

## Dr. Wolf W. Zuelzer—A Unique Phenotype Presentation of the Howland Award 1985

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It is my great honor and privilege to present the Howland Medal for 1985 to Dr. Wolf Zuelzer. My personal pleasure in this role has been mixed with concern over the enormous challenge of trying to capture, in a brief sketch, a meaningful picture of this man—pediatrician, scientist, teacher, and friend who has excelled as pathologist, hematologist, developmental biologist and administrator, as well as in the fields of literature and music. I thought it appropriate for this audience to approach the task by reviewing the genetic and environmental influences which conditioned his development and his work.

Over the years, Dr. Zuelzer illustrated the pedigrees of hematologic patients with symbols representing the specific characteristics of red cell morphology, such as target cells, spherocytes, or sickle forms, which were found in affected family members. In that tradition, we have depicted the outstanding characteristics in the Zuelzer family of scientists and in the Wolff family of musicians and artists which combined to produce the unique phenotype, the *propositus*, a Wolf Zuelzer (Fig. 1).

Wolf W. Zuelzer was born May 24, 1909 to George L. and Edith Zuelzer of Berlin, Germany. On his paternal side, almost every member of the family for two generations had been physicians, medical scientists, or biologists of some distinction. His grandfather, Wilhelm Zuelzer, had been offered the Directorship of the Reich Health Department by Bismark, but he declined the position, because it would have required that he convert from Judaism to Protestantism. The position was eventually filled by Robert Koch.

Wolf's father, George Zuelzer, 1870–1949, was a prominent physician, and a pioneer in the search for the antidiabetic principle. In 1908 he was the first to bring moribund patients out of diabetic coma using a pancreatic extract which he had prepared.

On his maternal side, music, art, and literary influences predominated. His maternal grandfather, Herman Wolff, was the founder of the Berlin Philharmonic Concerts, a friend and advisor of such musical giants as Brahms and Liszt, and sponsor of such young artists as Bruno Walter. When he died in 1902 his young widow, Louise Wolff, a native Austrian, vastly expanded the scope of her husband's work and contributed in a major way to making Berlin one of the musical capitals of the world. Her home was a cultural center where artists, musicians, actors, and writers mingled with government officials and diplomats. Thus, Wolf, who was very close to his grandmother, grew up in the very center of the Weimar culture of Berlin in the 1920's and 30's and was introduced in his home and that of his grandmother to such luminaries as Richard Strauss, Rachmaninoff, and Fritz Kriesler. His mother, Edith Zuelzer, was an accomplished pianist and had a trained voice. She was a brilliant woman, widely read, widely traveled, and with knowledge of several languages. Not surprisingly in this environment, Wolf studied music and became a competent pianist.

Having been brought up in this stimulating environment, the classical humanistic gymnasium which he attended as an adolescent seemed dull at best. When he graduated at the age of 17 it is not surprising that he embarked on a career in literature and the arts. He enrolled in the University of Heidelberg to study philosophy and romance languages and was later selected for a fellowship in Paris, designed to promote Franco-German cultural and political understanding between the German and French people in the aftermath of World War I. From 1928–1929 he studied at the Sorbonne, traveled widely, became fluent in idiomatic French, and was introduced at gatherings of the leading writers in Paris including André Gide. The year was intoxicating and he had, without realizing it, achieved far more than his sponsors could have hoped for.

He returned home to complete his Ph.D. and began to publish critical essays on contemporary French literature. At the age of 20 he was recognized publically as an authority in the field. Though enormously pleased, he felt he was too young to be taken that seriously and began to rethink his career direction. This was a moment of crisis and a major turning point; although he was within 6 months of his Ph.D. degree, he felt the need for more solid ground under his feet, abandoned his literary career and switched to medicine. He also wanted to please his father who would be happy to see him following in his footsteps. Real enthusiasm for medicine came later, once he had actually entered medical school.

He took his preclinical years at the University of Bonn, and, happily, graduated with honors. In 1932 he transferred to Berlin from whence he had intended to graduate. However, Hitler came to power in 1933 and Wolf, revolted by what was going on in Nazi Germany, left the country permanently in the autumn of that year. He continued his medical studies at the German University of Prague, graduating in 1935. That same year he emigrated to the United States arriving in New York in August, too late to get a regular internship. Finding no position in New York, he decided to try his luck in Boston. There, too, he ran into a stone wall, but through the exceptional kindness of Dr. Paul Emerson, a Pediatric Cardiologist at the Children's Hospital, he was eventually offered a position at Cambridge City Hospital. Subsequently, he obtained an appointment as a House Officer on the Children's Medical Service of the Massachusetts General Hospital.

At this point, he decided to go into academic medicine and aim at a career in research and teaching. Dr. Sidney Farber accepted Wolf as a volunteer in his Department of Pathology at the Boston Children's Hospital; there he spent a year that launched him on this career. It was 1938, and Pediatric Pathology was then a unique subspecialty whose virtually sole practitioner was Farber. Wolf found Farber to be demanding but stimulating and the field very exciting. Thus Zuelzer became the second Pediatric Pathologist in the country, and loved the fact that it was terra incognita with golden opportunities for exploration.

