and a manure pit built on a rise known as Cannonball Hill. The family scratched a living from a dozen milk cows and some chickens. They sold vegetables in the spring, and in the summer they took in boarders from the city. While the urban renters lived in the farmhouse and enjoyed the green outdoors, the Schatz family lived in tents. Julius joined the U.S. Army in World War One, and after he returned, he was delivering vegetables by horse cart to nearby Norwich one day when he met a pretty, dark-haired young woman named Rachel Martin who worked in a bakery. They soon married. Her parents were Jewish immigrants from Poland who had come to America via Britain.

On February 2, 1920, Albert Schatz was born in a Norwich hospital. The family stayed on the farm until he was three, when they moved to Passaic, New Jersey, where Julius's sister Rebecca and her husband, Abe, had a grocery store. They lived in a wooden three-story house with six apartments—three at the front and three at the back. Two girls were born, and the family moved back and forth from Passaic to the farm, wherever there was work. As soon as he was able, Albert helped out on the farm. He learned how to sharpen farm tools, milk cows, make butter and cheese, and drive the horse cart. When he was older, he shot groundhogs, mended his own clothes, and darned his socks. He attended the local one-room school-house, which had one teacher and twenty students, grades one through eight. The building was twenty by twenty-five feet and had two entrances, one for boys and one for girls. Albert wanted to be a farmer, like his father and grandfather.

During the Great Depression the family lived mostly in Passaic. They joined other immigrants from Eastern Europe—Hungarians, Czechs, Poles, and Russians. Albert witnessed much poverty and

sickness, people fighting for scraps on the garbage dumps and dying from infectious diseases, like pneumonia, diphtheria, and, of course, tuberculosis. It was a raw and sometimes violent period. One of the young boy's lasting memories was of the bloody police charges that ended the fourteen-month-long Passaic textile workers' strike involving fifteen thousand workers, in 1926–27. The police dispersed the strikers with horses and water cannons, and schools were often closed. Despite the disruptions, Albert managed to stay in classes and was a consistently promising student at Passaic High School.



*Albert Schatz, age twelve, with his mother, sisters Sheila and Elaine, and his maternal grandmother on the Connecticut farm in 1932.
(Courtesy Vivian Schatz)*

In his junior year, in 1936, when he was sixteen, he contributed three paragraphs to the school newspaper about his “life’s ambition,” to be a farmer. He did not seek wealth “for I should not know what to do with it.” He wanted to “sweat by honest labor” and to “roam the open fields.” He wanted to chop wood until his muscles ached. “**I want to LIVE.**”

Aged eighteen, Albert won a scholarship to the Rutgers’ College of Agriculture, the first in his family ever to attend an institution of higher learning. In his second year, he was elected to Phi Beta Kappa, a rare achievement for an “aggie.” The head of the Department of Soil Microbiology, Dr. Waksman, was another Jewish immigrant of Russian descent. He was always on the lookout for bright young graduates, and was happy to accept Albert as a Ph.D. candidate.

SELMAN ABRAHAM WAKSMAN, the man behind the intense wartime hunt for antibiotics at Rutgers, was no ordinary soil scientist. Like the Schatz family, Waksman had arrived in America at the beginning of the twentieth century, but he came from a different social order and had achieved much in the New World.

He was born on July 8, 1888, according to the old Russian calendar, in the small market town of Novaya Priluka, in western Ukraine, two hundred miles from the regional capital of Kiev. He wrote in his memoir that it was “**a mere dot** in the boundless steppes,” surrounded by chernozem, the fertile black earth on which wheat, rye, barley, and oats flourished, as long as the rains came. Without them, famine swept the land. The inhabitants of the small towns and villages of Western Ukraine were

recently freed serfs who scratched a living from smallholdings, and Jewish artisans and tradesmen who marketed the farm and forest products.

His life there was simple, but not uncomfortable. His father was the relatively well-off son of a coppersmith and had inherited property. His mother was the daughter of a successful businesswoman who ran a dry goods store, a “[prominent merchant](#) in the community.” His mother had inherited the store, and together his parents were able to pay for Selman’s private tutors.

Immediately after marriage, his father had been drafted, like all able-bodied men, into the czar’s army for five years, leaving Selman’s mother to carry on her business and fend for herself. When his father had returned from service, Selman had been born, but his father showed little interest in being with his son, most of the time living twenty miles away in the nearest large city, Vinnitsa, where he had inherited property. Selman was brought up by his mother, several aunts and maiden cousins, and his maternal grandmother, who had eight daughters. Selman was the son of the youngest daughter. Inevitably, [he was spoiled](#).

