

Profile of Werner and Gertrude Henle

Co-Founders of our Present Knowledge on Infectious Agents in Human Cancers

By Harald zur Hausen

Werner and Gertrude Henle belong to the founders of present tumorvirology. They married in 1937. Both became members of the National Academy of Sciences in 1975 (Werner) and 1979 (Gertrude).

A brief review of their lives elucidates the difficult time periods and personal fates, in particular during the 1930s in Germany and subsequently as immigrants settling in Philadelphia.

Werner was born in 1910 in Dortmund, Germany, as son of a surgeon. His grandfather was a famous anatomist in Göttingen, known among medical students and colleagues up to today as the discoverer of "*Henle's Loop*," a specific structure in kidneys. Werner studied Medicine in Heidelberg and received his M.D. in 1936.

He met Gertrude during his internship at the Kaiser-Wilhelm-Institute in Heidelberg. After finishing his internship he was barred from a professional career in medicine, due to his Jewish ancestry in the Nazi-controlled country. The political climate in Germany at the time offered no perspectives for their work and both left Europe, initially settling for a short period of time in Cuba before moving on to Philadelphia. There Werner became Instructor of Bacteriology in the Department of Microbiology at the University of Pennsylvania School of Medicine in 1939. Subsequently, he was promoted to Professor of Virology and joined the Department of Pediatrics at the Children's Hospital of Philadelphia. He retired from this position in 1982, but continued his research until a few months prior to his death in 1987.

Gertrude was born in Mannheim, Germany, studied medicine in Heidelberg to qualify for her Medical degree in 1936. She became Instructor in Virology in 1937 and subsequently Professor. She retired simultaneously with her husband in 1982.

During their early years in Philadelphia, Werner and Gertrude worked on influenza virus infection and the effectiveness of vaccination against these infections, viral interference and paramyxoviruses. They developed a rapid test for mumps diagnosis and evaluated a vaccine against mumps. They also analyzed the effect of gamma globulins against viral Hepatitis.

Their major contribution to virology was developing immunological tests to discover Epstein-Barr virus (EBV) antigens in lymphoblastoid cell lines from Burkitt's lymphomas, as well as establishing a careful seroepidemiology of Epstein-Barr virus infections. This work was initiated in collaboration with Anthony Epstein (at that time in Bristol, UK), who had discovered Herpesvirus-like particles in electron micrographic sections of cultured cells from Burkitt's lymphoma. The Philadelphia studies identified these particles as a new "Herpesvirus found in virtually all human populations. These studies were also performed in collaboration with George and Eva Klein at the Karolinska Institute in Stockholm. The most successful result from Henle's Philadelphia lab was the identification of EBV as causative agent for infectious mononucleosis and the discovery and development of test systems for its transforming activity for specific lymphocytes. In collaboration with our group we could demonstrate the persistence of EBV DNA in non-virus producing Burkitt's lymphoma cells and later in epithelial tumor cells of nasopharyngeal carcinomas.

I joined the Henle's laboratory at the end of 1968, despite being warned by many of my German colleagues that this was not the best place to go. Viral molecular biology was starting to develop in several other places, although not at this time in the Henle's laboratory. Nevertheless, I never deplored my decision. Despite the fact that both had been German immigrants harboring very bad memories of their last years in Germany, they opened their lab for many German postdocs almost instantly after World War II. Fritz Deinhardt, Volker ter Meulen worked there prior to my coming, Volker Diehl, Rainer Waubke joined there during my stay and several others followed. Indeed, the Henle's became a center to reshape German virology. At the same time they opened their lab for many other nationalities. It has, for me, been a fortunate coincidence to start in the Henle lab almost right from the beginning of their EBV studies. These years can be considered as the start/origin of studies on infectious agents being causative agents of human cancers, previously not seriously considered as human carcinogens.

Werner Henle passed away in 1987, Gertrude followed him 19 years later in 2006.

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