

## A Personal Autobiography

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Looking back on my career, from my earliest recollections as a child I had the intent to study medicine. I was particularly influenced by my father, who was among the first generation of radiologists in Sweden and a great supporter of mine in this regard. My mother was a painter of the West Swedish Göteborg Colorist School. Therefore, I was exposed from the beginning to strong academic and cultural traditions. I was born on August 9, 1923, the eldest of 3 children, in Göteborg but spent my early years in Stockholm, Sweden. My sister was born in 1925. My brother was born in 1932, and he later became a prominent archeologist, particularly exploring the Viking influences in Sweden and becoming head of the Swedish Historical Museum in Stockholm. Our household was always lively, and we especially enjoyed our summertime vacations near the sea on Sweden's west coast, where our grandparents spent their summers. We were exposed to outdoor life and spent many days exploring in the nearby woods and taking advantage of the seaside for swimming, fishing, and sailing. I attended school for my first 2 years in Stockholm. When I was 8 years old, my father became head of radiology at the regional hospital in Borås, a center of the Swedish textile industry, just to the east of Göteborg. At that time in this community, it was important to be proficient in athletics such as European football (soccer). I was fortunate in being a swift runner, especially for short distances. I quickly became accepted by the other children in Borås because of my athletic abilities. In the winter, it was possible to ice-skate on natural ice at the nearby lakes and ponds and to play a game akin to ice hockey called bandy. I excelled in bandy as well because of my quickness. However, it was in running that I had my greatest success, especially in the 100-m sprint. During my years in high school, I was among the fastest sprinters in Sweden, ultimately winning the 100-m championship

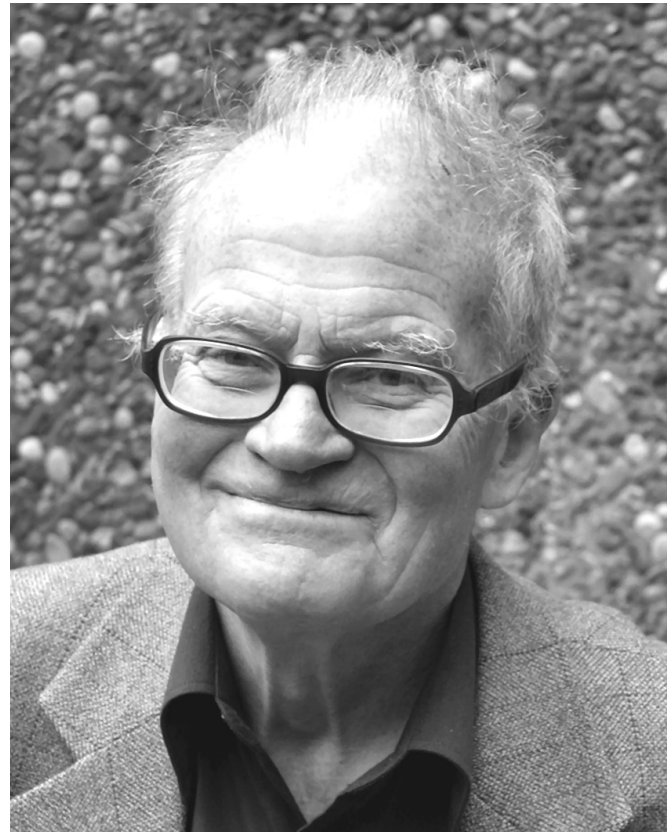
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among high school students. All the while, I was pursuing my high school academic studies, and in 1942 I entered the University of Uppsala, Sweden, as a medical student. I continued my running during these times, competing in the 100-m sprint and the 4 × 100-m relay. During World War II, we were isolated in Sweden. As a means of breaking out of this isolation after the war ended, Sweden was invited in 1946 to compete in a track and field competition in Zürich, Switzerland, with national academic teams from Switzerland and Denmark. Unfortunately, I was impressed with the sights and shops in Zürich, so my legs suffered, and I did not have my best running results there. We traveled by a primitive bus without toilet through partly war-destroyed main roads in West Germany and a totally ruined Hamburg and were met by many children seeking food. This made a lasting impression that I carried with me throughout my career.