His mother taught him to read and sent him to the local heder (private school) and then to private tutors. She also made sure that he studied the Bible and the Talmud. The young Selman quickly learned Hebrew and Russian literature, history, and geography. And he was frequently picked as the one to read a chapter from the Bible or deliver the blessing on the initiate at a bar mitzvah.

Jews and Ukrainians lived side by side in Novaya Priluka. The Waksmans lived in the wealthier part of town. His mother gave birth to a daughter when Selman was seven, but the daughter died less than two years later of diphtheria.

In the Waksman household there was usually money left over to help a needy niece or nephew, or the less fortunate on the town’s poorer side. Encouraged by his mother, Selman gave free lessons in Hebrew and Russian, and later private lessons to the sons of the wealthier inhabitants and the rich peasants.

The first Russian uprising of 1904–05 did not affect little Novaya Priluka, but revolution was in the air. Selman’s friends were divided on the future. One believed that socialism was inevitable, and another, the Zionists, looked for salvation in a new homeland in Palestine. Selman was uncommitted with divided sympathies—on the fringe of the two groups. Instinctively, he favored the revolutionaries, but he disliked the fierce arguments over the form of a future government, should revolution be successful. He was more interested in pursuing a higher education, but the way was blocked because he was a Jew. He could not enter the gymnasium or go on to university without passing a special competitive exam.

In 1908, he left with four friends for Odessa to be coached, at a price, for the crucial exam. He passed “with [flying colors](#)” and returned home a hero now set to attend university in Odessa. But suddenly he suffered a terrible blow. In the summer of 1909, his mother died of an intestinal blockage. During the seven days of mourning, he read and reread the Bible, “[perhaps for the last time](#).”

He returned to Odessa to find new political barriers. Candidates for the university had to have been born in Odessa or have spent the last twenty years there. Selman managed to bribe a government official to give him the necessary papers, but when his friends were refused admission, they decided to leave Russia for good. He thought briefly of going to Switzerland, a destination favored by his father, but his cousins in Philadelphia, having heard of his mother’s death, urged him to join them.

In October 1910, Selman and a group of five young people from Novaya Priluka, three men and two women, left by train for Bremen, and thence for America. They landed in Philadelphia on November 2.

BY THE BEGINNING of the twentieth century more than three million Russians had immigrated

the United States. Waksman, now aged twenty-two, went to work on his cousin's five-acre farm near Metuchen, New Jersey, thirty miles from New York City. He helped with the hens, learned how to make compost from stable manures, and planted vegetables in the spring for local markets. His cousin was a great teacher, and at the end of his first year Waksman published an article in the *Rural New Yorker* titled "How I Raised a Flock of Chickens," for which he was paid his **first ten dollars**.



Selman Waksman as he was about to leave Russia in 1910. (Special Collections and University Archives, Rutgers University Libraries)

But his goal was college. He thought of becoming a doctor, and was accepted at Columbia University medical school. Another cousin, who was a dentist, offered to help with the fees, but Waksman did not want to be tied down by debt.

So he had to take what was available, and in those days the most accessible institutions were the land grant colleges. These were created by the Morrill Act of 1862, which gave states land grants to fund public agricultural and engineering colleges. One of the first such establishments was at Rutgers College, established originally as Queen's College in 1766 and still a small institution at the turn of the twentieth century.

Rutgers was only eight miles from Metuchen, and Waksman's farmer cousin suggested he should go and see Jacob Lipman, another Russian immigrant, who was then head of the Department of Bacteriology. By 1911, Lipman was an established figure in soil science, having made his reputation on studies of bacteria that make nitrogen available for crops.

Waksman was persuaded that a course in agriculture would satisfy his curiosity about the biochemistry of living organisms, plus he was awarded a full scholarship. Aged twenty-three, he found it hard, at first, to be among much younger boys of seventeen, who teased him for his clumsy English and dislike of sports. He also found the level of teaching poor. In his sophomore year, his chemistry professor was "an **unimaginative bore**," physics was "a **great disappointment**," he found the courses of American and English literature uninteresting, and he disliked Shakespeare. The French teacher was enthusiastic, but he felt he already had enough knowledge of foreign languages. The only courses that earned his approval were zoology and botany.

At the end of his second year, he yearned for independence and moved into a room in an old house on the college farm, paying for his accommodation by working in the college greenhouse and helping out in the laboratory. He bought cracked eggs from the Poultry Department at eleven cents a dozen.

Another and more important reason for striking out on his own was the arrival in New York from Novaya Priluka of a young woman named Deborah Mitnick. The daughter of a prosperous grain

merchant, she was the sister of Waksman's best friend, Peisi, back in Ukraine, and after finishing grade school she had come to stay with her cousins, braving the voyage from Riga on her own in the middle of winter. She was good looking, bright, and energetic. In America, she quickly joined Peisi in New York—he had come to America with Waksman, in 1910. She [worked in a sweatshop](#), became a member of the International Ladies' Garment Workers' Union, and took singing lessons. She was affectionately known as Bobili, Russian for young grandmother, a nickname given in the hope that she would reach a ripe old age. Waksman had been her tutor in Novaya Priluka, had always admired her, and planned to marry her.

