Lucy Balian Rorke-Adams

ANNUAL REVIEWS

Annual Review of Pathology: Mechanisms of Disease

My Journey

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Annu. Rev. Pathol. Mech. Dis. 2023. 18:1–18

The *Annual Review of Pathology: Mechanisms of Disease* is online at pathol.annualreviews.org

https://doi.org/10.1146/annurev-pathmechdis-031621-025854

Keywords

neuropathologist, Philadelphia General Hospital, The Children's Hospital of Philadelphia, vaccine, forensic pathology, autobiography

Abstract

This is the life story of Dr. Lucy B. Rorke-Adams, who was raised in the rural Midwest of the United States by Armenian immigrant parents during the Depression. The youngest in a family of five girls, she was lovingly nurtured by her parents and sisters. She was encouraged to become educated in order to lead a worthwhile life and contribute to society. She chose medicine, specifically the specialty of pediatric neuropathology, and over her long career succeeded in advancing the field. In particular, she made major contributions to understanding childhood brain tumors, central nervous system (CNS) malformations, and pathophysiology of abusive CNS injury in infants and children.

INTRODUCTION

I was the fifth and youngest daughter of my parents and was born in St. Paul, Minnesota. My father, Aram H. Balian, was Armenian but was born in Turkey. He was a descendent of the famous architects and landscape artists, favorites of the Turkish sultans, who commissioned these masters to design palaces and gardens in Istanbul, then Constantinople. His mother died when he was a teenager and his father remarried. His stepmother was the personification of evil, as she was unkind not only to her stepchildren (three boys and a girl) but to her husband as well. My grandfather abandoned the family and went to Constantinople to join his father, leaving my father and the other children in the hands of his ill-chosen wife. My father's sister was rescued by a kind neighbor, and my father left home when he reached 18.

My father was a skilled cabinetmaker and eventually got a job working on the section of the Berlin to Baghdad railroad that traversed Turkey. Construction was supervised by a German engineer who was a widower; his only son had also died. In 1913, this man decided to return to Frankfurt and invited my father to go with him, as he had developed a fatherly interest and wanted to adopt him. After considering this offer, my father chose not to accept it. Upon his refusal, the engineer advised him to leave Turkey, as he had read an article in the *Frankfurter Zeitung* newspaper reporting that the Young Turks, then the political leaders of the country, were developing a plan to exterminate the Armenian minority. Hence, the German suggested that if my father did not go to Germany with him, he should leave the country. My father took his advice and convinced his two brothers and his brother-in-law to emigrate to America.

The fate of my mother (Karzouhy Ousdigian) was quite different. She was born in Trebizond, a town in eastern Turkey on the Black Sea. Her father was a wealthy merchant, and the family lived a comfortable life. She had one brother and three sisters all younger than herself. Mass deportation of women and children began in the spring of 1915. My grandfather was killed and tossed into the Black Sea. My grandmother was separated from her children, and the children were separated from each other. They were told to leave their homes within 24 hours and could only take what they could carry. Two sisters were sheltered by Turkish neighbors, and my uncle became a slave of a Turkish farmer and shepherd. The youngest child disappeared.

My grandmother divided her jewels among the children, and on the appointed day she and my mother were marched off in separate groups. Just before leaving, my mother decided to take scissors, a thimble, and a tape measure with her. She had been educated in a French school and had learned the art of dressmaking. Her march lasted 19 days, and when the surviving deportees reached the last town before their journey was to end in the desert, the group stopped to rest in a marketplace. While there, my mother overheard two Turkish ladies inquiring among the group whether any of the deportees knew how to sew. When my mother identified herself as one who had such a skill, one of the ladies asked for proof. The scissors, thimble, and tape measure came out of her pocket, providing the required proof, and she was rescued from certain death. The daughter of one of the ladies was to be married and required a trousseau.

A short time thereafter, my mother learned that the group with whom my grandmother was marching would be coming to town. The lady who rescued my mother agreed to let my grandmother come to the house. My grandmother had had nothing to eat except grass from the hillsides during her long journey and died of an incarcerated hernia three days after she had been given shelter. My mother subsequently became a servant to other Turkish families until the war ended in 1918. She settled in Constantinople and succeeded in finding her brother and two of her sisters. She supported the family by working in the sewing room of the Near East Relief, a branch of the Red Cross.

My father, in the meantime, had settled in Minneapolis and decided it was time to marry and establish a family. As there were few eligible Armenian girls in the Twin Cities, he wrote to a friend

in Constantinople to determine whether she had any suggestions. In a roundabout way, my mother learned of this young man and agreed to correspond with him. This correspondence eventually led to the arrival of my mother and her siblings at Ellis Island in March 1921, where my father had gone to fetch them. My parents were married in Minneapolis one week later and were together for 54 years before my father's death. They eventually settled in St. Paul and lived comfortably until October 1929, when my father lost his job because of the stock market collapse. Thus, the years of my childhood and youth were difficult for our family. However, even though we did not have much in the way of material goods, our home was filled with love, intellectual stimulation, and music. As the youngest of a family of five girls, I also benefited from the mentoring and love lavished upon me by my sisters.

My parents were devout Christians; hence, we were taken to church at an early age. There were too few Armenians in the Twin Cities for an Armenian church, so we attended the Baptist church located across the street from the hospital in which I was born. We lived in a rural part of St. Paul and had as our playmates three cousins next door and five more next door to them. In those days, before television, we created our own games and pastimes. Reading became a passion, and aside from the school and public libraries, I had access to a marvelous collection of classical literature belonging to a remarkable friend from church, Dorothy Baumgart. She taught English at Central High School where Charles M. Schultz of *Peanuts* fame was one of her pupils. She would occasionally lament that a pupil of hers preferred to draw rather than learn about great literature.

Music was a constant, either through the medium of the radio or the piano in the living room. My parents noted that I had a lovely voice, and I was always made to sing for visiting family and friends. A friend of my oldest sister, Patricia Barker, happened to be a close friend of Gladys Swarthout, a diva of the Metropolitan Opera. When in my teens, Patricia arranged an audition for me with Miss Swarthout, who was considering taking on a protégé. To my extreme distress, the audition was canceled because Miss Swarthout had cardiac decompensation consequent to childhood rheumatic fever. Although I continued to sing in the church choir, high school choir, and university choruses, I decided that my future was not on the operatic stage.

