PORTRAITS OF SCIENCE

1200
1300
1400
1500
1600
1700
1800
1900
2000

Damn the Torpedoes. Full Speed Ahead!

Sharon Bertsch McGrayne

Although Elion never finished her Ph.D., motivated by personal tragedy, she went on to do pioneering research in drug discovery.

Gertrude Belle Elion met Leonard Canter, the love of her life, in July 1937, when she was 19 years old and full of bubbly charm (*1*). She had recently graduated in chemistry with highest honors from Hunter College, the women's branch of the free but fiercely competitive City College of New York (CCNY). Ever since her grandfather's death from cancer, scientific research had been her goal. The stock market crash in 1929 had bankrupted Elion's father, however, and she needed financial aid for graduate school.

Despite her academic record, 15 chemistry departments around the United States rejected her application, largely because she was female. For almost a decade she would be confined to marginal jobs, and she was never able to earn a Ph.D. Yet in 1988, she shared the Nobel Prize in Physiology or Medicine for the development of a scientific approach to drug discovery based on a knowledge of cell growth and purine chemistry. She also synthesized or developed compounds that helped make organ transplantation, chemotherapy, and antiviral pharmaceuticals possible.

More than 300 love letters, written by Elion and Canter between 1937 and 1941 and discovered after her death, cast new light on how she developed the philosophy that enabled her to overcome personal tragedies and the lack of a doctoral degree.

When Elion met Canter, he was a handsome and brilliant statistics student at CCNY. Smitten, Canter saw in the redheaded Elion "a brilliant woman ... sincerity ... a vital, fresh, spontaneous, sparkling spirit ... the soft loveliness in my life." Within weeks, Elion had gently dismissed two other beaux. Canter addressed his second letter to "Dearest Gertie," and she was equally forthright with him: "It would be like an ostrich hiding it's [sic] head in the sand to ignore the general tone of your letter.... A little confidence between us—I frighten away easily when people get too serious on certain subjects. I know that you have enough good taste and good sense for me to stop worrying about it right away."

The author, a science history writer, can be reached at 5233 Pullman Avenue, NE, Seattle, WA 98105, USA. E-mail: McGrayne@alum.swarthmore.edu

Over the next 4 years, the couple dated weekly, attending New York's concerts and plays, discussing thermodynamics and the Method of Least Squares, or visiting city parks and her parents' summer cottage in Suffern, New York. Between dates, they used the telephone to transmit prosaic data and the post office to analyze their growing love.

Because a 2-cent stamp delivered a letter within hours, the correspondence has much the immediacy of e-mail. Thus, Elion sent Canter a penny-postcard saying that she loved music, poetry, spring—and him. And she reported in an 8 July 1938 letter, "I received a letter of rejection today from Penn State which elated me almost as much as if it had been an acceptance. It really deserves to be framed as a fine example of courtesy, kindness, encouragement and a score of other virtues." More disheartening experiences appear in her diary. A job interviewer at the Chemist's Unemployment Committee was "unnecessarily rude and made me feel really terrible. Very upset by it." The uncertainty of her professional prospects depressed her. "Don't know what will happen this winter. Worried. Business school? Volunteer work? Chemistry job? Salesgirl? Courses at Hunter or Columbia? No money." Once she was told, "You're qualified. But we've never had a woman in the laboratory before, and we think you'd be a distracting influence." Years later, Elion recalled, "I almost fell apart. That was the first time that I thought being a woman was a real disadvantage" (*2*). She added, "It surprises me to this day that I didn't get angry. I got very discouraged. But how could I say, 'No, I won't be a distracting influence?' How could I know what the men were like? I wasn't bad-looking. I was kind of cute" (*3*).

In desperation, she entered secretarial school but quit as soon as she landed a 3-month, part-time job teaching chemistry to nursing students for $200. Later that winter, Elion faced a dilemma when a family friend offered her an unpaid post in the chemical laboratory of the Denver Chemical Company. Should she take the chance that it might lead to research science, hold out for a paid laboratory job, or give up her dreams entirely and become a public school teacher?