In his studies, Waksman had at last found a subject that interested him: general bacteriology under Dr. Lipman. "I felt that I was [finally under the tutelage of a master](#)," he wrote. Waksman was the only student majoring in soil microbiology. For his senior thesis he listed the different groups of microbes—bacteria and fungi—but he was fascinated by the actinomycetes. He dug trenches on the college farm and mapped the different horizons of the microbes he found in the soil. He took samples from each layer, suspended them in water, put the microbes on petri dishes of nutrient agar, let them grow for a week, and then counted the different colonies that had developed.

The actinomycetes, hardly noticed in America, had been known for more than forty years in Europe, having first been described by German researchers as a microbe responsible for a disease of cattle known as "lumpy jaw," literally lumps on the animal's cheek containing a growth of the microbe. Russian researchers had also published papers on the actinomycetes, and Waksman had a distinct advantage over his colleagues because he could read German and Russian. He cataloged the different species and played an important role in their early classification into five genera, depending on a microscopic examination of the degree of branching of the cells, whether they produced spores in chains or singly on stalks, and whether they could live with or without oxygen. Thus, as Waksman would write forty years later, began his interest "in a group of microbes to which I was later to devote much of my time and which were to remain for the rest of my life as my [major scientific interest](#)."

He was elected to the scholastic fraternity Phi Beta Kappa, and on his graduation in 1915, Lipman offered him a job as a research assistant in soil microbiology and a stipend of fifty dollars a month, which in those days meant he could continue to live comfortably in his room in the farmhouse and study for his master's degree.

By the end of 1915, he had written [his first academic paper](#) on bacteria, actinomycetes, and fungi in the soil. He was twenty-seven. The paper was published in February 1916, the year he became an American citizen and the year he married Deborah "Bobili" Mitnick.



Selman Waksman married Deborah Mitnick, his childhood sweetheart, in 1916. (Special Collections)

“I had [sent my roots into the soil](#) in search of its microbiological population,” he later wrote. “I was now on my way. I knew now exactly what I wanted and how to get it. The rest was merely to follow my plan. California was to prove whether I was on the right track.”

The new couple moved to the University of California at Berkeley, where Waksman studied for two years for his doctorate on the enzymes produced by microbes, mostly the actinomycetes. During his last year he supplemented his income by working at Cutter Laboratories, a local commercial laboratory producing antitoxins and vaccines against bacterial infections. It was the start of a lifelong connection between his research as a microbiologist and industry.



IN THE SUMMER OF 1918, AS World War One was drawing to a close, Waksman returned to Rutgers to take up a new position as the farm college “Microbiologist.” His somewhat mundane task was to continue the search for microorganisms that would produce more fertile soils, but he insisted on the rather grand title, with a capital *M*, as a mark of the importance he attached to the emerging science, and his own place in it.

The war had taken its toll, even on the quiet backwater of the New Jersey Agricultural Experiment Station. There were no graduate students and no lab assistants in the Department of Soil Microbiology. Waksman found the laboratory benches covered with **dirty petri dishes**, and the cultures of fungi and actinomycetes he had put into the culture collection before leaving for California were either dead or in need of prolonged resuscitation.

The sorry state of the laboratories reflected the scarcity of funds. His mentor, Dr. Lipman, could offer him only one day a week and fifteen hundred dollars a year, less than he had been getting as a part-time bacteriologist in the Cutter Laboratories in California. Personally, he had no funds in reserve, and he was forced to look for another part-time job in industry to supplement his income. This did not present a problem.

Before the war, America had been dependent on Germany for supplies of chemicals, laboratory glassware, and even scientific literature, but was gradually severing these ties and establishing its own infrastructure of scientific research. Waksman was now a bacteriologist and a biochemist, a good combination for employment amid the expansion of microbial research after the war. The brewery and food industries were studying yeasts and cheese-producing molds, public health officials were looking at new ways to use microbes in sewage disposal, and drug companies were beefing up their research into medicines to cure infections. In agriculture, researchers concentrated on identifying soil-enriching microbes to grow bigger and better crops.

This bustling activity was a natural progression of the work of the nineteenth-century European pioneers of bacteriology—Louis Pasteur, who first formulated the germ theory of disease, and the German bacteriologist Robert Koch, who discovered the TB microbe. On the eve of World War One, German researchers had found a new purpose for the dyes that had been used to identify bacterial cells under the microscope. In 1910, a young German chemist, Paul Ehrlich, and his Japanese assistant Sahachiro Hata, found an arsenic-based dye that worked against the syphilis microbe. They named it salvarsan, and it became the first of the so-called magic bullets that would cure bacterial infections.