About that time, I read a book, *The Magnificent Obsession* by Lloyd C. Douglas, that changed the course of my life. This was the story of a feckless playboy who inadvertently caused the death of a renowned neurosurgeon. Consequently, he decided to go to medical school and prepare himself for a career in neurosurgery. This work of fiction inspired me to consider a career in medicine.

I had a rocky start in kindergarten where I spent my first week crying because I could not understand anyone. At five years of age, Armenian was my only language. The teacher was a loving person and tolerated this behavior with the help of my oldest sister who was in the eighth grade. They convinced me that I had no option other than to learn English.

From kindergarten through high school, I was blessed with many remarkable teachers. Grade school was a 3-mile walk from home and high school an additional 2 miles. Those years predated the luxury of school buses, so the typical Minnesota winters challenged our stamina. Mother kept us healthy with a daily teaspoon of cod liver oil followed by a wedge of an orange to make the endeavor palatable.

My parents emphasized the importance of learning, and the excellence and enthusiasm of my teachers made school a marvelous place. There were wonderful libraries in both the grade school and the high school, and during summer vacations these libraries remained accessible. Each week we would select an armload of books, which were exchanged for another armload the following week. Reading expanded my knowledge of the world beyond the relative isolation of the rural home environment, shaping my concept of the world and planting the seeds of what my place in it might be.

In addition to the stimulation of school, the other major influence that shaped me was the church. My parents took me to church starting when I was five. Sunday School was a delightful place as I had the opportunity to meet other children, and the teachers, who were for the most part spinsters, lavished maternal affection on the children of others. There were also group activities for teens, typically led by a young couple who may or may not have had children of their own. During those years there were weekly Bible classes, prayer meetings, and choir practice in addition to morning and evening worship on Sundays.

The Second World War was raging during my teenage years, and the radio carried detailed news of terrible events occurring in faraway places. My awareness of the conflicts was part of daily existence and seeded a lifelong interest in both subsequent historical accounts and biographical descriptions of survivors. This profound interest was probably also a consequence of my parents' accounts of what they had experienced in the First World War.

A DECADE AT THE UNIVERSITY OF MINNESOTA, 1947–1957

Undergraduate and Graduate School

I entered the University of Minnesota in the fall of 1947 and departed 10 years later after earning four degrees: a bachelor of arts in psychology in 1951, a master of arts in 1952, a bachelor of science in 1955, and a doctor of medicine in 1957. These were difficult but wonderful years. Difficult because I had to work to pay for tuition and books, but wonderful because of the rich personal and intellectual stimulation. During my undergraduate years, I was girl Friday to a surgical supply salesman.

The first four years allowed me to spread my wings beyond the circle of family and church. These were early postwar years, and enrollment in 1947 had reached 27,000, as a consequence of returning veterans taking advantage of the G.I. Bill. Many lectures were held in auditoria, although others were held in ordinary classrooms and thus were more intimate. The classroom venue made interaction with the faculty easier than in the auditorium setting, and during those four years I developed warm personal relationships with several professors. As a member of the university chorus, I had the great pleasure of participating in an incredible performance of Mendelssohn's *Elijah* conducted by Dimitri Mitropoulos. Shortly thereafter he left to conduct the New York Philharmonic, and Antal Doráti became conductor of the Minneapolis Symphony (now called the Minnesota Orchestra). Under Maestro Doráti, the chorus performed Handel's *Messiah*.

My most life-changing event during my undergraduate years occurred in the summer of 1950, which I spent in Innsbruck, Austria. In 1947, a group of idealistic students at the University of Minnesota and several other colleges in Minnesota had decided that there might be a way to prevent future wars and reasoned that friendship among citizens of different countries would reduce the possibility that they would set out to kill each other. They formed an entity called Student Projects for Amity Among Nations based at the University of Minnesota. Students interested in participating in the program were invited to propose a research question that could only be answered by collecting data in the foreign country of choice. Four countries were selected each summer, each of which had a faculty advisor. For the summer of 1950, there were four choices: England, France, Germany, and Peru. At the urging of a fellow student, I applied to join the group going to Germany. My research question was whether a psychological test, in this case the Minnesota Multiphasic Personality Inventory, developed in one culture could be used reliably in a different culture. A fellow student, Norman Sundberg, had done a German translation of the test, which I revised with the help of a German professor. Scholarship funds were solicited from businessmen in the Twin Cities. I received a scholarship to be a member of the German group.

To carry out this study, I needed to have access to a population of psychiatric patients as well as a "normal" group. Efforts to find a psychiatric hospital in Germany failed, but through my

work with the surgical supply salesman, I established contact with Professor Hubert Urban, chief of psychiatry at the University of Innsbruck. Hence, after spending two weeks with the group in Berlin, I traveled by train through the Russian zone to Innsbruck. It was an adventurous journey. I reached Innsbruck at midnight on a Sunday on the wrong train and found no one to meet me. A kind porter loaded my baggage on his bicycle, took me to Professor Urban's home, and roused the household. The professor was in India, but his wife provided a bed, and I was rescued the next morning by the psychologist the professor had assigned to help me with the study.

For a girl who had never been far from the warmth of the family circle, the challenge to succeed in a totally foreign environment, which required communication in another language, was enormous. The two months spent doing my work and living in a land that was trying to resume some measure of normality five years after the end of the cataclysmic war required personal resources of which I had been hitherto unaware. When I returned home, I was a different person.

As my goal was to become a psychiatrist, I opted to do a master's degree in psychology, followed by an internship in clinical psychology at the Anoka State Hospital. Shortly after I began this internship, it became apparent that two of the four staff psychiatrists were themselves in need of therapy. In fact, one of them had been under treatment by the famous psychoanalyst, Frieda Fromm-Reichmann.

After the internship and receipt of my master's degree, I was an itinerant psychologist for the State of Minnesota for a short time. This involved traveling from place to place testing children whose parents had applied for state assistance in their schooling. My assignments also included testing the intelligence of teenage girls who were giving up their babies for adoption. However, this was a short-lived assignment, as I was asked to assist the psychologist at the State Hospital in Rochester, Minnesota, home of the Mayo Clinic, and served there for a few months before entering medical school in the fall of 1953. Those months at Rochester were a joy. The clinical psychologist who I worked for as an assistant was a marvelous mentor with a warm personality, and the work was engrossing. Many evenings I went to the clinic to sit in on teaching conferences.