During the medical student years, I became active in the Medical Student Association, for which I was chairman in 1947-1948 and represented Sweden at the Medical Students First International Study Group held in the United Kingdom in 1948. I was much interested in pediatrics from the beginning. After receiving my MD in 1950, I entered pediatric training at the University of Uppsala and spent the next 3 years (1950-1953) with Professor Bo Vahlquist, a leading pediatric academician of Scandinavia through the 1950s and 1960s. In the Swedish system, one is expected to complete the equivalent of a PhD degree to enter academic medicine. My dissertation project was in the area of pediatric hematology, entitled "Studies on the Plasma Transport of Iron." This was presented and published in April 1953, part of it as Supplement 93 in *Acta Paediatrica Scandinavica*.<sup>1</sup> Beginning with my first months as a pediatric trainee, I was fascinated by the manifold unsolved and challenging diagnostic enigmas and therapeutic problems found in infants and children with neurologic abnormalities. The field of pediatric neurology at that time (in the late 1940s and early 1950s) was only beginning to emerge within Swedish pediatrics. I soon found the problems associated with pediatric neurology to be an ever-expanding sector, appearing to be encountered about 10 times more often in daily clinical work than hematologic problems in that "pre-oncology" era. As the result of my interest, I then spent an additional 3 years training in adult neurology and internal medicine, in the latter placing special emphasis on neurologic problems. This was a busy and challenging time as I divided my training between the Swedish neurologic departments of Professor Ekblom in Uppsala, Professor Broman in Göteborg, Professor Wohlfart in Lund, and the research-oriented internal medicine center of Professor Waldenström in Malmö, Sweden. For a short period (a couple of months), I also worked with Assistant Professor Sven Brandt in Copenhagen, Denmark, the first and only pediatric neurologist in Scandinavia at that time. Thereafter, I entered the medical faculty in Uppsala first as assistant professor of pediatrics in 1956 and was named lecturer in pediatrics from 1960 to 1964.

During my university studies, I was fortunate to meet Gudrun Wranne, also a medical student, in fact serving as her instructor in anatomy and histology. This was the beginning of a long-lasting relationship, both personal and professional. We were married in 1947 and soon began a family. Our family quickly expanded to include 5 now-grown children. Three are daughters, one an architect, another a teacher, and the third a physiotherapist, and there are twin sons who are both physicians, one a leading specialist in oncology in Uppsala and the other a professor in infectious diseases in Göteborg. Gudrun and I now have 14 grandchildren and 2 great-grandchildren. Caring for the children, Gudrun ended her medical education, but she subsequently acquired further education in statistics and epidemiology.

In the absence of any broad Swedish experience in pediatric neurology, I was mainly self-taught as a pediatric neurologist. During the latter part of the 1950s and through the whole of the 1960s, my experiences were devoted to clinically intensive years in the routine diagnosis and management of neurologic disorders at the dynamic department of pediatrics in Uppsala. At that center, subspecialization within pediatrics was developing. My focus was clinical and was necessarily broad because I had to solve many different problems as they appeared. Without a large cadre of pediatric neurologists, it was necessary to make myself available throughout the countryside providing consultations, performing examinations, and making recommendations for further study and investigation. In fact, it was during this time in 1960 that I encountered my first patient with what is now known as Rett syndrome. The father of this young girl said, "This must be something very special" and insisted on intensive investigations, including brain biopsy to find a basis for this unique disorder. Within a few years, I had observed another 15 girls with the same clinical picture. I called the disorder Vesslan disease after the family name of the first patient, and it was to occupy me fully in later years. In 1964, I was fortunate to receive a personal clinically oriented research appointment in pediatric neurology from the Swedish Medical Research Council. This research appointment allowed me to focus for the first time on special questions such as longitudinal examination of infantile hydrocephalus and cerebral palsy in Sweden, as well as rare and progressive neurometabolic disorders such as Krabbe disease, metachromatic leukodystrophy, and the special infantile form of neuronal ceroid lipofuscinosis. In 1967, I was promoted to associate professor in pediatric neurology, and in 1969 I was named to the first professorial position of ordinarius in pediatric neurology in the Nordic countries. In 1971, I was named professor of pediatrics in Göteborg, remaining in this position until my retirement and entrance into emeritus status in 1990. I had many administrative responsibilities during this period, including 2 as administrative head of Children's Hospital in Göteborg, first from 1973 to 1981 and then from 1984 to 1987, and as head of the administrative block for pediatrics, pediatric surgery, child psychiatry, and child health from 1978 to 1981. These years brought a number of national posts, including scientific advisor of the Swedish Social Council through the 1980s and member of the national expert commissions for "small and less known handicap groups" through the 1990s. Since 1990, I have been professor emeritus and consultant child neurologist at Queen Silvia Children's Hospital in Göteborg.

