A lifetime quest for a cure

Driven by the death of loved ones and a commitment to science, Gertrude Elion helped launch a new wave in medicine.

BY JULIE L. McDOWELL

It seemed as if Gertrude "Trudy" Elion's college plans would be among the many dreams shattered when the stock market came tumbling down in 1929. A high school graduate at age 12, Elion was determined to dedicate herself to scientific research. Fortunately for the medical and drug discovery fields, Elion found her way to college and beyond. Shortly after the stock market crash, Elion received news that she was accepted at Hunter College, the women's branch of the free but competitive City College of New York (CCNY).

Born in New York in 1918 to parents who had emigrated from Lithuania and Poland, Elion was torn between careers in science and medicine, but because of her grandfather's illness and subsequent death from cancer in 1933, she decided to study chemistry with the hope of finding a cure for the disease.

She earned her chemistry baccalaureate in 1937 at age 19, but even though she graduated Phi Beta Kappa, she was denied financial assistance by the graduate programs to which she applied. In addition, America was still in the throes of the Great Depression, so jobs were hard to find, especially for women: "I hadn't been aware that there were doors closed to me until I started knocking on them. I went to an all-girls school. There were 75 chemistry majors in that class, but most were going to teach it.... When I got out and they didn't want women in the laboratory, it was a shock.... It was the Depression, and nobody was getting jobs. But I had taken that to mean *nobody* was getting jobs.... [Then I heard,] 'You're qualified. But we've never had a woman in the laboratory before, and we think you'd be a distracting influence'" (*1*).

Soon after Elion graduated from Hunter College, she met Leonard Canter, a brilliant statistics student at CCNY. By all accounts, they were smitten with each other from the start. In fact, over 300 of the couple's love letters exchanged between 1937 and 1941 were recently discovered, revealing a deep personal and intellectual connection. During these four years, the couple enjoyed weekly outings to concerts and plays in New York, along with intense discussions about thermodynamics or their own, more prosaic data.

Meanwhile, Elion was determined to continue her education in spite of the lack of job opportunities for women in chemistry. She took graduate chemistry classes at New York University on weekends and at night while working several jobs to pay for tuition. She worked as a doctor's receptionist, high school chemistry and physics teacher, and at A&P grocery stores, where her jobs included analyzing the acidity of pickles and monitoring the color of mayonnaise.

While Elion was working days and studying nights, Canter completed his bachelor's degree studies with the highest grade-point average in CCNY history. Given the bleak economy, though, even he was also having trouble finding a job. But worse news came shortly after graduation. A routine medical examination revealed that Canter had a heart condition. The couple was shocked by the news, and Canter encouraged Elion to leave him. "You mustn't love me, Gertie," he wrote in a letter. "I'm not a full man" (*2*). But Elion rejected his pleas and pledged her devotion to him. Within a few months, the couple was engaged. Elion soon earned her master's degree in chemistry from New York University (1941), where she had been the only female in her class.

Sadly, the couple's happiness was short-lived. In November 1940, Canter became ill with bacterial endocarditis, an infection of the heart valves. At the time, penicillin was not widely available. Canter was in the hospital for several months and died on June 25, 1941, with Elion at his side.

Motivated by heartbreak and grief, 23-year-old Elion committed herself to advancing her chemistry career. Even though opportunities in the chemical industry were still limited for women, many jobs opened up when a large number of men joined the armed forces during World War II. In 1944, Elion was hired by Burroughs Wellcome as a senior research chemist working for George Hitchings, who had done his doctoral research at Harvard on the metabolism of nucleic acids. She was one of only two women among a staff of 75 in Hitchings' laboratory. Hitchings was focusing on a scientific approach to drug discovery based on knowledge of cell growth. Initially working in organic chemistry, Elion became involved in all aspects of drug discovery in the laboratory—biochemistry, pharmacology, immunology, and

GERTRUDE ELION PHOTO COURTESY OF THE GLAXOSMITHKLINE HERITAGE CENTER

virology. "It was one new field after another, and the compounds were taking me there, and that was wonderful," she told an interviewer in 1991 (*2*). "Hitchings was great; he let me do it."