Medical School

I entered medical school in September 1953. Quarterly tuition was $50. The freshman class numbered 120 students, 10 of whom were women. One never came because of serious personal problems. A second attended opening lectures but transferred to law school after she confronted the cadaver in the anatomy lab. A third dropped out when her husband, also a freshman, decided he preferred to be an engineer. A fourth developed serious psychiatric problems and dropped out. I do not recall why the fifth one left, but by the end of the first year there were 5 women and 110 men in the class.

The first day was traumatic. We had lectures in the morning and a lecture in gross anatomy after lunch followed by 3 hours of dissection in the lab. Four students were assigned to a cadaver. We named ours the Headless Horseman because his head was missing, having already served to educate dental students. Each of us was given a complete disarticulated skeleton to take home for study. We were told that we would have a test the next day on the hip bone. We were expected to know the anatomical names of all parts of the bone, the muscles attached thereto, and the nerves serving those muscles.

By the end of the first week, I was overwhelmed and decided to drop out. I shared my despair with my anatomy instructor, who had been a classmate in some undergraduate classes. He sternly reminded me that (*a*) the admissions committee must have thought I was capable of meeting the challenges, and (*b*) if I dropped out, it would be difficult for young women in the future to enter medical school, especially considering that three had already dropped out that first week. His final

comment was, "They thought you could do it so stay until they ask you to leave." Well, that never happened, so four years later I graduated.

Those were four incredible years. For the first two, we were drilled in the basic sciences. Physical diagnosis was added in the second year. Classes and labs ran from 8 AM to noon and resumed from 1 to 5 PM. The anatomy professors would use the noon hour to draw on the blackboard, so if you did not go to the amphitheater and munch on your sandwich while simultaneously trying to keep up with the drawings, you were totally lost when the lecture began at 1 PM. At 5 PM I drove to the psychiatric hospital to see consults for psychological testing until 10 PM. I downed a sandwich and a couple of cookies and fruit en route. I was usually home by 11 PM, when I showered, got into pajamas, and studied until 2 AM. The alarm sounded at 6 AM, awakening me for a new day.

During my sophomore year, I added an externship at a small hospital in Minneapolis to my schedule, serving there primarily on weekends. My mother was the only family member with whom I interacted regularly during those years, as she was always up early to provide a hot breakfast and to make sandwiches for my lunch and dinner.

The faculty were all male except for a clinical psychologist who lectured in the fourth year. Each was outstanding and most communicated the material well except for the professor of neuroanatomy, Olaf Larsell, whose talents as a lecturer were sadly lacking. As a consequence of my inability to follow his lectures, I received a grade of D in the midquarter exam. I was devastated, as this was the first such grade that I had ever received. My only recourse was to study more diligently and pray, promising God that if he would help me pass this course, I would never have anything more to do with the subject. Well, God fulfilled his side of the bargain, but I fell woefully short on my part.

The most outstanding professor was Dr. James Dawson of Dawson's inclusion body encephalitis fame (1). He conveyed a sense of enthusiasm and wonder in explaining how tissue changes led to organ malfunction. I had no idea when I was a sophomore medical student that I would become a pathologist rather than a psychiatrist and that Dr. Dawson and I would become close friends some years hence.

The material we were expected to learn during those first two years was exceptionally detailed, and we often grumbled that so many details were unnecessary to become good practitioners. How wrong we were, for later I was amazed by the frequency with which I was able to call up some obscure fact to assist in solving a problem.

The two clinical years involved clerkships, some of which required night duty. It was thus difficult to continue my practice as a clinical psychologist. I approached Dr. Starke Hathaway, head of clinical psychology and coauthor of the Minnesota Multiphasic Personality Inventory, to ask whether there might be a job in the division. It seemed that a businessman in Minneapolis had a schizophrenic son and he had given money for research in this disorder. Dr. Hathaway suggested I give him a proposal for a study and if it were acceptable, I could do the work under the guidance of his associate, Dr. William Schofield. There would be no rigid schedule to do the study, so I could fit it in when not otherwise occupied by classes or clerkship duties.

There was a theory at that time that mental illness was a consequence of childhood trauma. Since detailed histories of such events were only taken from patients, I posited that those without psychiatric problems also had similar experiences, but the medical community was unaware of them, as detailed histories of "normal people" were not taken. My basic postulate was that severe mental illnesses, i.e., the psychoses, were not the result of psychic trauma. Even though I was a neophyte in the field, I suspected that this group of disorders might have an organic or genetic basis. Thus, for the last two years of medical school, I investigated this question and published the findings with Dr. Schofield (2).

Sometime during my senior year, Dr. Hathaway suggested that I forego a clinical internship and join the staff in the Division of Clinical Psychology, with a focus on research. At that time, I had begun to rethink my goal of becoming a psychiatrist, as my close contact with the psychiatrists at Anoka Sate Hospital soured my opinion of the field. This was reinforced during my clerkship on the psychiatry rotation. Although the students in my clerkship group (all men) were congenial and we got along well, the behaviors of one resident and one faculty member were such that I told myself that if these behaviors were characteristic of others in the field, I did not want them as colleagues. I shared my misgivings with Dr. Hathaway and, although greatly flattered, refused his offer.

Match Day found me telling myself that the slip of paper inside the small white envelope held the key to my destiny, a somewhat melodramatic thought, but nevertheless true. I matched to Philadelphia General Hospital (PGH), the oldest hospital in the country; it had 1,800 beds. They selected 108 interns to serve the needs of the indigent citizens of Philadelphia. I was one of 10 women in this group. I was thrilled, but my mother did not share my enthusiasm. Her last words to me as I boarded the train that would carry me eastward were, "Don't stay any longer than a year."

POSTGRADUATE YEARS, 1957–1962

Internship

My internship year was the most remarkable year of my life. We were provided room and board, uniforms, and a salary of $57 a month. This odd figure was selected by the city fathers, as it was $1 more than the monthly income limit above which a citizen was no longer eligible for welfare. There was some embarrassment when a few interns had applied for relief when their monthly salary was $25.

We were instructed to appear on June 28. At the end of the orientation, the assignments were distributed. Although I was delighted to see that my first rotation was neurosurgery, I was equally horrified to note that duty began at 2 PM and I was on call that night. Each time the phone rang, I was overwhelmed to realize that someone was sick and needed a doctor and that I was that doctor.