My epidemiologic research on neuropediatric disorders such as cerebral palsy and infantile hydrocephalus was begun during the Uppsala period. When I moved to Göteborg, organized research projects were established in the West Swedish region together with my wife, Gudrun, who joined me as a most competent and efficient epidemiologist and statistician. She became an appreciated

coworker to physicians in various medical disciplines, particularly those specializing in child neurology. Therefore, I was especially pleased and proud when Gudrun received an honorary doctor of medicine degree at Göteborg University in 1989. The changing panorama of cerebral palsy in Sweden was investigated and described in a series of articles (1975-2005), all representing large population-based series of cases born between 1954 and 1998. These studies were performed in collaboration with Dr Ingemar Olow at the Regional Habilitation Center Bräcke-Östergård (1975-1982). Other epidemiologic investigations covered severe forms of mental deficiency with Professor K.-H. Gustavson, Uppsala (1977), and milder forms (IQ range, 50-70) in studies from Göteborg in the 1980s, as well as infantile hydrocephalus (with Dr Elisabeth Fernell, 1987-1989) and peripheral neuropathies (with Dr Barbro Westerberg, 1980-1983).

With my appointment in 1971 as professor ordinarius of pediatrics in Göteborg, I finally had a broader platform and better resources for pediatric subspecialization, especially in pediatric neurology, as it was becoming an intensive field of interest in Scandinavia. I recognized the need to expand expertise in pediatric neurology and to create a national network that could meet the needs of country. Children were being referred from wide areas throughout Sweden. Although most of the population lived in the southern third of the country, Sweden is in fact a long country, such that some citizens lived far from organized medical centers. It was necessary to build a system of regional centers staffed by neuropediatricians to alleviate the requirement that families travel long distances to find expertise in pediatric neurology, while developing a feeder system that could refer the most vexing problems to the major centers. In this leadership position and in an effort to provide an interim solution, I traveled the countryside providing consultations, making suggestions in special situations, and, most important, building a series of contacts that would serve as the basis for a national network for pediatric neurology. (Editor's note: Although Bengt is too modest to suggest this, he is widely regarded as the "father" of pediatric neurology in Sweden.) Together with my group of collaborators, we built up during a few years a center with neuropediatric emphasis that integrated neurodevelopment, child neurology, and habilitation of the handicapped child. Furthermore, a close collaboration was started with the Regional Habilitation Center Bräcke-Östergård, directed at the time by Dr Ingemar Olow. As such, I had created a Swedish "neuropediatric school" in the broad sense, parallel to my administrative efforts to structure a decentralized organization in Sweden for neuropediatrics and for care of the handicapped child at the county level. Through a hectic decade, positions were created in neuropediatrics throughout Sweden, in fact successively in all the Swedish counties, even the most northern ones. Young pediatricians passed through Uppsala and later Göteborg for periods of specialized training in basic clinical neuropediatric knowledge and thinking, including learning what could be managed at home and what should be referred to the

regional university centers. A large number of such "county neuropediatricians" spent a period in my neuropediatric school at Uppsala and in later years at Göteborg for clinical work, training, and sometimes small structured research projects. In time, I was able to initiate this system for neuropediatrics, starting with young more or less "barefoot neuropediatricians," who then continued with subsequent postgraduate training through the years. This successively built up (and spread countrywide) neuropediatric competence, which was fundamental for the decentralized Swedish neuropediatric structure with emphasis on the county level (Swedish counties have populations ranging from 250 000-400 000). In Göteborg, I succeeded in building up a well-functioning regional neuropediatric university center with 4 head positions in neuropediatrics, each with somewhat different emphasis. I achieved this through my positions as administrative chairman of the Pediatric Hospital Block in Göteborg and as head of the department of pediatrics at the university level.

With my collaborators, I participated in clinical research, publishing more than 410 peer-reviewed articles between 1951 and 2007. Pediatric neurology, epidemiology of handicapping conditions, neurometabolism, care load evaluation, and pediatric hematology (during the early period) have been the main targets of these publications. A research area in which I have been particularly eager to contribute is the delineation of various progressive brain disorders. As a clinical counterpart during 30 years to Professor Lars Svennerholm (professor of neurochemistry) and Professor Patrick Sourander (professor of neuropathology), we formed a strong 3-part collaboration resulting in a series of original contributions on many neurometabolic and neurodevelopmental disorders that included various lysosomal diseases, particularly the sphingolipidoses and the neuronal ceroid lipofuscinoses (the infantile form was first described in 1968 by our team<sup>2</sup>), and Rett syndrome. In the process, I succeeded in constructing clinical staging systems for late infantile sulfatidosis (metachromatic leukodystrophy), Krabbe disease, and Rett syndrome. For Rett syndrome, we provided prevalence figures and the first reports on the natural history from infancy to middle age (together with Dr Ingegerd Witt-Engerström), on genetic aspects, on brainstem and spinal cord neurophysiology, and on the neuropathology.

