Medicine in Stamps

Elie Metchnikoff (1845–1916): discoverer of phagocytosis

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Medicine remained empirical and largely ineffective throughout most of the 19th century, with everyday life carrying the very real danger of illness and swift death, usually from infections. However, at the turn of the century, a number of European scientists made landmark discoveries in microbiology. One such luminary was Elie Metchnikoff, a Russian scientist who was the first to discover phagocytosis, a cell-mediated immune response to foreign matter. Prior to his findings, white blood cells, for example, were thought to take up bacteria not to fight disease, but to spread it. Metchnikoff showed instead that such cells, called phagocytes, could engulf and destroy microorganisms. For his discovery, he became a co-winner of the 1908 Nobel Prize.

EARLY LIFE Ilya Ilich Metchnikoff was born near Kharkoff, Russia on May 16, 1845, the youngest of five children. As a child, he was active and spirited, earning the nickname "Mercury." He attended high school in Kharkoff, frequently skipping classes to audit university courses. Graduating at the top of his class, he then journeyed to Würzburg, Germany, hoping to work under the eminent zoologist, Rudolf von Kölliker, but quickly took the train back to Russia because of homesickness. He had planned to study medicine, but his mother dissuaded him, believing him too sensitive to bear the suffering of patients. At Kharkoff University, Metchnikoff studied biology. Deeply dissatisfied with the rigid teaching and poor quality of the laboratories, he embarked on research studies on nematodes alongside Rudolf Leuckhart, a zoologist in Helgoland, Germany. When Leuckhart failed to acknowledge him as a co-author in his publications, Metchnikoff angrily left for Naples to begin work with Alexander Kovalevsky in a new field, comparative embryology. His parents and a two-year stipend from the Russian Ministry of Education supported his studies away from Russia, but the support was meagre, and he had to forgo meals on a number of occasions. Still, by 1867, he had earned his doctoral degree, and was honoured with the prestigious von Baer Prize for his work on the origins of the germ layer of invertebrate embryos.

SUBSEQUENT CAREER Metchnikoff taught briefly at Odessa University in Russia, handicapped by his candour and dogmatism. He moved to St. Petersburg, and there met Ludmilla Feodorovitch, a frail and sickly woman who became his first wife. Stricken with tuberculosis, she had to be literally carried to their wedding, and died only five years after their marriage. Depressed, Metchnikoff attempted suicide by ingesting a large vial of morphine, but survived the attempt as the large dose of morphine acted as an emetic.

Metchnikoff then returned to Odessa University, battling bouts of depression as he toiled in newly-installed laboratories. He rented an apartment above a house that belonged to a large, noisy family, and there he met Olga Belokopitova, the landlord's 16-year-old daughter, who was studying the natural sciences. Tutorship quickly turned into romance, and they married in 1875. Although barely an adult when she was married, Olga proved to be a loving wife, an invaluable assistant and his eventual biographer.

In 1881, Olga fell ill with paratyphoid fever, and this coincided with the further deterioration of his work conditions at Odessa University brought on by political unrest. Metchnikoff's depression worsened, and he again attempted suicide, this time by inoculating himself with the spirochaete of a relapsing fever. Being the true scientist, Metchnikoff then tried to determine if the agent causing the disease could be transmitted through the inoculation of his blood! Fortunately, he recovered from the relapsing fever, and Olga too survived her illness. Around this time, both her parents died of unrelated

causes, leaving them with a sizable inheritance. With his newfound financial independence, Metchnikoff was able to leave Russia to eventually end up at the Pasteur Institute in Paris, France. However, it was at his first destination in Messina, Italy, that the stage was set for his momentous discovery of phagocytosis.

THEORY OF PHAGOCYTOSIS One morning in 1882, as Metchnikoff observed cells moving freely within transparent starfish larvae, he hit upon this theory: "*These wandering cells in the body of the larva of a starfish, these cells eat food... but they must eat up microbes too! Of course the wandering cells are what protect the starfish from microbes! Our wandering cells, the white cells of our blood—they must be what protects us from invading germs*." To test his hypothesis, he inserted small thorns from garden plants into the starfish larvae. The following morning, he noted that the cells within the larvae were no longer moving around aimlessly, but were instead aggregated around the foreign bodies, as if to drive them out.

The theory of phagocytosis was thus taking shape. He theorised that under appropriate conditions, protector cells within an organism would mount an immune response by attacking and ingesting foreign matter. Metchnikoff coined the term, phagocyte, from the Greek words, "phages", meaning "to eat", and "cite", meaning "cell". In another telling experiment, he mixed *Daphnia*, a type of water flea, with spores of an infectious fungus, and again observed phagocytes in action: mobile cells in the fleas surrounded and engulfed the infectious spores, just as white blood cells would aggregate at the site of an infected wound. He later observed similar reactions in mammals (rabbits) that were exposed to microbes such as anthrax, especially the less virulent and attenuated forms. The scientific world greeted his findings with excitement, but phagocytosis, the cellular basis of immunity, was to take a temporary back seat when German scientist, Emil von Behring, discovered humoral immunity (antibodies) in 1890. There erupted an intense debate as to which theory was correct, with the French supporting Metchnikoff, and the Germans, von Behring. Eventually, both theories would become entrenched as being fundamental to the body's fight against microbial infections.

LIFE AT THE PASTEUR INSTITUTE Metchnikoff had moved to France in 1882, adopted it as his home, and changed his first name to Elie. He received many job offers, but chose to work at the Pasteur Institute in Paris. There, in 1888, he was warmly received by Pasteur, and gained an entire laboratory for his continued research on phagocytosis, a theory later applied to vaccinotherapy that would save innumerable human lives.

He remained at the Pasteur Institute for 28 years. With Olga as his wife-assistant, he continued his research, publishing many papers and books, the best-known being *Immunity in Infective Diseases*. He surrounded himself with bright young scientists, the most famous of whom was Jules Bordet, who won the Nobel Prize in 1919.

During his last 15 years, Metchnikoff became fascinated with the biology of ageing and death. He believed that the ageing body was gradually poisoned by waste products from harmful bacteria in the intestines, which could be neutralised by lactobacilli in yogurt and sour milk. He had two major publications during this time: *The Nature of Man: Studies on Optimistic Philosophy* and *The Prolongation of Life: Optimistic Studies*. In 1914, stunned by the war that had broken out in Europe, Metchnikoff called for an end to the "unexampled butchery", pleading: "*Let those who have preserved the combative instinct direct it towards a struggle, not against human beings, but against the innumerable microbes, visible or invisible, which threaten on all sides and prevent us from accomplishing the normal and complete cycle of our existence*."

Elie Metchnikoff died of myocarditis and heart failure on July 15, 1916, at the age of 71, and his ashes remain preserved in the library of the Pasteur Institute. Metchnikoff, the Russian scientist, variously described as fiery, contentious and emotionally unstable, was invited to spend his dying days in Pasteur's personal apartment. It was an honour that brought him much happiness.

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