Things got off to a rocky start and continued that way for many rotations. The resident on neurosurgery was a genial young man. Two days after the internship began, he had surgery for acute appendicitis and did not return for the remainder of the month. That left me with no supervision, as the staff neurosurgeon responsible for the service had a busy practice outside the hospital and only appeared for rounds between 7 and 9 PM.

The second month I was assigned to the psychiatry ward. After reviewing the patient charts, the resident informed me that she was leaving for a month-long vacation. If I had not had training and experience in clinical psychology, this would have been a disaster for both myself and the patients.

The next rotation was pediatrics. That month there was a severe flu epidemic. One of the eight interns assigned to the service contracted flu complicated by staph pneumonia and died. The patient load for the seven remaining healthy interns was enormous.

The next assignment was divided into two two-week periods. First came laboratory service, during which the intern was the night lab technician for the entire hospital. The second two weeks were an assignment to the anesthesia service. There was no sleep to be had on that service either, as we spent nights in the operating room dealing with a regular stream of emergencies.

The month on the obstetrics ward was a nightmare. One of the eight interns in that rotation developed staph abscesses on his neck and hence was barred from patient contact. The typical schedule consisted of 12 hours on and 12 hours off. Because we were short one intern, this changed to 18 hours on and 6 hours off for the entire month. During that month, we delivered 500 babies and I never stepped out of the hospital.

During the month on surgery duty and the tuberculosis (TB) ward there was a different problem. My fellow intern on surgery duty began to manifest erratic behavior as a consequence of a frontal lobe tumor diagnosed a few months later. He was unable to carry out his duties, so I basically had a double load, including taking all his night calls.

Three interns were usually assigned to the TB service. One of the three had become psychotic and had dropped out. The service was doable with two interns, but unfortunately my partner was almost never available when he was on night call.

Despite all these extra challenges, or perhaps because of them, I learned a great deal about clinical disease and how to treat patients who came under my care. A decision about residency had to be made during the internship year, and I was thinking about my future path. Even though I considered going into neurosurgery, I realized that I did not function optimally without sleep and realized that the life of a surgeon is basically sleep deprived. I had been stimulated by Dr. Dawson's pathology lectures, and I reasoned that because pathology was basic to all clinical fields, I would apply for a residency position at the hospital and leave the decision about surgery for a later time.

Residency and Fellowship

The chairman of pathology was Dr. William Ehrich. He was a native of Germany and had been the prize pupil of Ludwig Aschoff. Aschoff's mentor had been Friedrich von Recklinghausen, who had been a student of Rudolf Virchow. A distinguished scientific lineage indeed! Dr. Ehrich was being groomed to succeed Aschoff, but this plan was derailed for two reasons: (*a*) Dr. Ehrich decided to get married but failed to ask Aschoff's permission, and (*b*) his bride was Jewish. The climate for Jews in Germany in the 1930s was not salubrious, so Dr. Ehrich chose to leave for a position at the Rockefeller Institute in New York City. From there he was recruited to the University of Pennsylvania and PGH.

Dr. Ehrich was a superb mentor and had daily contact with the residents. The most important and unforgettable lesson was ingrained at the outset. Pathologists, Dr. Ehrich said, are consultants to clinicians and, in order to interpret findings in tissues and organs, the pathologist must have a firm knowledge base of clinical medicine. Clinical-pathological correlation was paramount. I would note here that I learned this lesson early and followed it throughout my career. It was priceless advice that I passed on to my students.

On the first day of residency Dr. Ehrich came into the room where the residents awaited him, looked around, walked over to me, and said, "You're the only girl here, pediatrics is the province of ladies, so you have to do all the pediatric autopsies." Of course, I did not realize it at the time, but it was the most wonderful gift he could have given me. Pathological aspects of children's diseases had not received much attention up to that time. However, two pioneers in the field were at St. Christopher's Hospital for Children (also in Philadelphia). I was told that I could take any problem cases to them. Because of the emphasis on clinical-pathological correlation, I went to the pediatric conferences and not only broadened my knowledge of clinical pediatrics but developed warm collegial relationships.

During the three-year residency in anatomical pathology (AP), I saw an extraordinary range of diseases. There were roughly 1,500 autopsies yearly, and the program was organized such that when the autopsy was completed the organs were laid out on the table. A signal was sent to the office to alert the staff and residents to come to the morgue. The clinician would have been informed that his or her patient was being autopsied, so they congregated along with the pathologist. The clinical history was reviewed and then the resident would describe the changes in the organs. Following this, Dr. Ehrich or one of the other staff pathologists would discuss the case. That procedure allowed the trainee to learn from all the available material.

Over the three years of my AP residency, I did approximately 200 autopsies each year, half of which were pediatric cases. A considerable number were prematurely born infants, most of whom had died of what in those days was called hyaline membrane disease but later renamed respiratory distress syndrome. It quickly became clear that there were abnormalities in other organs, especially the central nervous system (CNS). I always examined the CNS; that is, it was not sent to the neuropathologist, Dr. Helena Riggs.

This exam was a challenge, as the brain of premature newborns, especially those weighing between 500 and 1,500 g, was soft and gelatinous, often disintegrating in the process of removal. To deal with this problem, I decided to inject 1–2 cc of formalin into the subdural space on either side of the anterior fontanelle and 1 cc into the cisterna magnum when the body arrived in the morgue. I waited for 24 hours before doing the autopsy. By that time, the outer rind of the cerebral hemispheres had fixed so that the specimen was easier to handle.

Aside from the premature newborns, there were also several babies with malformations of all sorts, most commonly involving the cardiovascular system or the CNS. Those involving the CNS were especially frustrating. While there were a few well-known types of malformations, such as Arnold-Chiari with meningomyelocele, the majority were complex defects about which there was little in the literature. Even after consultation with Dr. Riggs, there was nothing to be done beyond a careful dissection and photographs of the specimen to accompany the written description. The field of genetics was still in its infancy.

In view of the fact that many babies had disturbances of pulmonary function, I began to identify CNS lesions stemming from hypoxia. As my experience grew, it became apparent that there were lesions in the brain that were unique to prematurity and related to factors operative during development that were rare in the mature newborn or were basically never seen later in infancy or maturity. A few years later, when I began my association with the Children's Hospital of Philadelphia (CHOP), my experience with neuropathological findings in newborns and infants expanded dramatically. I summarized these findings in a monograph (3).