As my research work expanded in pediatric neurology, neurometabolic diseases, handicap epidemiology, general pediatrics, and care load, so too did my international connections and collaborations. I was elected secretary general of the European Federation of Child Neurology Societies from 1970 to 1977, serving as an initiator of this organization together with the legendary Dr Ronald MacKeith in the United Kingdom and Professor Johannes Melchior in Denmark and subsequently as a member of the organization's council group from 1978 to 1981. I arranged the first European Federation of Child Neurology Societies conference at Kungälv, Sweden, in 1973. I also served as chairman

of the Section for Pediatric Neurology and Habilitation within the Swedish Pediatric Association from 1975 to 1978 and as chairman of the Swedish Medical Research Committee on Medical Research in Mental Retardation and Neurohandicaps in Children from 1977 to 1989. I also became a member of the council of the Folke Bernadotte Foundation for crippled children in 1970 and its vice chairman in 1973, a board member of 4 other foundations providing support for neuropediatric research, vice president of the International Association for the Scientific Study of Mental Deficiency from 1988 to 1992, and scientific coordinator of the 1996 Rett World Congress in Göteborg.

Two international meetings came to be especially important and thrilling for my research. First to be among those invited in 1953 by Ronald MacKeith to participate in what became a series of Oxford, United Kingdom, conferences at St Edmund Hall devoted to cerebral palsy, I remember creating a stir when I insisted on examining the youngest small children on a mat on the floor. Everyone scoffed at the idea that anything could be learned from such a position, but on subsequent visits I was pleased to see that many had adopted this examination method. At this first meeting, we were exposed to children with different types of cerebral palsy, and huge discrepancies between participants were obvious. We were sent home with the lesson to delineate criteria for the different cerebral palsy types. Together with Dr Ingemar Olow from Göteborg and Dr Marcel d'Avignon from Stockholm, I was happy to find our suggested Swedish classification to be internationally accepted and used worldwide and the impetus for a series of dissertations, including theses on hemiplegic cerebral palsy (P. Uvebrant), tetraplegic cerebral palsy (K. Edebol-Tysk), and dyskinetic cerebral palsy (M. Kyllerman). The other extremely important meeting for me was that organized by the European Federation of Child Neurology Societies in Manchester, United Kingdom, in 1980. I presented my 16 patients with what I called Vesslan disease and asked if anyone else had seen something similar. Dr Jean Aicardi (France) and Dr Karin Dias (Portugal) immediately recognized a number of similar girls. We prepared a manuscript for *Annals of Neurology* that described 35 girls with a syndrome that included autism, dementia, ataxia, and loss of purposeful hand use. By chance, a collaborator of Jean Aicardi's had come across a chapter by Dr Andreas Rett from Vienna, Austria, in the *Handbook of Clinical Neurology*<sup>3</sup> in which Dr Rett described a syndrome that was associated with hyperammonemia (this association was subsequently found to be spurious) and very much resembled what I had called Vesslan disease. At the time, we were unaware that Professor Rett had already described his syndrome in 1966 in a local German-language medical newsletter in Vienna.<sup>4</sup> Little was known about his observations outside of Austria, and in fact his observations were not regarded highly there. This was not an unusual attitude, as many accomplished clinicians did not consider Rett syndrome to be a unique entity. I encountered

similar skepticism among my colleagues in Göteborg. Then in 1982, I was invited to survey mental retardation syndromes at the World Neurology Congress in Toronto, Ontario, Canada, and I mentioned the similarity between the syndrome Rett had described and what I had observed in Sweden. During the discussion following my talk, a large man approached from the back of the lecture hall shouting repeatedly, "Ich bin Rett." I managed to finish with the general discussion period, and then Andy Rett and I went to the back of the hall, spending some time discussing our mutual experiences. We were both convinced that our syndromes were the same, further confirmed at a meeting at his clinic in Vienna. Following this encounter, "Rett's syndrome" was added to the title of the article published by *Annals of Neurology*.<sup>5</sup> This widely read article published in 1983 drew international attention to this "new" disease, neglected since the original description at Vienna in 1966 by Andy Rett.<sup>4</sup>

In the late 1960s and early 1970s, we started intensive exchange meetings between Professor Folker Hanefeld and his group, first in Berlin, West Germany, and later in Göttingen, West Germany. It was thus that I developed a long-standing friendship and collaboration with Folker Hanefeld. We were able to work together on many pediatric neurology problems, in particular progressive brain disorders.

