Eloise R. Giblett

BIOGRAPHICAL

A Biographical Memoir by Arno G. Motulsky and Stanley M. Gartler

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Eloise Giblett, or Elo as she preferred to be called, was born in Tacoma, Washington in 1921. Her mother had been reading "Eloise and Abelard" during her pregnancy and was so taken with the famous love story that she chose the name Eloise for her daughter. Her mother also gave Eloise a love of music, dance, and song—for a short period as a child, Eloise was thought to have the potential to become a second Shirley Temple. At the time of Elo's birth, her father was a machinist working on the shipbuilding docks around Tacoma. When Eloise and her older brother started school, their father became an insurance salesman for the Metropolitan Life Insurance Company. Successful at his new job, he was promoted to manager of the Spokane office, and the family moved there and lived a comfortable life through the Great Depression.



Eloin R Liblet

By Arno G. Motulsky and Stanley M. Gartler

Elo did well in school and excelled at the violin but was not particularly interested in science in her early years. That changed when her brother told her about a high school chemistry course he was taking and she became fascinated with atoms and molecules. Thereafter, she started taking science courses while still maintaining her interest in music. Upon graduation from high school in 1938, she received a scholarship to Mills College in California and spent two years there majoring in chemistry. She transferred to the University of Washington in the fall of 1940 and changed her major to microbiology. Following her graduation in December, 1942, she was offered a position as Teaching Fellow in Microbiology, but for family reasons returned to Spokane and spent a year living and working there.

Following Pearl Harbor, Elo wanted to contribute to the war effort. Hence, in the fall of 1944, she joined the WAVES and was inducted into the service in New York City. While there, she had the unusual experience of having her unit reviewed by two of the most important leaders in the fight against the Axis Powers: President Franklin D. Roos-

evelt and General George C. Marshall. Elo was assigned to the US Naval Hospital in San Diego, which was then the largest hospital in the world with 14,000 patients. She learned a great deal of medical technology while there and wrote her first paper about detecting meningitis in blood smears.

Elo was discharged shortly after the war ended in August, 1945 and resumed her education at the University of Washington, where she received a M.S. degree in Microbiology in August, 1947. That fall she enrolled in the new Medical School at the University of Washington. At the end of her first year as a medical student, she began carrying out research with Dr. Charles Evans, the Chair of Microbiology, who was interested in the effect of aging on the bacterial flora of skin. This work led to a publication in the *Journal of Investigative Dermatology* (1950). Given her attraction to research and success with her early projects, it was becoming clear that Elo was headed toward an academic career.

While Elo was a resident at Harborview Hospital in Seattle, in July of 1952, she recognized a man, Richard Czajkowsky, the director of the King County Central Blood Bank when she encountered him talking to a receptionist in an agitated state. Czajkowsky had a degree in biology from the Sorbonne and had been director of blood banks in New Orleans and San Joaquin, California, before coming to Seattle, where he became Director of the King County Central Blood Bank in 1944. He is credited with having organized the Blood Bank in an innovative way, centralizing donations and laboratory work—a model that has been widely emulated by other regional blood banks. She discovered that he had brought a seriously ill employee to the hospital the previous night and was trying to find out what had happened to him. Elo stepped in and straightened out the situation, earning Czajkowsky's gratitude. A year later Elo would realize just how grateful he had been.

After Medical School, an internship, and her residency, Elo began a research fellowship with Clem Finch at the University of Washington. Finch, who was working on erythrokinetics, had an international reputation as a blood researcher. During the first year of her fellowship, Elo co-authored five papers with Finch, including three on which she was first author. One of these publications, which included improved measurements of red-blood-cell lifetime and a clear description of hemolysis became a classic paper in the field (Giblett et al. *Blood* 11:291, 1956).

For the second year of her fellowship, Czajkowsky was considering Elo for a co-directorship. Elo was not even asked if she was interested—Clem Finch, a close friend of

Czajkowsky's, had recommended her and Czajkowsky remembered her from their earlier interaction at Harborview Hospital. The Blood Bank needed someone with laboratory

Elo's careful curation of these samples had an unexpected sequela: one of them was found to contain the first known example of human immunodeficiency virus (HIV) in man... experience to cover the increasingly complex problems of red-cell serology and genetics, especially as they applied to the hemolysis associated with blood-transfusion reactions and hemolytic disease of the newborn. Czajkowsky had already arranged for the candidate to spend six months in Patrick Mollison's Medical Research Council Blood Transfusion Research Unit in London to learn the latest technology. A senior technologist there named Marie Cutbush trained Elo and they became lifelong friends.

Elo returned to Seattle in July 1955 to work at the King County Central Blood Bank as co-director with Czajkowsky. Elo took over the lab and worked on the genetics of red-cell antigens and the newly discovered genetic variations in serum proteins. She realized that any genetic variation in blood—involving red cells, white cells, or serum proteins—could have relevance to transfusion safety and recognized the potential of starch-gel electrophoresis as a tool for studying genetic variation in serum proteins. Elo became expert with this new technique, which had been developed by Oliver Smithies, publishing several papers on the topic including one with Smithies (Giblett, Hickman and Smithies, 1959).