The hospital had a busy surgical service that provided abundant material for study. We were closely supervised by the three staff pathologists, including Dr. Ehrich, and signed out the microscopic findings of both surgical and autopsy cases with one of them. We were expected to have studied the slides ahead of time and to have done some reading about the case so we could have a meaningful discussion with our mentor. Aside from the current material, there were slide sets available for study. We focused on these in the evenings, when two or more of us would go to the lab, look at the slides, and discuss what we were seeing.

Sometime during the residency, I learned that Dr. Ehrich had slides of Einstein's brain. He never discussed them with us, but the story behind them is fascinating. The pathologist who did Einstein's autopsy, Dr. Thomas Harvey, had trained at PGH and knew that Dr. Ehrich had a histology lab at the University of Pennsylvania and a highly skilled technician, Mrs. Marta Keller. Mrs. Keller was expert in the use of the sliding microtome and celloidin embedding technique. This technique, no longer in general use, allowed preparation of larger pieces of tissue than the small fragments typically placed on 1- by 3-inch slides. Dr. Harvey removed Einstein's brain without permission, as he had decided that examination of it was important scientifically although he was not a neuropathologist. At any rate, he brought it to Dr. Ehrich from Princeton, New Jersey. Mrs. Keller made five sets of slides, each consisting of two serial sections of multiple brain regions, one stained with cresyl violet and the second by the Weigert technique.

Dr. Harvey gave one set to the neuroanatomist at Women's Medical College (no longer in existence); a second to Dr. Harry Zimmerman, a neuropathologist at Yale University; the third to Dr. Percival Bailey, a neurosurgeon in Chicago; and the fourth to a neuroanatomist in California whose name I do not know. The fifth box was a gift to Dr. Ehrich. This box contained 46 slides,

most of which were 2 by 3 inches and had been sampled from many areas, although none were from the cerebellum. When Dr. Ehrich died, his widow gave these slides to Dr. Allen Steinberg. He had been an intern and resident with me and was an assistant to Dr. Ehrich. After Mrs. Enrich died a few years later, Dr. Steinberg gave them to me.

Einstein died at age 76 of a ruptured aortic aneurysm, but his brain was that of a young person. There was no significant vascular disease or gliosis and minimal intracellular lipofuscin. In 2012, I gave the slides to the College of Physicians of Philadelphia, which houses the famous Mütter Museum. The slides were beautifully preserved thanks to Mrs. Keller's skill and her use of celloidin rather than paraffin. Einstein had specified that he wished to be cremated and that his ashes were to be thrown into the Delaware River, as he did not want his grave to be a pilgrimage site. His family did fulfill his instructions, but years after his death the slides of his illegally removed brain became a focus of intense interest for countless visitors.

I met Robert (Bob) Rorke, a businessman, under a sprig of mistletoe on Christmas Eve of 1959, and we married six months later at the end of my second year of residency. He was a widower with two children, a son aged 10, and a daughter aged 17. As these children were in school, I was free to continue with my career. I had the strong support of my husband, and it was he who suggested that I pursue my interest in the brain and specialize in neuropathology. The neuropathologist at PGH, Dr. Riggs, was a remarkable woman. She had graduated from the University of Pennsylvania Medical School in 1925 and specialized in neurology. Her plan to marry a neurological colleague was crushed when he died of a brain tumor. About that time, Dr. Robert Winkleman, also a neurologist, invited her to join him at PGH where he was trying to establish a neuropathology laboratory. It was the custom at that time for neurologists and neurosurgeons to do their own pathology, as most pathologists found the complexities of neuroanatomy too challenging.

Dr. Riggs was a pioneer in the field and as a neurologist approached neuropathology with a firm knowledge of clinical neurology. Following three years as an AP resident, I received a National Institutes of Health (NIH) fellowship for one year to study with Dr. Riggs. The neuropathology fellowship was even more fantastic (if possible) than the three years of AP residency. That year Dr. Riggs had three students. Two of us were NIH fellows and the third was a neurosurgeon. The other fellow, Dr. Joan Short, was a pediatric neurologist. The neurosurgeon, Dr. Frederick Pitts, had completed his residency and decided to study neuropathology before entering practice. The three of us had a wonderful year together, as we had a common goal and enthusiastically studied neuroanatomy by doing dissections of the pyramidal system, the rhinencephalon, and the vasculature of the brain.

During this year I focused on the pathology of the infant nervous system and was perpetually frustrated to find little literature to help me. Most glaring was a lack of information on myelination. It rapidly became obvious that without knowledge of normal development we could not recognize deviations from what was expected at a given age. By that time, I had already been invited to join the staff following completion of the fellowship. Hence, Dr. Riggs and I decided to apply for an NIH grant to study the issue. Some years later, a member of the review committee told me that they decided to give us the grant because "it was something that had to be done and they are requesting only a modest sum of money." We studied myelination in newborns weighing 500 g and higher, dividing them into groups from 500 to 999 g, the stage of viability, through to term.

MY CAREER FROM 1962 TO 2015

Philadelphia General Hospital

As noted above, I joined the staff at PGH following completion of training as chief of pediatric pathology and assistant neuropathologist. As such, I supervised the training of AP residents doing the pediatric cases and assisted in evaluation of the surgical and autopsy specimens of the CNS,

nerves, and muscles. There was a large case load of approximately 100 pediatric cases and 1,000 neurological specimens each year. Although we dealt with specimens from individuals of all ages, I focused my attention on infants and children. As noted above, I was dismayed at finding only scant information in the English literature on brain development and disorders of the newborn in particular. The German literature was somewhat richer, and my knowledge of that language was helpful in filling the gap.

Pediatric neuropathology is especially challenging, as knowledge of the developing brain is basic to understanding the pathology. To do pediatric neuropathology well, the pathologist must have considerable knowledge of obstetrics, including placental pathology, as well as developmental neuroanatomy and physiology, as these are constantly changing. We received the grant to study myelination in 1963 and reported our findings in a monograph published in 1969 (4).

I was privileged to study and work with Dr. Riggs from 1961 until she died in 1968. She was a phenomenal mentor who refined my knowledge of neurology and reinforced the necessity of combining both clinical and pathological features of a case in arriving at a diagnosis. In addition, she honed my writing skills and urged me to actively participate in discussion of presentations at the meetings of the American Association of Neuropathologists (AANP).

Dr. Ehrich died in 1967, and about a year and a half later I was named chairman of the Department of Pathology. Unfortunately, there are no courses in medical school that provide instruction in administration, so I had to learn by doing. Unbeknownst to me at the time, this was only the beginning of future assignments as an administrator. In 1973, I became the first woman president of the medical staff in the 241-year history of the hospital. During my tenure as staff president, the medical director died, and for a 10-month period I found my job becoming a 24-7 responsibility.