She gambled and began volunteering at the Denver Chemical Company in March 1938. "Now that I've actually begun working, I can't understand why I was so hesitant," she told Canter. "There are inconveniences of course—the 2½ hours spent in the subway every day, the rushing home for supper and rushing downtown again to school, the coming home after 10, too tired to study—but it's worth it, if only for the feeling of self-confidence I am rapidly acquiring."

CREDIT: BURROUGHS WELLCOME/AP PHOTO

Gertrude Belle Elion (1918—1999)

A personal crisis loomed when Canter won a year's scholarship to study in Paris. Canter worried that he would lose her. Frankly, she admitted that he might, but promised that, when he returned, "No matter what the answer is, it will be the truth." While he was away, Elion worked during the day (eventually earning a salary), took evening education and chemistry courses, applied for jobs, and studied for the rigorous examinations given to prospective schoolteachers. "Tired," she summarized. Also depressed by the coming war, "the insane futility of slaughtering bodies and crippling minds."

When Canter returned from France in 1939, they found their love as strong as ever. Using $450 earned during Canter's absence, she enrolled for a year of graduate study at New York University (NYU) in Manhattan. Like Canter, Elion lived at home in the Bronx with parents; a morning job (as a doctor's receptionist) covered lunches and subways. "Sometimes, I think I have more luck than I deserve."

Graduate school had its difficulties though. "It isn't as much fun as some people would think, being one of four girls in a class of about 60 boys," she said. And most classes were "very dull ... lots of facts, but no 'whys or wherefores.'" She preferred the physical chemistry professor who explained "the most difficult concepts with such clarity that I am positively spellbound."

"Just a few minutes ago I thought I was on the verge of understanding 'entropy,' but just as I had gotten the molecules into a suitably random distribution, I somehow became rather disorganized myself, and poof! It was gone. Well, perhaps when my mind is a good deal fresher than it is at the moment, I will recapture the faint glimmerings and the light will dawn. In the meantime," she wrote Canter, "let's listen to that lovely *Overture to the Bartered Bride* the Ford Symphony is playing" on the radio.

Early in 1940, Canter graduated from CCNY with a bachelor's degree and the highest academic record in the college's history. Yet, such was the state of the economy that his 13 job application letters elicited "eight no's" and one 4-minute interview. Later, Macy's comptroller rescinded a job offer when a routine medical examination revealed that Canter had a heart condition. Reeling from the news, Canter felt as though "the ground has been cut from under my feet.... You mustn't love me, Gertie," he wrote. "I'm not a full man."

Elion refused to abandon him. To lighten his spirits, she mailed Canter her antidote for spring fever: "One large dose of L.C. [Leonard Canter], taken as frequently as possible during the day, and always upon retiring. And now, having taken a dose, let's see how strong it's made me. Hmm! I actually opened the book. Won't you sit here and hold one hand while I turn pages with the other? Thanks. Here we go."

After more than 5 months of job-hunting, Canter was hired by a stock brokerage. In celebration, Elion and Canter danced all night and reached an understanding about their future. Whatever it was, it did not include Elion's giving up chemistry. Canter assured her that he would "wait for her a thousand years," and Elion responded, "In you I find most of what others must find in religion—faith, hope, consolation, beauty, ecstasy of an almost unearthly quality, and a deep transcending love."

By the fall of 1940, Elion's job prospects had improved. She was teaching chemistry and physics at Jamaica High School in Queens and working evenings on a master's degree in chemistry at NYU. Lectures there were exhilarating—"a little over my head so that I have to stretch upward to reach them."

Their elation was short-lived. In November, Canter contracted bacterial endocarditis, a strep infection of the heart valves. Penicillin was not yet generally available, and after months of hospitalization, Canter died, with Elion at his side, on 25 June 1941. Elion was 23 years old. She did not consider marriage again for years and eventually told any would-be suitor that she did not have time to marry.