Farber recommended him to Joseph Brenneman of the Children's Hospital in Chicago for a dual residency in pathology and pediatrics and it was Farber who recommended that Jim Wilson

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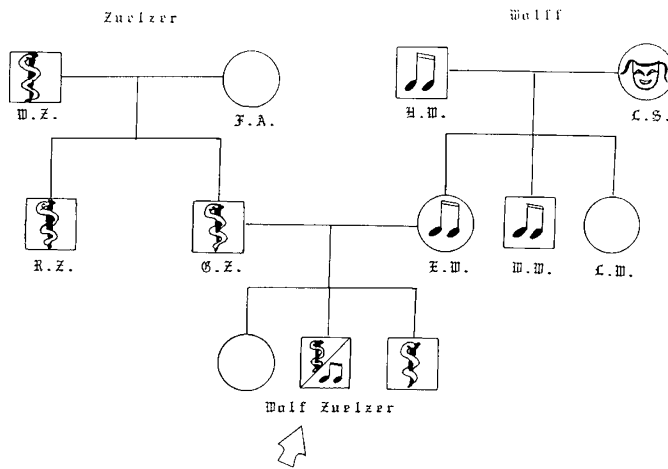


Fig. 1. The family tree of Wolf Zuelzer showing phenotypes.

consider Wolf for the position as the first pediatric pathologist at the Children's Hospital of Michigan. Wolf and Jim Wilson clicked and he got the job, initially that of an autopsy pathologist. He was later entrusted with the hematology service as well as additional clinical responsibilities and ultimately with the direction of the entire laboratory service. He began to build both the hematology and oncology services as well as the anatomic and clinical laboratories. His direct access to both the clinic and laboratory gave him the opportunity to satisfy his zeal for understanding the bases for the diverse pediatric disorders he encountered at the Children's Hospital.

After Jim Wilson left, Wolf temporarily served as interim chairman of the Department of Pediatrics. When Paul Woolley came to Detroit to direct that service in 1946, Wolf returned to the laboratory and built divisions of chemistry, bacteriology, and virology, as well as pathology and hematology. In 1955 he was appointed director of the Child Research Center of Michigan.

Wolf persuaded two people, Abner Robinson, a biochemist and Cyril Stulberg, a virologist and microbiologist, to take a chance on the future of the Child Research Center and to work in the hospital laboratories as well. Research programs began to attract funds and he was able to utilize a team approach toward solving problems in pediatrics, utilizing a whole arsenal of techniques including biochemistry, hematology, immunohematology, histology, cytogenetics, and virology. It was this freedom to work in clinical pediatrics, teaching, and research that was the major attraction to Wolf, and despite tempting offers from other institutions, he stayed with the Child Research Center and the Children's Hospital in Detroit for 35 years. During that time the variety of problems attacked in depth were quite astonishing. Ultimately, his publications totaled more than 250.

It is difficult to reduce Dr. Zuelzer's publications to their essence. His ability to attack and to answer questions brought to his attention by patients in the hematology clinic or at the autopsy table, regardless of the discipline or the subspecialty area, resulted in many classic "firsts" in an extraordinary array of fields. I have selected some of these classic papers to illustrate not only the variety, but the insight and the conceptual "leaps" which they represent.

One of his first major contributions was the delineation of the defect in megaloblastic anemia in infancy, for which Wolf received the first Mead Johnson Award for Pediatric Research in 1949 (1). This observation was the subject of the first Ross conference in 1950; the participants, including William Castle, Dave Cox, Charles May, Allan Butler, and Wolf are shown with others during this conference at the Massachusetts General Hospital (Fig. 2).

His papers often contain the modest phrase, "It seems to have

been overlooked by others that . . .," for example, so-called "functional intestinal obstruction" in infancy had a congenital neurogenic basis. Thus, his not overlooking the pathology of Hirschsprung's disease, led to the first description of the underlying defect in that disorder (2). His not overlooking the occurrence of kernicterus in premature infants without Rh hemolytic disease led to the first description of this phenomenon (3). His not overlooking the fact that a ubiquitous virus might cause widespread visceral disease led to the first description of herpes simplex hepatitis in the newborn (4).

His not overlooking the fact that ABO blood heterospecificity between mother and infant could lead to isoimmunization, led to the first description of ABO hemolytic disease of the newborn, in a series of papers with Gene Kaplan (5). His not overlooking the reciprocal relationship between hemoglobins A2 and F in patients with  $\beta$  chain thalassemias, led to the hypothesis that more than one gene was capable of producing the stigmata of thalassemia, and to his concept of the evolution of the hemoglobin chains (6, 7).