The mayor of Philadelphia closed the hospital in 1977, which marked the end of a remarkable period in American medicine. The hospital originated as an almshouse in 1731, but as many of the poor were also sick, it was rapidly transformed into a hospital by the next year. The history is fascinating and has been well documented (5). Many of the greats of Philadelphia and American medicine served as staff or learned the practice and art of medicine there. Included among them are David Hayes Agnew, Samuel Gross, S. Weir Mitchell, Benjamin Rush, and, perhaps most famous of all, William Osler.

Osler was a native of Canada but was on the faculty of the University of Pennsylvania for five years. As the university was located next to PGH, Osler took advantage of the patient population for the purposes of teaching. He was also passionately interested in pathology and did postmortem exams in a small building on the PGH campus called the Dead House. As I was chairman of pathology at the time the hospital was closed, I arranged to have the contents of the building transferred to the Mütter Museum at the College of Physicians of Philadelphia. These included the autopsy table, dissecting instruments, and handwritten postmortem reports.

Although it is inappropriate here to expand on the importance of the loss of this great hospital, one little-known piece of history was of special interest to me. Marie Curie brought radium to Philadelphia for the first use in treatment of patients in this country who had malignancies. It was placed in a room in the Pathology Building, called the Radium Emanation Room. In honor of the occasion, the street fronting the hospital campus was named Curie Avenue. It carried that name when I arrived in Philadelphia in 1957, but some years later the city fathers decided to call it Civic Center Boulevard, as the Civic Center was located across the street.

The Children's Hospital of Philadelphia, 1965–2015

While still busy at PGH, I was invited in 1965 to serve as neuropathologist at CHOP. Dr. Charles Kennedy, chairman of neurology, wished to strengthen the training program and was convinced that instruction in neuropathology was important. At first, I retained all my duties at PGH and

spent 2 hours daily plus Saturdays at CHOP. After PGH closed in 1977, I worked full-time at CHOP.

My 50 years there were fantastic! I had freedom to do my work and superb secretarial and technical support as well as a remarkable group of colleagues with whom to interact. At both hospitals, I was confronted daily with diagnosing a wide variety of disorders, some familiar but many unique and challenging. In consequence, I expanded my knowledge and was stimulated to develop new ways of approaching diagnostic problems. As there were few pediatric neuropathologists, I was often asked to assist colleagues with their research work. Even though I was unfamiliar with the issue in question, I seized the opportunity to expand my horizon.

My modus operandi throughout my life was to think carefully about the world around me and to seek answers to questions when confronted with something puzzling. From time to time, a unique problem would arise. In 1965, there was a rubella epidemic in the eastern United States, and I began to see infants whose mothers had had rubella in the first trimester of pregnancy. The existing literature documented occurrences of cataracts, deafness, congenital heart disease, and mental retardation in survivors. The morphological basis of the mental retardation was not known. My study of the brains of the infants disclosed two major abnormalities: a striking unusual vasculopathy with associated ischemic lesions and retardation in myelination.

The manuscript reporting these findings was submitted to a leading pediatric journal but was rejected because the referee noted that "no one else has ever reported such findings, hence Dr. Rorke must be mistaken." If all new observations were rejected on such grounds, we would never have pulled ourselves out of the Dark Ages. The paper was published elsewhere, and I learned to trust my own observations and proceed in the face of criticism (6). I put this lesson to use some years later when I challenged prevailing teaching relative to the nature and biology of medulloblastomas.

Roughly 20% of pediatric tumors fall into the category of medulloblastoma. This tumor is composed primarily of primitive neural cells and occurs most commonly in the cerebellum. It was thought to arise from external granular cells, a cell unique to the cerebellum. However, tumors with similar histological features arise in other regions of the CNS. In such cases, a different diagnostic label was attached depending on the location. For example, if in the cerebrum it was called a cerebral neuroblastoma, and if in the pineal it was called a pineoblastoma. If in the brain stem or spinal cord, a number of other names were created.

This practice troubled me, as other CNS tumors were not diagnosed on the basis of location. I decided to use the forum of my presidential address to the AANP in 1982 to discuss the dilemma (7). My aim was to encourage colleagues to probe the biology of this group of tumors, all of which were composed of primitive neuroepithelial cells, regardless of their origin in the CNS. Reception was mixed. Dr. Lucien Rubinstein, who at the time was a leading authority on brain tumors, was not pleased. At the same time, others were stimulated to look at the problem with fresh eyes. Although this probably would have happened eventually, it stimulated investigators to probe the issue in the laboratory. Over the ensuing four decades, there has been significant progress regarding embryonal tumors.

I had the good fortune to be surrounded by a remarkable group of colleagues, and we shared a common goal, namely, to expand our knowledge of CNS diseases of infants and children in the hope that these diseases could eventually be prevented or cured. For example, early in my tenure, I began to find brain stem infarctions, especially in low-birth-weight infants who had been ventilated because of pulmonary problems. These infants were placed on a neck roll in a position of hyperextension of the neck. In discussing my observations with Dr. George Peckham, chief of the Neonatal Intensive Care Unit, I suggested that the lesions were iatrogenic. Specifically, I told him that because of immaturity of the ligaments that provide stability for the upper cervical vertebrae,

this position of hyperextension was compromising the flow of blood in the vertebral arteries by allowing subluxation of the bones through which they traversed. Following our discussion, I no longer saw these lesions.

We had a remarkable team of specialists who focused on children with tumors. We generally met for a light supper once a month to discuss the patients who were undergoing treatment; following the meal, one member of the group would report on current research. The enthusiasm, collegiality, and exchange of ideas were priceless. Many CNS tumors in infants and children are different from those that occur in adults, and one must be alert to recognize unusual types. As we saw many children with medulloblastomas and other embryonal tumors, we had in-depth knowledge of their clinical and pathological features. Advances in the field of genetics made it possible to investigate their genetic footprints as well; hence Dr. Jaclyn Biegel, the geneticist, was an especially valuable member of our team.