"The thrill of seeing people get well who might otherwise have died of disease...cannot be described in words."

Work became her salvation. She earned a master's in chemistry from NYU—her highest degree, other than a host of honorary Ph.D.'s. Testing food quality for A&P supermarkets taught her about instrumentation. When the work became repetitious, she moved on to Johnson & Johnson. And at the still-young age of 26, as the World War II shortage of male chemists finally opened research laboratories to women, Elion landed a job at Burroughs Wellcome (now merged into SmithKlineGlaxo).

Here, Elion worked with George Hitchings, who was developing a scientific approach to drug discovery based on a knowledge of cell growth. "What turned me on was what the compounds did, although I did organic chemistry for probably the first 15 years I was there, I got involved later on with the biochemistry, the pharmacology, and eventually the immunology, the virology. It was one new field after another, and the compounds were taking me there, and that was wonderful. Hitchings was great; he let me do it" (*4*).

Dividing the nucleic acids among his staff, Hitchings assigned the purines to Elion. For 2 years, she worked at Burroughs Wellcome during the day and on a Ph.D. at Brooklyn Polytechnic Institute at night. She did not abandon her dream of a doctorate until the institute ordered her to study full time. She refused. Drug discovery had become a personal mission, motivated by the deaths of her grandfather and Canter and later her mother and the patients for whom her first drugs were not effective enough.

Elion's close collaboration with Hitchings had its cost. Elion said that she regarded them as a team but that Hitchings did not. She worked so smoothly with him for 22 years that no one could identify their separate contributions. But when I interviewed Hitchings for a biography of Elion, he emphasized that he—backed by Elvira A. Falco, Peter Russell, and others—had discovered pyrimethamine, an antimalarial, and trimethoprim, which, combined with sulfa, treated septicemia and meningitis and still is used to treat urinary and middle ear infections, as well as *Pneumocystis carinii* pneumonia, a complication of AIDS. Hitchings credited Elion's early career with 6-mercaptopurine (6-MP), sold as Purinethol, which helps cure about 80% of children with acute leukemia; azathioprine, marketed as Imuran, to prevent rejection of transplanted organs; and allopurinol, marketed as Zyloprim, to treat the gout often associated with chemotherapy.

When Hitchings retired from active research in 1967, Elion said, "At 55, I had had enough already of being junior." Finally on her own, she developed the first antiviral drug, acyclovir (Zovirax), "my crown jewel.... That such a thing was possible wasn't even imagined up until then." The antiherpes drug became Burroughs Wellcome's most profitable product. Afterward, Elion trained the team that developed AZT, the most widely used retroviral drug for treating AIDS.

When the Nobel Committee wondered whether Elion should share a Nobel Prize with Hitchings, her academic supporters pointed to her early articles, where she was first author, and to her antiviral work, conducted after Hitchings' retirement. The prize was eventually awarded to Hitchings and Elion and to Sir James W. Black.

How did Elion herself explain her ability to overcome years of discrimination, personal tragedy, and being Hitching's "junior"? "Time passes rapidly when you are having fun," she said. "The thrill of seeing people get well who might otherwise have died of disease ... cannot be described in words. The Nobel Prize was only the icing on the cake."

"Keep your eye on the goal," she advised, paraphrasing Admiral David Farragut, "Damn the torpedoes. Full speed ahead!"

References and Notes

1. J. L. Elion, M.D., described his aunt as "full of bubbly charm." Dr. Elion kindly gave permission to read and quote from her letters and diaries. He is her executor and copyright holder.
2. S. B. McGrayne, *Nobel Prize Women in Science: Their Lives, Struggles, and Momentous Discoveries* (Joseph Henry Press, Washington, DC, 2nd ed., 2001).
3. M. Holloway, *Sci. Am.* (Oct. 1991), pp. 40 and 43.
4. G. Elion interview with McGrayne, 6 January 1991, Research Triangle Park, NC.