From among the many companies making offers, Waksman chose the Takamine Laboratory, in nearby Clifton, New Jersey, one of the more successful of the new companies producing antibacterial products, including salvarsan. Waksman’s job was simple enough for a postgraduate biochemist—he had to test each batch of salvarsan for toxicity to human cells. He was paid good money for those days, forty-five hundred dollars a year, and the company was close enough to Rutgers for him to combine his work with a day a week at the college. The money even allowed him to move into Manhattan, where his wife, Bobili, could enjoy the music, theater, and culture missing in rural New Jersey.

Over the next two years, Waksman was exposed to much more than how to test a drug for toxicity. The Takamine Laboratory produced and marketed **adrenaline**, a natural product of animal adrenal glands. His experience “**suggested the possibility**” of finding other useful natural products—perhaps

even among his favorite microbes, the actinomycetes.

Waksman was a rising star in microbiology at a time when researchers were focusing on a ghoulis question. What became of all the microbes that caused deadly diseases—typhoid, dysentery, cholera, diphtheria, pneumonia, bubonic plague, and tuberculosis—when a dead body was buried in the earth? When scientists searched the nearby soil, they found few of these germs, and they concluded that either the microbes could not exist in the soil, because the environment didn't suit them, or they were consumed by predators larger than themselves, or, a far more intriguing possibility, they were destroyed by other microbes.

In London at the turn of the twentieth century, researchers found that the cholera bacterium, *Vibrio cholerae*, survived in clean, deep water but not in surface water containing microbes present in the air. Cholera bacteria disappeared quickly, in a matter of hours, in sewage sludge, and also in seawater. *E. coli* was rapidly crowded out in manure piles teeming with other species of microbes. On the microbe battlefields, researchers in Europe and Australia found actinomycetes to be active warriors, but Waksman was reluctant to become involved. He had no medical training and preferred to concentrate on microbes that were useful in agriculture.

When finances at Rutgers improved in the early 1920s, Waksman became a full-time assistant professor in his chosen pursuit—the microbiology of the soil. The condition of his labs was pitiful, and he complained to Dr. Lipman. The division of soil chemistry had only two workers but had “three laboratories and three large closets,” and his division, soil microbiology, “had four workers and only one laboratory.” Recent alterations to the Administration Building had not included painting the walls, which “absolutely demoralizes the assistants and discourages the workers,” he wrote to Lipman.

In 1923, Waksman and his graduate assistant, Robert Starkey, saw actinomycetes producing clear zones when matched against other bacteria. “A zone is found free from fungus and bacterial growth,” their joint paper concluded, and “numerous” microbes, including bacteria, fungi, and actinomycetes “bring about injurious or destructive effects upon themselves or upon other soil organisms.” But Waksman was interested only in the effects on the fertility of the soil. He did not link this strange activity to the possibility of curing human infectious diseases. “Unfortunately our own observations on the growth inhibiting effect of actinomycetes upon other microbes were not pursued further at that time,” he later wrote.

In 1924, Waksman took six months off from Rutgers to go to Europe on a “grand scientific tour” with his wife and their four-year-old son, Byron. It was the first of five European tours that he would make with his wife before the outbreak of World War Two. In 1924, the main attraction was a conference on soil science in Rome organized by Jacob Lipman, who allowed Waksman to continue to be paid his small Rutgers salary but gave him no expenses for the trip. Despite his tight budget, Waksman packed in a hectic schedule of visits to major soil microbiology laboratories in Britain, France, Germany, Sweden, and Holland. In Paris he met and struck up a thirty-year friendship with the Russian pioneer of soil microbiology, Sergei Winogradsky, now an émigré in Paris. And in Holland he visited Martinus Beijerinck, who made his reputation by discovering viruses in 1898 and went on to find bacteria that make nitrogen available to plants. According to Waksman, Beijerinck greeted him with the words “You are the actinomyces man.” Waksman also went to Moscow and even his hometown, Novaya Priluka, in Ukraine. There he witnessed the ravages of the revolution and the civil war and saw again the little house where he was born. “It looked like a hole of a troglodyte,” he wrote later. He returned to America determined to write source books to fill the gaps in the literature of soil science.

“I was primarily a soil microbiologist,” he wrote, “studying soils and composts, peat bogs and manure piles ... concerned with products of microbes that are used in green plants.” He “scarcely

dreamed of becoming profoundly involved in problems dealing with human health.” He was “[too busy](#) completing [his] work on the distribution of different groups of microorganism in the soil, their role in the decomposition of organic matter and formation of humus.” His studies resulted in several major works that said almost nothing about the possible medical application of his fighting microbes.