As I was a slide reviewer of all tumors in children diagnosed with medulloblastoma who were treated under protocols of the Children's Cancer Study Group, I had access to a large number of pathological specimens. Whereas the hospital pathologist who made the diagnosis initially was correct in most cases, there were a small number that displayed unusual features. The accompanying report tended to be longer than usual and the pathologist expressed some uncertainty. I began seeing similar cases at CHOP and in consultation cases from elsewhere and was intrigued. These tumors had fields of embryonic neuronal cells but often contained other cell types that were squamous, mesenchymal, or epithelial in nature. Most prominent, however, were fields of rhabdoid cells. The latter were unfamiliar to me but were identified by my colleague, Dr. Jane Chatten. Such cells were characteristic of infantile renal rhabdoid tumors. All these features suggested the possibility of a teratoma, but immunoperoxidase preparations for germ cell tumors showed no expression of these antigens.

Consultation with Dr. Roger Packer and Dr. Biegel yielded a distinct clinical and genetic profile. Children with these tumors were primarily less than two years of age, and the primary genetic signature involved chromosome 22 rather than chromosome 17, which is most typically found in medulloblastomas. Moreover, they were highly malignant, as the babies usually died within a year of diagnosis.

I named them atypical teratoid/rhabdoid tumor, and prior to definitive publication of our findings I presented our data at a symposium on brain tumors at an International Congress of Neuropathology. This presentation was greeted with considerable disdain by a distinguished neuropathologist who made uncomplimentary comments about our work. However, he returned to his institution and reviewed cases in his files and a year or so after our manuscript was published came out with a me-too paper (8).

My years at CHOP involved more than doing neuropathology. After several requests to become the first female president of the medical staff, I finally agreed, as I had been assured repeatedly that this was primarily a social position that would not interfere with my professional duties. Alas, these were false promises. A few days after I became president, the hospital board fired the CEO, and the COO and I were given the responsibility of running the hospital until a new CEO arrived 18 months later. Unfortunately, administrative responsibilities did not terminate with his arrival. About 10 years later, I was asked to take on the duty of chairman of the Pathology Department for six months. Five and a half years later, I was relieved of that responsibility.

Forensic Pathology

In 1972, the Department of Pathology at PGH and the Office of the Medical Examiner of Philadelphia moved into a new building on the PGH campus. Before that time, I had been

consulted by the forensic pathologists on their cases involving CNS issues. When we occupied the same building, interaction became more frequent and I began to develop more in-depth knowledge of this specialty. While there were diagnostic problems of many kinds, I was drawn to dealing with the infants and children. Inevitably I became involved with those in whom there was a question of abuse, as 60–70% of abused children die because of CNS injury. A major proportion of these infant deaths fell into the category of shaken baby syndrome. Investigations at that time focused on brain damage consequent to the shaking, and although a characteristic pattern of brain injury is a component of shaking, I posited that spinal cord damage also occurred when the infant was shaken.

There was only spotty information regarding this issue, most likely because the spinal cord was not examined, or if it was the lesion was probably destroyed because of the dissection technique. When both brain and spinal cord are removed, they are typically separated at the high cervical level. Following a change in technique wherein the brain and cord were removed in continuity, we found a high frequency of injury to the cord and roots (9, 10).

Involvement in the forensics of child abuse led me into the courtroom. This is a unique world. Because our court system is basically adversarial, the defense is required to find experts to challenge objective evidence gathered by the forensic pathologist. In consequence, there has developed a group of experts who testify under oath that subdural hematomas, for example, are not a consequence of trauma but result from hypoxia or a host of other nontraumatic conditions that are put forward, e.g., vaccinations, infections, coagulopathies, genetic disorders, etc. The challenge for the forensic pathologist in the courtroom is to explain to the lay jury, in terms they can understand, what actually happened. The forensic pathologist has an awesome responsibility. Evaluation of each case must be meticulous, and all possibilities outside of trauma must be excluded. To accuse an innocent person of crime is reprehensible.

This work was very discouraging, as even highly educated judges sometimes could not grasp the science. This was especially obvious when I appeared before three bewigged lord chief justices of the High Court of Justice of England and Wales in London in 2005. The court was hearing an appeal of approximately 80 individuals who had been convicted of child abuse on the basis of a publication by a neuropathologist whose testimony had led to their conviction, but who had subsequently done a study purporting to show that subdural hematomas and retinal hemorrhages were caused by hypoxia not trauma (11).

A guilty verdict for the defendant is a hollow victory in my estimation. In these situations, there are no winners: the baby is dead, the family is broken, and the perpetrator's life is changed forever.

The Wistar Institute

The Wistar Institute is the oldest biomedical research institute in the United States. Whereas it was established in 1892 to house anatomical specimens to further study comparative anatomy and experimental biology, the focus later shifted to cancer research and viral diseases.

In the late sixties and early seventies, pediatric neurologists were challenged to diagnose and treat an alarming number of children with a mysterious, devastating, lethal disease. Because one of the prominent pathological features consisted of intranuclear inclusion bodies, it was postulated that it might be caused by a virus. Dr. Michael Katz, a pediatrician-virologist who was working at the Wistar, asked me to share some of the biopsy tissue so he could inoculate ferrets in the hope of transmitting the disease and thereby determining whether it was, in fact, caused by a virus. Several months following inoculation of brain suspension into the ferrets, a behavioral change from aggressivity to docility was noted. Pathological features of the brains of these animals disclosed inflammation and, at the ultrastructural level, myxovirus nucleocapsids characteristic of measles.

The disorder had been described by my pathology professor, James Dawson, in the 1930s (1). It was eventually named subacute sclerosing panencephalitis and fortunately has largely disappeared consequent to widespread vaccination preventing measles infection.

Following success with the ferret studies, we turned our attention to multiple sclerosis (MS), as it was postulated at the time that this disease was also caused by a virus. This work was done in cooperation with a different group of investigators led by Dr. Donald Gilden. Design of the study involved removal of the brain of the MS patient within a few hours of death, selection of tissue in and around plaques, preparation of cell suspensions, and inoculation of the suspension into the brains of infant chimpanzees housed in a primate colony in San Antonio, Texas.

To accomplish this, I was on permanent call, as timing in obtaining the brain of the patient was crucial. Once the animals were inoculated, we had only to wait for a year or two to note whether the chimp became ill. If it did, we flew to San Antonio to deal with the situation. Typically, we assessed the status of the animal, and if it was ill a postmortem was done, following which we returned to Philadelphia on the next available flight. While we found some interesting abnormalities in the chimps, we were unsuccessful in producing MS and the research was terminated 20 years later.