Other new diseases described together with my collaborators include the following: malignant hyperlipidemia in infancy (with Lars Svennerholm in 1964), Niemann-Pick-simulating oligosaccharidosis (with Lars Svennerholm and colleagues in 1978), genetic dysequilibrium syndrome (with G. Sanner in 1972), Hagberg-Hansson disease (a familial ataxic diplegia with cellular immune deficiency, in 1972), a Swedish form of lysosomal Salla disease variant (with Lars Svennerholm and colleagues in 1986), disialo-developmental deficiency disease (congenital disorder of glycosylation syndrome) (with B. Kristiansson and colleagues in 1989), and 2 different familial forms of 3-methylglutaconic aciduria (in 1978 and in 1983 with various authors).

Following my move to emeritus status, I was fortunate to continue my research in a number of areas. These include cerebral palsy, mental retardation-related syndromes (and neurometabolic disorders), and, especially, Rett syndrome.

Cerebral palsy research and epidemiology studies include the following research: ongoing cerebral palsy panorama in western Sweden within the broad Swedish research group for birth years 1954 to 1998, now more than 1400 cases; projects with the University of Tübingen, Germany (Professor R. Michaelis and colleagues) and the University of Perth, Australia (Professor F. Stanley and colleagues); international projects within the Little Foundation, United Kingdom; origins and neuroimaging of ataxic cerebral palsy in 10 Swedish counties (with Dr E. Esscher and colleagues); and Surveillance of Cerebral Palsy in Europe, a collaboration of 14 regions from 9 European countries.

Mental retardation and progressive neurometabolic brain disorder research includes the following: epidemiology of severe and mild mental retardation (with G. Hagberg and collaborators), Rett syndrome (project leader of the Swedish Rett Research Project since the 1960s, including medical genetics and genealogy, with Professor J. Wahlström and Professor H. O. Åkesson), congenital disorder of glycosylation syndrome (project in Sweden with Professor H. Stibler and Professor B. Kristiansson), progressive neuropiloid disorders (with the Svennerholm team), mitochondrial disorders (with Professor A. Oldfors, Professor E. Holme, Professor M. Tulinius, and collaborators), and care load (with Dr K. Edebol-Tysk).

Special attention to Rett syndrome research resulted in the publication of 56 clinical and basic research articles from 1983 to 1996. I was editor of a textbook in the Clinics in Developmental Medicine series, published in 1993.<sup>6</sup>

Throughout the years, I guided a dozen PhD students in writing their dissertations, mainly on neuropediatric topics. I mentored scores of other neuropediatricians from Sweden and abroad.

I have been distinguished as an honorary member of a number of European societies and as the recipient of numerous mainly neuropediatric awards, including the following: Lennander Award (Stockholm, 1974), Malte Award (Oslo, Norway; 1979), Ronnie MacKeith Lecturer (British Paediatric Neurology Association, 1981), Gesellshaft F. Neuropädiatric (Germany, 1983), Honorary Big Lottery Fund Lecturer (Helsinki, Finland; 1972 and 1983), Guest Professor Award of the University of Dundee (Scotland, 1985), Oskar Medins Award (1987), Folke Bernadotte Award (1988; together with my wife, Gudrun Hagberg), Honorary Segawa Prize Lecturer in Child Neurology (Japan, 1989), Guest Professor at the University of Göttingen (1991 and 1992), Per Dubb Price Lecturer (Göteborg, 1991), Child Neurology Society Hower Award (1993), Rosén von Rosenstein Award (Uppsala, 1994),

Cornelia de Lange Award (Utrecht, the Netherlands; 1994), Ågrenska Award (Göteborg, 1996), and the Philipsson Award for Rett syndrome research (shared with Professor Huda Zoghbi, 2004).

For all of these honors and for my long career in general, I owe much to my many colleagues. This has been a rich experience for me. I am pleased to have been able to participate in the advancement of pediatric neurology from the time of the introduction of ventricular shunts and ultrasonographic measurements of ventricular size, to the expansion of knowledge and the ever-emerging techniques in neuroimaging and molecular genetics. I have been privileged to be part of it. I am also pleased to see this field in the good hands of highly competent pediatric neurologists whose formation was through our system.

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