In a 360-page book, *Enzymes*, published in 1926, he devoted only one paragraph to antagonistic bacteria. In his 894-page tome *The Principles of Soil Microbiology*, he wrote only two pages on “[antagonism and symbiosis](#) among microorganisms.” On another page, he mentioned the “inhibitory effects” of fungi and actinomycetes. In a [smaller book](#), *The Soil and the Microbe*, written with Starkey, now Waksman’s deputy, in 1931, they discussed the role of microbes in the life cycle of soil organisms. But he wrote only one sentence about bacteria fighting among themselves.

In his lectures and scientific papers, he would remind his students and readers that the soil was a complex system, our knowledge of it limited, our methods crude, and we were still unable to understand how it works. In the basement lab, his students followed “a semi-military regime,” often working weekends during the depression years because they had no money to spend. They wrote brief descriptions of each day’s projects in five-by-seven-inch lab notebooks, which Waksman reviewed at the beginning of each week. One student recalled what was known as the “book parade.” “Waksman would spot Harry and say, ‘Let me see your book.’ Waksman would glance at it and add, ‘Tell Dave to bring his book.’ Harry, disarmed, would go down to the basement lab and pass the word. Dave would submit his book and come back to order another student up to the office. The books were returned when Waksman spotted an error, or something unclear, but he never accused anyone of being a sloth and all partings were amiable. The book parade seemed to me [a little Teutonic](#).” Waksman rarely visited his students in the basement lab, even then. But once a year he held a spring cleaning, which he obviously enjoyed. All drawers and cabinets had to be open for inspection, and Waksman would walk in followed by his assistant, who carried a laundry basket. The student wrote, “If he found equipment lying on the bench, or chipped, or unlabelled, he would say, ‘Vat’s this for?’ in his Russian accent (which he never lost) and if there was any doubt, he would tell his assistant, ‘[Throw it in the basket](#).’”

In those days, Waksman’s students were still not looking for medical applications. “The soil and the microbe,” Waksman wrote, “await the investigator [who] is not looking for practical gains but for explaining the obscure and observing the unknown. The application will doubtless come.” Undoubtedly, Waksman missed a great opportunity. Had he pursued what he had observed with Pasteur’s “prepared mind,” he, not Alexander Fleming, might have been the first to discover an antibiotic.

But he was not a physician, like Fleming, and Rutgers had no medical department. In his daily life Waksman was not exposed to faculty discussions about the therapeutic value of “magic bullets” like salvarsan, or the sulfa drugs that followed. In 1932, the German doctor Gerhard Domagk, working at the giant chemical company I. G. Farben, found a bright-red dye that cured mice infected with pathogenic streptococci. This new compound, named Prontosil, was good for fighting a wide range of bacterial infections and later gave rise to the sulfonamides, or sulfa drugs, which had a major impact on the treatment of infectious diseases. (The life of Winston Churchill was saved by a sulfonamide when he developed pneumonia after the Tehran Conference with Stalin and Roosevelt at the end of November 1943.)

Yet Waksman still lacked funding to expand his research. In America, medical research, like other scientific research, suffered from a lack of public assistance. In the 1920s and ’30s, the National Institutes of Health and the National Science Foundation did not exist. Waksman relied on his wits to attract support. He was a good salesman, a scientist-entrepreneur who never seemed short of industrial sponsors.

He helped tanners find enzymes for [defatting hides](#); brewers, enzymes to clarify beer. He convinced the local mushroom industry that providing funds to investigate a compost mix of alfalfa, peanut shells, and tobacco stalks was a better bet than relying on horse dung from the declining stables of the Philadelphia police department. These links with industry provided rare funding during the depression years, and endeared Waksman's graduate students to him for providing them with beer and mushroom tastings. There were some unexpected delights. On one famous evening in the college auditorium, female models paraded in then-daring off-the-shoulder evening dresses with fringes of miniature orchids bred in Dr. Waksman's Department of Soil Microbiology. The event was sponsored by a local businessman hoping to sell the orchids at debutante balls.

A few independent foundations gave research grants, and in 1932, the National Tuberculosis Association funded Waksman to study the fate of TB germs in people and animals who died of TB and were buried in the soil. He assigned the task to [one of his graduate researchers](#), who found that the tuberculosis bacteria were greatly reduced in some soils. But Waksman did not follow up the interesting result. Similar results were being obtained by other researchers, and Waksman thought they all seemed to lead nowhere. He was not "yet [prepared to take advantage](#) of these findings."