Vaccines

During the AP residency, Dr. Ehrich asked us to assist in the evaluation of animal tissues, primarily of rats and dogs, that were utilized by Wyeth Laboratories in their toxicological studies of drugs under development. Dr. Ehrich was a consultant pathologist for Wyeth and was responsible for this aspect of drug development.

When I became a neuropathologist, I was invited to undertake the responsibility for the neurovirulence studies required in establishing safety of the Sabin polio vaccine. The protocol established by the Division of Biologic Standards required injection of a sample of each vaccine lot into the thalamus and spinal cord of 18 monkeys. The animals were monitored for 21 days and then killed. My assignment was to examine the brain and spinal cord for evidence of excessive inflammation or contamination with B virus. The B virus is a subclinical infection of monkeys, but it is lethal for humans. After some years, both Wyeth and Lederle Labs, the other American manufacturer, threatened to stop producing the vaccine because of increasing litigation problems. Along the way, I also cooperated with my colleague, Dr. Stanley Plotkin, in the development of rubella vaccine. Dr. Plotkin was working with SmithKline and a pharmaceutical house in France, the Institut Mérieux. Because of increasing allegations of serious side effects of vaccines, the pharmaceutical companies threatened to discontinue production. The public health consequences of such action led the government to assume liability for alleged injury from all vaccines. I was asked to evaluate those cases involving children whose parents alleged that one or more vaccines had produced a CNS problem in their child. Over the years that I reviewed these cases, I identified many fascinating diseases, none of which could be ascribed to the vaccines in question (12).

Academic Life

My career at PGH and CHOP included appointment at the University of Pennsylvania. Initially, I was appointed as an assistant instructor in the Pathology Department and some years later became a clinical professor of pathology, neurology, and pediatrics. My most important duties were instructing residents and fellows in pathology, neurology, and neurosurgery as well as lecturing to medical students. I enthusiastically embraced the responsibility and derived considerable satisfaction from it. I soon realized that teaching is gifting the student with part of one's self, and when this gift is accepted and used, joy at the subsequent success of the student is great.

In this academic milieu I was blessed with many remarkable colleagues. As pediatric neuropathologists were in short supply, I was often asked to assist in research projects, the subject of which were often unfamiliar. I always agreed to help and enjoyed the challenge of exploring the unknown. As a consequence, my career flourished.

At the same time, I pursued investigation of issues that continued to puzzle me. Chief among these, aside from the fascinating realm of brain tumors, was the issue of CNS malformations. As time progressed, I saw fewer complex malformations as advances in obstetrics led to their identification in utero and termination of the pregnancy. However, malformations falling into the category of migration disorders remained a challenge, especially since they varied widely and many were not lethal. In fact, a large number occurred in children who had poorly controlled seizure disorders, which were treated by surgical excision. The migration disorders were so-named by Max Bielschowsky in 1915 (13). He postulated that the malformation occurred early in development and resulted from the inability of the postmitotic neuroblast to find a permanent home on its way from the internal limiting membrane of the neural tube to what would eventually become the cortex. This would account for cortical dysplasias and heterotopias. However, examination of surgical specimens and brains postmortem showed additional abnormalities including too many or too few neurons, neurons that were too large or too small for the cortical layer in which they resided, and disorganized laminae or neurons with bizarre morphology.

As I pondered these issues, I turned to the growing body of literature in developmental anatomy, especially the studies of John Sulston and Sydney Brenner. Sulston studied the worm *Caenorhabditis elegans* and Brenner focused on *Drosophila*. As the field broadened and others provided increasing information, I realized that developmental abnormalities produced by mutant genes in these lower forms paralleled what I was seeing in humans. Thus, in 1994, I published a hypothesis paper in which I reviewed the subject and postulated that this was indeed the case (14). It has been gratifying to follow the subsequent literature validating that hypothesis.

Personal

Although my professional responsibilities were demanding, I found time to enjoy other things. Music and reading were paramount. As a child I was imprinted with music, and aside from singing I played both piano and violin. Although my early ambition to become an opera singer came to naught, I never lost my enthusiasm for opera, and for many years my husband Bob and I were regulars at the Saturday matinees at the Metropolitan Opera House. Bob had a wonderful sense of humor and taught me to laugh. He gave me a long leash to pursue my career and helped me in many ways. We were married for almost 42 years before he died quietly in his sleep on Easter morning in 2002.

Two years later I married Boyce Adams, a longtime friend; his wife had died seven months after Bob's death. Sadly, he did not survive aggressive prostatic cancer and died two years later. He was a financial wizard and inventor.

After seven years of widowhood, I married a third time. My husband, C. Harry Knowles, had been a close friend of Boyce. Harry was a genius and had more than 400 patents. He formed a company called Metrologic whose primary product was the handheld laser barcode reader. He sold the company and established a foundation dedicated to assisting young high school science teachers in improving their teaching skills in mathematics, chemistry, physics, and biology called the Knowles Teachers Initiative, which has been successful in fulfilling that goal. We shared a deep love of music and following my retirement reveled in the opera and concert offerings in New York and Philadelphia. This marriage too, was short-lived. His death in 2020 was consequent to complications of radiation therapy for carcinoma of the prostate.

THE SUMMING UP

There is a famous poem entitled "How Do You Live Your Dash" by an Irish poetess, Linda Ellis (15). It questions how one has lived his or her life between birth and death. I lived my dash as well as I could because I was blessed from the beginning. I was born in a land of freedom to loving, wise parents who nurtured my body, mind, and soul. I was encouraged to live life so that by the end I would have accomplished something of value for others.

I incorporated two parental exhortations in particular and kept them uppermost in my thoughts throughout my life. They were as follows. First, learn as much as you can because you never know when you will need that knowledge. Second, if someone gives you a job, do it as well as you can with a smile.

I was not a clock-watcher. The tasks had to be finished regardless of how long it took. Most importantly, whatever success I achieved was because I loved what I was doing. Without that enthusiastic approach, life could have become drudgery. Responsibilities thrust upon me often required hours in and out of the hospital beyond the limits of a routine eight-hour day. That this devotion to my duties was applauded by colleagues and the larger medical community has been a side benefit.

While I am grateful for the honors I have received, I am most proud of two things: (*a*) my efforts to improve the lives of infants and children, and (*b*) that I have transmitted my knowledge to future generations of physicians who have taken what I taught them as a base and are advancing knowledge in undreamed-of directions.

DISCLOSURE STATEMENT

The author is not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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