His seminal paper in 1964 on long-term survival of children with acute leukemia was the first clear statement of the curability of childhood leukemia by early combined chemotherapy (8). In the late 1960's many of his papers had a genetic theme; several, including the important work on the significance of the Philadelphia chromosome represent collaborative efforts with Ruby Thompson, now Mrs. Zuelzer (9).

Some of Wolf's hypotheses were considered heretical, and therefore were criticized, or worse, not accepted for publication. One such hypothesis was his prediction of the order and sequence of the genes for the  $\gamma$ ,  $\delta$ , and  $\beta$  globin chains. It was 10 years before development of the laboratory tools to validate this concept. In an address to Pediatric Pathologists, Wolf pointed out that he did not advocate indiscriminate speculation as a substitute for data, but he emphasized that our craving for objectivity can lead to the substitution of data for the essentially creative act of formulating concepts (10).

To those who wish to enjoy the marriage of creative scientific thought with masterful prose, I highly recommend the reading of what he calls his "fun papers." His Presidential address before the Society for Pediatric Research, given more than 30 years ago, is still well remembered to this day. In this address he called upon his intimate knowledge of the history of art to draw an analogy between the influence of the patron on art, and the potential impact of targeted funding on medical research (11). It was his response to the "disease of the month" pattern of research funding, which he felt would stifle free scientific inquiry.

These "fun papers" include a short biographical sketch of Thomas Cooley whose hematology clinic Wolf had inherited (12), and the delightful paper read before the Pediatric Pathology Club entitled "Who Has the Last Word, A Look at Pediatric Pathology" (10). In it he suggested that conventional roles in the CPC be reversed and that the pathologist be deflated by requiring him to reconstruct the clinical signs from the morphologic findings!

His more recent papers, "The Pediatrician and The Species, Some Implications of Our Achievements," as well as "Ethical Dilemmas in Current Obstetric and Newborn Care," reflect his long-standing concern for ethical issues in pediatrics (13, 14).

In his SPR Presidential Address, Wolf also gave a glimpse of his own approach to research, which explains in part the variety of fields in which he made so many major contributions. He wrote: "It would do me no good to try to hide from you the fact that where medical research is concerned, I am an eclectic, or worse, an opportunist. I admit to having yielded to intellectual temptation on more than one occasion, and to have picked such flowers as I have been able to find in more than one garden. My only excuse is that I don't believe in fences."

During the many years at the Children's Hospital he trained more than 200 young scientists; some found the going hard, all found it exciting and were caught up by the intense spirit of



Fig. 2. The First Ross Pediatric Conference, Massachusetts General Hospital, November 16, 1950. Back row (left to right): Arnold Welch, Conrad Elvehjem, William Castle, David Cox. Front row (left to right): Charles May, James R. Wilson, Allan Butler, Wolf Zuelzer.



Fig. 3. Portrait of Wolf W. Zuelzer at the time of retirement from the Children's Hospital of Michigan.

inquiry. The atmosphere, as we peered through the clinic microscope with him at marrows and blood smears, was charged with an air of expectation that something no one had seen before might be seen; that we might begin to formulate a new concept not thought of before.

Figure 3 shows a portrait of Dr. Zuelzer made at the time of his retirement and now placed in honor at the Children's Hospital of Michigan. When Dr. Zuelzer left Detroit, he became Associate Director of the National Heart Lung and Blood Institute and

Director of the Blood Resources Section. While in this position he was able to influence research policy in hematology on a national scale.

Recently, Dr. Zuelzer returned to his once abandoned literary career, publishing a biography of an extraordinary German physician and pacifist, Dr. G. F. Nicolai, whose writings Wolf had discovered during a sabbatical in Zurich. Wolf's book, "*The Nicolai Case—A Biography*," has been awarded the Eugene Kayden National Book Prize of the University of Colorado for the best book in the humanities published by an American University Press.

He has been contributing to a prominent German literary-political magazine, *Merkur*, since 1973, and in 1974 he published his first book in Germany, "*Self Destruction of Democracy*," which examines Watergate in historical perspective.

Wolf has done all this while continuing another aspect of his family tradition—music. He plays the piano, participates in chamber music recitals, and regularly accompanies his daughter, Jacqueline, a violinist and member of the National Symphony Orchestra. Her sister Barbara is also musically talented as was their mother Margery who died in 1966.

It is highly appropriate that you, Dr. Zuelzer, have been selected to be the 1985 recipient of the John Howland Medal. In many ways your career, like Dr. Howland's, has been devoted to investigating clinical problems, working from an hypothesis, using both intellectual analysis and the newest laboratory techniques available. During the period of 1912–1926, Dr. Howland is credited with having modernized pediatrics by working in the laboratory himself, setting a personal example that the special problems in child health can be effectively probed and answered with the proper balance of hypothesis and laboratory analysis. Clearly, you have continued that tradition and we recognize your contributions today with the highest award of The American Pediatric Society, the John Howland Medal for distinguished service to pediatrics.

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