In late 1935, Fred Beaudette, Rutgers's director of Poultry Pathology, brought Waksman a test tube containing a TB bacterium specific to poultry that had been destroyed by a fungus that had accidentally contaminated the tube. This was indeed a "happy accident" of the kind that Fleming had encountered seven years earlier with penicillin. Yet Waksman was still not ready to seize the opportunity, this time staring him in the face.

There was, of course, a perfectly good and understandable reason for not wanting to test the microbe's ability to destroy pathogenic bacteria: the risk of catching the disease. In his writings, Waksman [never mentions this as a factor](#), but it must have been on his mind. His underfunded laboratories were poorly equipped to protect the workers against infections, or even the hazards of handling dangerous chemicals. In the basement laboratory, protective clothing consisted of worn and torn white lab coats and some "very crusty, black, rubber lab aprons designed to catch splashes of hydrochloric acid." These coats were "[hung on spikes](#) driven into the wall" when not in use.

BUT WAKSMAN COULD not ignore the research coming out of Europe and Russia. In the mid-1930s, the Russians led the world on research into the antagonistic properties of Waksman's precious actinomycetes. By 1935, Russians had published four papers on the subject; Waksman had published none. A key Russian paper reported that actinomycetes were antagonistic to *Bacillus mycoides*, one of the standard bacteria tests for antibiotics. The paper concluded, "The question of interrelationships between soil microbes deserves profound research." Waksman had an enormous advantage over his peers in America in being able to read these papers, not just the English summary that was always included but the whole paper, and some have speculated that the Russian research [started to turn his mind](#) toward the possibility of antibiotics, a suggestion he never acknowledged.

In 1936, at the Second International Congress for Microbiology in London, Alexander Fleming discussed the [antibacterial properties](#) of his penicillin, a debate which Waksman later listed as an important event in the evolution of his own thinking. One of Waksman's graduate students recalled that Fleming's discussion was when Waksman became "[seriously interested](#)" in antibiotic research.

Later in 1936, Waksman began to study the published papers on warrior microbes and wrote two papers for *Soil Science*, the journal started at Rutgers by Dr. Lipman. The first paper reviewed the current literature, including the four Russian papers. A measure of Waksman's absence from basic research in this area is that of the 107 papers he listed, only 2 were written by him.

In the second paper, also finished in 1936, Waksman and a graduate student, Jackson Foster, tested

a fungus, a bacteria, and an actinomycete from a Scottish peat bog. They were all capable of producing “[substances which are antagonistic](#)” to other soil microbes when grown in petri dishes containing artificial nutrients. In 1937, another Russian researcher found that antagonistic actinomycetes were “widely distributed” in different soils in the Soviet Union. [Of eighty cultures](#) isolated from various soils, forty-seven possessed antagonistic properties, but only twenty-seven were found to be capable of liberating toxic substances into the nutrient agar on a petri dish.

In 1938, Waksman was especially influenced by the work of one of his former students, René Dubos. A Frenchman who had qualified in agriculture and immigrated to America in 1924 after hearing Lipman speak at the conference on soil science in Rome, Dubos worked for his Ph.D. under Waksman at Rutgers. He discovered a soil microbe that produced an enzyme capable of breaking down cellulose, the key ingredient of plant stalks and tree bark, and turning it into plant food. Similar work was being carried out at the Rockefeller Institute for Medical Research, in New York City, where Dubos later moved. There, he eventually isolated a bacterial enzyme that destroyed the sugary coat of the bacteria that causes pneumonia. Unfortunately, the enzyme was too toxic to be used by humans suffering from pneumonia, but Dubos was sufficiently encouraged to begin the first systematic search for antibiotics in the soil.

In 1939, he found an antibacterial agent produced by a bacterium, *Bacillus brevis*, and named it tyrothricin. The Rockefeller biochemist Rollin Hotchkiss helped him recognize that it was made up of two compounds, tyrocidin and gramicidin. Tyrocidin was toxic to mice, but gramicidin cured experimental infections in mice, without side effects. Gramicidin was too toxic to be administered to humans intravenously, but it was effective when used on open wounds. The Russians produced their own version of Dubos’s discovery, known as [gramicidin S](#) (for Soviet), and used it throughout World War Two as their main antibiotic.

That same year, the Russians struck again. Two researchers, N. A. Krassilnikov and A. Korneyako, again found that many species of actinomycetes produced antibiotics. The Russians concluded that “[one cannot escape the possibility](#) of using the bacterial factor of actinomycetes” to treat bacterial diseases. For the first time, they discovered two that were active, even so slightly, against *Mycobacteria*, the group that causes tuberculosis. To anyone searching for a cure for TB, this was a powerful clue that such an antibiotic might be found.