In Seattle, Arno Motulsky had become a close colleague of Elo's, dating to their days in the Finch lab. Motulsky carried out a population study in the Congo in 1960 and sent back hundreds of blood samples that Elo analyzed for polymorphisms; this collaboration led to a publication describing many previously undescribed variants (Population genetic studies in the Congo; Giblett et al., 1966). Thirty years later, Elo's careful curation of these samples had an unexpected sequela: one of them was found to contain the first known example of human immunodeficiency virus (HIV) in man, and the sequence of this virus continues to figure prominently in studies of the genealogy of HIV.

As still another example of a discovery that grew out of her work on genetic variation in serum proteins, she helped characterize the first example of a mosaic individual whose conception involved dispermic fertilization of two egg nuclei followed by cell fusion (Giblett et al., 1963). In 1969, Elo published a reference book entitled *Genetic Markers in Human Blood*, which made information about biochemical variation in blood acces-

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sible to a much wider audience than had previously been the case (Giblett, 1969). In a review in the *American Journal of Human Genetics*, H. E. Sutton described Elo's book as "a remarkable achievement for a single individual."

Known for her meticulous experimental work, as well as her command of the relevant literature, Elo was a natural choice to join the team led by Donnall Thomas that pioneered bone-marrow transplants to cure cancers of the blood. If the donor was the same gender as the recipient, there was no way to tell if a graft had taken. Elo developed markers based on blood antigens and blood-cell enzymes to help distinguish recipient from donor (Thomas et al., 1971; Storb et al., 1974; Hansen et al., 1980).

In 1972, Elo was asked to screen the genetic markers of a child with severe combined immunodeficiency disease (SCID) who was a candidate for bone-marrow transplantation from her mother. One of the markers routinely used for this purpose was adenosine deaminase (ADA) expression, which is known to be polymorphic in most populations. Surprisingly, Elo found no ADA expression in the child's hemolysate and reduced expression in both parents. Within a short time she and her colleagues discovered a second case in which ADA deficiency appeared to underlie immune dysfunction (Giblett et al. 1972); within several years, over 30 patients with SCID and ADA deficiency had been reported. It is now known that approximately 15% of SCID cases are due to ADA deficiency.

This finding was a major breakthrough in our understanding of the basis of immunodeficiency. The discovery prompted her to consider the possibility that deficiencies of other enzymes associated with purine and pyrimidine metabolism might underlie additional forms of immune dysfunction. In 1975, she received a specimen from a child with lymphopenia and chronic infection. The child's blood had normal ADA activity, but there was no detectable purine nucleoside phosphorylase (PNP). This case was reported in 1975 in *Lancet* (Giblett et al. *Lancet i*, 1975), and within several years 10 more cases were reported. Among Elo's diverse contributions to biomedical research, her discovery of the relationship between immune function and pyrimidine and purine metabolism stands out as a high point of her career.

In 1979 the blood bank in Seattle, which had by then been renamed the Puget Sound Blood Center, underwent a major reorganization. Richard Czajkowsky had retired some years earlier and Elo was asked to take over as Director with full administrative responsibility. Although taking on this job would mean the end of her research career, Elo felt she owed this sacrifice to the institution; hence, she became the Blood Center's reluctant

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director in 1979. She spent much of her time during the next six years increasing the supply of blood to meet rapidly increasing demand in the Pacific Northwest. She also tended to the many administrative demands associated with the construction of a new physical facility.

In 1981 a new disease associated with severe lymphopenia and immune deficiency appeared abruptly in the United States. Many of the initially diagnosed cases clustered among homosexual men in large cities on both coasts. Epidemiologists suspected that the disorder was transmissible by blood as well as sexual contact and therefore could compromise the safety of the nation's blood supply. This risk became manifest almost immediately when a number of hemophiliacs, who had received regular blood transfusions, developed the signs and symptoms of AIDS. The Puget Sound Blood Center, along with many other blood banks in the United States, began to discourage donations from homosexuals. Some voices in the local media criticized the Blood Center for this action. At the same time, as evidence accumulated associating blood transfusion with HIV infection, some members of the public gained the impression that they were at risk of becoming infected just by donating blood. Elo expended a great deal of physical and emotional energy attempting to allay these fears. More generally, the stress in dealing with the many policy decisions all major blood banks had to make as they navigated the terrifying early years of the AIDS epidemic took a toll on Elo, a conscientious leader who had always preferred to stay out of the public eye.

Elo retired on her 66th birthday, January 17, 1987. Her lifelong love of music found renewed expression during her retirement as she helped form a new music school and, once again, lifted up her violin to play chamber music with several local groups. For Elo, music and a close circle of family and friends were life-sustaining for the next 22 years.

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