Hitchings divided the nucleic acid work among his staff, and he assigned the purines to Elion. For more than two years, she spent her days working in the Burroughs Wellcome laboratory and her nights at Brooklyn Polytechnic Institute working toward her doctorate. Eventually, the institute demanded that she leave Burroughs Wellcome and pursue her Ph.D. on a full-time basis. But drug discovery had become Elion's passion, and she refused to leave the laboratory—the deaths of her fiancé, grandfather, and later her mother impelled her to pursue effective drugs to fight disease. She quit her doctoral studies, although she was later awarded numerous honorary Ph.D.'s.

Over time, Elion and Hitchings' relationship evolved into a 44-year partnership that changed medical research forever. Trial and error had been the standard method of medical research, but Elion and Hitchings based their research on understanding the fundamental workings of human physiology and on the behavior of nucleic acids. Hitchings and Elion found that normal cells, cancer cells, and infectious microbes all use nucleic acids differently to reproduce. While analyzing these differences, the research team developed "target drugs" that blocked the replication of cancerous and infectious cells without damaging healthy cells. In 1988, *The Boston Globe* reported that Elion and Hitchings "developed six different drugs against nine serious medical conditions and paved the way for others, including AZT."

In 1953, Elion and Hitchings developed a cancer-fighting drug, 6-mercaptopurine, also known as 6-MP, which caused remission in 40% of children with leukemia. The research team went on to develop additional drugs using the 6-MP research. One of these new drugs, azathioprine (Imuran), suppressed the immune system and allowed successful organ transplants to take place. Elion and Hitchings also developed allopurinol, which is used to treat gout by reducing the body's production of uric acid in the joints.

In 1967, Elion was named the head of experimental therapy at Burroughs Wellcome (now Glaxo Wellcome). She and her research team continued to pioneer new drug discoveries, including acyclovir (Zovirax), the first drug used against viral herpes; pyrimethamine (Daraprim), used to fight malaria; and trimethoprim–sulfamethoxazole (Septra), used to combat bacterial infections.

Elion retired from Burroughs Wellcome in 1983, but soon accepted an offer to join the Duke University faculty part-time to mentor medical and graduate students. Her primary focus was working with students in the neuro-oncology and pediatric bone marrow transplant programs. At Duke, she published 25 papers with her students.

In 1991, Elion was the first woman inducted into the Inventors Hall of Fame, and she was awarded the 1988 Nobel Prize in Physiology or Medicine along with Hitchings and James W. Black for "their discoveries of important principles for drug treatment." Her association with Duke continued until the end of her life. She came into the laboratory every day and was still teaching until she died in February 1999.

Before her death, she was asked how she achieved such professional success while facing discrimination and personal tragedy. "Time passes rapidly when you are having fun," she said. "The thrill of seeing people get well who might have otherwise died of disease . . . cannot be described in words. The Nobel Prize was only the icing on the cake" (*2*).

References

(1) McGrayne, S. B. *Nobel Prize Women in Science: Their Lives, Struggles and Momentous Discoveries;* Birch Lane Press: New York, 1993.
(2) McGrayne, S. B. Damn the Torpedoes, Full Speed Ahead! *Science* **2002,** *296,* 851–852.

Further reading

Gertrude B. Elion; National Academy of Sciences; www.nap.edu/html/biomems/gelion.html.
Gertrude Belle Elion: A Lifeline; Chemical Heritage Foundation; www.chemheritage.org/EducationalServices/pharm/chemo/readings/lifeline.htm.
Wasserman, E. *The Door in the Dream: Conversations with Eminent Women in Science;* Joseph Henry Press: Washington, DC, 1999.

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