By late 1939—in the wake of pioneering research by the Russians, a major discovery by Dubos in New York, and the beginning of the war in Europe—Waksman, the soil microbiologist who had pledged his life to microbes that could be used in plants and industry, was finally ready to change the direction of his research to look for antibiotics to cure human diseases. All he needed was a sponsor.



Twelve miles down the railroad track from the Rutgers campus is Rahway, New Jersey, once an old Indian settlement and a stop on the stagecoach run from New York to Philadelphia. Since 1900, Rahway has been the home of Merck & Co., then and now one of the most important pharmaceutical concerns in the country. Friedrich Jacob Merck opened the original family-owned apothecary, the Engel-Apotheke (Angel Pharmacy), in 1656 in Darmstadt, Germany. In 1827, the Merck company started producing morphine, codeine, and cocaine. By the 1890s, Merck was selling so many products in America that the family dispatched the twenty-four-year-old George Merck to set up shop there. He settled in Manhattan, bought 150 acres of Rahway, and later sent his son, George Jr., a blond, blue-eyed giant at six feet five inches, to Harvard. On George Sr.'s death in 1926, his son took over the business.

By the beginning of World War Two, Merck was also producing vitamins. First came vitamin B1. Until the Merck chemists figured out how to synthesize the compound, tons of rice bran went into one end of Merck's Rahway plant, and fractions of an ounce of vitamin B1 came out the other end. So there was vitamin B2 for pellagra, vitamin B12 for anemia, vitamin C for colds, and vitamin A for eyesight. George Merck was also keeping a watchful eye on the Rutgers Department of Soil Microbiology. Like many other microbe researchers, Selman Waksman was experimenting with ways to use fungus fermentations to make citric acid, used in foods and soft drinks, and fumaric acid, used in dry cleaning.

At the beginning of 1939, Merck engaged Waksman as a consultant on microbial fermentation, first at \$100 a month and then \$150. In the summer of that year, Merck funded a \$150-a-month student fellowship specifically to find new ways of making citric acid. The program was successful, and the consultancy and the fellowship were renewed on an annual basis.

None of Waksman's students knew about his consultancies with Merck, **not even his deputy**, Ben Starkey. Some of the funds went into fellowships and stipends for his graduate students, some for "collaboration" between Merck and his laboratory, and some for "private consulting" between himself and Merck.

Toward the end of 1939, Merck expressed interest in hiring Waksman as a consultant on antibiotics, although in those days the word *antibiotic* was not in common usage. Merck called them "antibacterial **chemotherapeutic agents**." One such agent was penicillin. Although Alexander Fleming had discovered penicillin's antibacterial powers in London in 1928, he had never found a method of storing, concentrating, or purifying it, and it had remained a laboratory curiosity.

American scientists had read about Fleming's discovery, and in 1933 a graduate student at Pennsylvania State College had studied Fleming's microbe for his doctoral thesis. He confirmed Fleming's claims about the instability of the drug and, being unable to extract it himself, made no further investigations. Still, two other American drug companies, Eli Lilly and E. R. Squibb, looked at penicillin's potential. Squibb researchers carried out their own literature search and produced a well-reasoned statement, now a classic in the history of penicillin, concluding that "in view of the slow development, lack of stability and slowness of bacterial action shown by penicillin, its production and marketing as a bactericide **does not appear practicable**." Penicillin was sidelined in favor of the readily available sulfa drugs.

In 1936, a chemist at Merck was shown a culture of Fleming's *Penicillium notatum* by a physician

from New York's Beth Israel Hospital who predicted that more interesting antibiotics were on the way. Three years later, Merck's research director, Randolph Major, asked Dr. Waksman's advice, and he suggested taking penicillin seriously. Other similar agents would probably soon be found, he forecast. Merck immediately hired three new staff members to "study isolation of therapeutic substances from micro-organisms."

In Britain, the start of the world war had revived interest in Fleming's penicillin. At Oxford University, Howard Florey, an Australian pathologist, and Ernst Chain, a German Jewish chemist who had fled the Nazis in 1933, began work on purifying penicillin.

In the fall of 1939, Merck returned to Waksman with another proposal. This time the company offered him a second consultancy—of another \$150 a month—for information about "chemotherapeutic agents." "I informed them of my own interest in antibiotics," Waksman noted later. "They placed another fellowship in my laboratory and engaged me to help Merck in this field of research." Merck agreed to carry out "chemical, bacteriological and biological tests for the production, purification, plus identification and evaluation and to arrange for clinical trials." These were the kinds of tests that could not be carried out at Rutgers because of a lack of facilities. In exchange, Merck would have the **exclusive right** to develop any new drug that resulted from the research. The company would pay Rutgers a royalty of 2.5 percent of net sales.

