Editor-in-Chief's Note

A Tribute to Gertrude Belle Elion on the 100th Anniversary of her Birth

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About 25 years ago, when I directed and taught in a course called Graduate Pharmacology, I would regularly ask students to tell me the names of scientists who deserve a place in the pantheon of great drug discoverers. At least four names were typically offered (the names varied a bit from year to year), and the most frequently mentioned names were Alexander Fleming for penicillin, Paul Ehrlich for Salvarsan (arsphenamine) and its use for syphilis, Friedrich Serturner for morphine, Felix Hoffmann for acetylsalicylic acid (aspirin), and Frederick Banting and Charles Best for insulin. I liked to point out that Nicolae Paulescu isolated insulin (he named it pancreine) before Banting and Best and that Arthur Eichengrun was the actual discoverer of aspirin but that he was denied credit because he was Jewish.

I would next point out that there were no women's names suggested; I should note that at least 50% of our graduate students were women. Someone would usually ask, "What about Madam Marie Curie?" Someone else would add that her work on radiation had nothing to do with drug discovery. I would point out that it was her separation of pure radium chloride from pitchblende (uraninite) that made its therapeutic uses possible. Whenever Curie's name came up, it would be an opportune segue to talk about laboratory safety and good laboratory practice by reminding them that Curie died of aplastic anemia secondary to radiation exposure.[1] I would add that Karen Wetterhahn, whose work on heavy metals our students had studied, died of exposure to dimethylmercury in her own laboratory; this liquid organic mercury form accidentally penetrated her latex gloves.

Before 1991, I was unaware of any famous female pharmacologists. We have an annual lectureship at Tufts that was endowed by Sterling Drugs to honor Dr. Louis Lasagna, who was then the dean of the Sackler School for Graduate Biomedical Sciences at Tufts and a professor in our newly minted Department of Pharmacology and Experimental Therapeutics (DPET). In 1991, as DPET's first chair, I asked Dr. Lasagna to suggest a name for the Sterling Lectureship. Without hesitation, he suggested Gertrude Elion. When I did not recognize her name, he laughed and told me about her. I soon had the opportunity to meet with her at length and to talk with her at a dinner in her honor. What follows is short version of what I learned from her and from subsequent reading.[2–6]

Gertrude Belle Elion was born in New York City 100 years ago (January 23, 1918). During her teenage years, her mother's father died of cancer. Having been close to him, she decided to devote her life to finding cures for cancer. She entered Hunter College in New York City and majored in chemistry, graduating summa cum laude at the age of 19. She then worked part time while working toward a master of science degree at New York University, which she received in 1941. Next, she worked as a chemist at several short-lived jobs at the Quaker Maid Company and Johnson & Johnson. She also began taking night courses toward a PhD at Brooklyn Polytechnic Institute. While World War II was raging and commuting to school was taking its toll, she was told that she could no longer be a part-time doctoral student. She then came to a critical decision point, realizing that she could not simultaneously work part time and study full time at a level that met her own high standards. Because of the shortage of men working in science and the increased job openings, she reluctantly decided to drop her PhD studies and seek full-time work.

In 1944, Elion began to work as a senior research chemist at Burroughs Wellcome's research laboratory in Tuckahoe, New York. In 1968, she moved with the laboratory to Chapel Hill, North Carolina, where the laboratories are now known as the Wellcome Research Laboratories. From that point on, Elion continued to live in Chapel Hill, North Carolina, and was still serving as a scientist emeritus at the Wellcome Research Laboratories in Research Triangle Park until she had an intracranial hemorrhage and died on February 21, 1999.

I learned more from our conversations, but most of it was not relevant for this tribute. Although she was engaged once, she never married. Her fiancé unfortunately died of an infection, and his death added to her drive to develop useful medicines. She also discussed her more than 30-year collaboration with George Hitchings with whom she shared the Nobel Prize in Physiology in 1988 and who had hired her as the second person to work in his research group. In his Nobel biography, he describes her as "intelligent, hard working and ambitious."[7] Hitchings died in February 1998, almost exactly a year before Elion. I would be remiss not to mention that Sir James Black also shared the 1988 Nobel Prize with them.

Because of their desire to integrate knowledge of illnesses and biochemistry, Elion and Hitchings created new procedures for developing new chemical entities. The following are some of the important drugs for which Elion was centrally responsible: 6-mercaptopurine for leukemia, acyclovir as an antiviral agent, pyrimethamine for malaria, allopurinol for gout, azathioprine as an immunosuppressant, trimethoprim as an antibacterial agent, and azidothymidine for HIV/AIDS. Elion also led the team that developed nelarabine, a prodrug of ara-G. Synthesized in the 1970s, an injectable formulation was finally fast-tracked by the US Food and Drug Administration in 2003 and approved in 2005 for the treatment of T-cell acute lymphoblastic leukemias and lymphomas.[8]

She received 45 patents throughout her career. Elion was both a pioneer and a lasting force because her work has been the basis for the development by many others of important therapeutic agents. She received many more well-deserved awards during her illustrious career, including the National Medal of Science from President George H. Bush in 1991.

From my conversations with Elion, I had the distinct impression that she was never a self-promoting recognition seeker. She clearly devoted her life to making the world a safer and healthier place. Does Gertrude Belle Elion not deserve a prominent position in the drug discovery pantheon? In my opinion, she was one of America's all-time top scientists, a remarkable achievement for anyone and particularly for someone who never completed a doctoral degree.

STERLING DRUG AND GLAXOSMITHKLINE: CURIOUS CONNECTIONS AND A COMMENT ON SOME MISSTEPS

I suspect that most of our readers have never heard of Sterling Drug. I had to look it up in 1991 in conjunction with the lectureship and again for this Note.[9,10] Sterling Drug was established in 1901 in Wheeling, West Virginia, by Albert Diebold and William Weiss. Years later it became Sterling-Winthrop, and it was eventually subsumed into what is now GlaxoSmithKline (GSK). In 1940, the Winthrop component inadvertently contaminated its antibiotic sulfathiazole with phenobarbital.[11] Winthrop was fined; this incident fortunately contributed to the establishment of the good manufacturing practices guidelines through the Public Health Services Act of 1944.[12]

American-born pharmacists Henry Wellcome and Silas Burroughs started a company called Burroughs Wellcome & Company in London in 1880. This company also eventually morphed into GSK.[13,14] My guess is that Elion would have been very distressed by the troubles that beset GSK after her death. In 2012, GSK agreed to a $3 billion settlement with the US government after pleading guilty to several major missteps: nondisclosure of safety concerns (eg, rosiglitazone, paroxetine) and promotion of their products (all big sellers) for unapproved indications (eg, paroxetine, bupropion, ondansetron, sumatriptan, valacyclovir).[15] With the exception of valacyclovir, I could not find any evidence that linked Elion to any of these products; for valacyclovir, she was not involved beyond discovery and preclinical development. None of this should tarnish her stature and contributions.

For perspective, it is important to note that other companies have been penalized for similar violations.[16–19] In 2013, Johnson & Johnson was fined $2.2 billion for similar reasons. They pleaded guilty to off-label marketing for unapproved indications for their antipsychotic agent risperidone and for paying kick-back monies to certain clinicians and pharmacists; these large monetary amounts sent a clear signal to the pharmaceutical industry.[16]