In August 1940, the Oxford team published their first promising results of the use of penicillin on ten patients, and the team was eager to start development. But British industry was overstretched, and under constant air attack. Florey and a colleague, Norman Heatley, brought penicillin to America and found a government not yet at war, and drug companies eager to be the first in the antibiotic market. Merck, Squibb, Lederle Laboratories, and Pfizer & Co., in the East; Abbott, Parke, Davis, and the Upjohn Company in the Midwest. Merck agreed to be part of a massive, U.S. government-sponsored war effort to produce penicillin. George Merck sent a telegram to Vannevar Bush, director of the Office of Scientific Research and Development: "**Command me** and my associates ... if you think we can help you." The Roosevelt administration launched an astonishingly successful example of government-science-industry cooperation, second only in wartime to the atomic bomb project. It would eventually involve ten American and five British firms, combining efforts to make the drug for Allied troops.



George Merck of Merck & Co. with vial. (The Merck Archives, 2011)

WAKSMAN'S DEAL WITH Merck caused quite a stir in the offices of the Rutgers administration. They wanted to make sure the university got its share. Like many universities of the day, Rutgers had no policy for dealing with faculty who made patentable discoveries. The most recent case, in 193

concerned a [professor of pomology](#) named M. A. Blake, a well-known breeder of peaches who was called the father of the New Jersey peach industry. He was especially proud of his latest nectarine crosses and wanted to apply for a patent.

Whether Blake himself had the right to take out a patent depended on his contract, the Rutgers lawyers advised. If he had been employed specifically to breed nectarines, he would have to assign the patent to Rutgers, but if he was a “general employee” in the fruit-breeding department, and he had bred this spectacular new nectarine in the course of other work, then he would be entitled as an individual to apply for a patent and collect royalties. The lawyers noted, however, in view of Rutgers’ duty to make agricultural discoveries available for free to the public, that Professor Blake “might be embarrassed” if he started to profit from the patent. In that case, there was a third way: He could assign it to the nonprofit Rutgers Endowment Foundation, a body originally set up to receive alumni donations. A percentage of the royalties could be paid to the professor, the lawyers said, in line with similar arrangements at other universities.

This quickly became Rutgers’s policy; the only question was what percentage, if any, of the royalties to allow the discoverer. In 1937, Rutgers agreed to a [50-50 split](#)—until it found out that it was being overgenerous compared with other universities, or, as the Rutgers comptroller, A. Johnson, observed, that it had been “decidedly [off on the wrong foot](#).” Rutgers reduced the discoverer’s share to 25 percent, but even that was above what other institutions were paying. Purdue’s was fixed at 20 percent, the University of Wisconsin’s at 15 percent. Wisconsin’s Alumni Research Foundation director, A. L. Russell, advised Johnson to “keep in mind” that university patents are “to be taken out primarily in the interest of the public rather than for the inventor.”

While the Merck deal with Waksman was being worked out, the first of [Waksman’s graduate students](#) to work on the antibiotic project arrived at the Department of Soil Microbiology. Boy Woodruff, a tall, confident, genial farmer’s son from South Jersey, joined Waksman’s laboratory in July 1939. His parents were determined that he should have a university education, but all they could afford was the state-supported agricultural and engineering course at Rutgers. He lived with other students [above the chicken house](#), which at that time accommodated 125 white Leghorns. Woodruff earned pocket money selling farm eggs.

Woodruff had found the college experience exciting and sometimes a little overwhelming. He had gone to a concert for the first time, and had celebrated with his fellow students all night in 1937 when the Rutgers football team scored its first victory, 29 to 27, over Princeton since 1889. He graduated in soil chemistry, and Waksman offered him a college fellowship of \$900 a year—20 percent more than fellowships elsewhere. The money came from Merck’s generous contributions to Waksman, now totaling \$3,600 a year.

As a result of his European tours, Waksman attracted students worldwide. Eleven graduate students crammed into the two upstairs laboratories of the Department of Soil Microbiology. They came from China, South America, Europe, and across the United States. At first Woodruff was “terribly discouraged” when Waksman put him to work on composts and gave him little direction. He relied heavily on Waksman’s deputy, Robert Starkey, as had most of Waksman’s graduate students over the years. As one of them recalled, Starkey was their “[great provider](#) of materials and receiver of complaints—the equivalent of an assistant in a steel mill. He remembered; he got things done. He told us how to make our cases to Dr. Waksman. Modest to a fault, totally loyal to the Department—it is inconceivable that Dr. Waksman could have operated without him.” Woodruff worked alongside a visiting student from China who was trying to find out the minimum temperature needed to kill all the harmful bacteria in human feces so that it could be used for compost. Since human feces were not used for compost in America, Waksman suggested that Woodruff should study horse dung, horse

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