The History of Rett Syndrome

In 1954, Dr. Andreas Rett, a pediatrician in Vienna, Austria, first noticed two girls as they sat in his waiting room with their mothers. He observed these children making the same repetitive hand-washing motions. Curious, he compared their clinical and developmental histories and discovered they were very similar.

Dr. Rett checked with his nurse and learned that he had six other girls with similar behavior in his practice. Surely, he thought, all these girls must have the same disorder. Not content with studying his own patients, Dr. Rett made a film of these girls and traveled throughout Europe seeking other children with these symptoms.

Meanwhile, in 1960, young female patients in Sweden with quite similar symptoms caught the eye of their own physician, Dr. Bengt Hagberg. Dr. Hagberg collected the records of these girls and put them aside, intending to return to them when he had more time to study this curious phenomenon.

Then, in 1966, Dr. Rett published his findings in several German medical journals, which, however well-known in that part of the world, were hardly mainstream reading for much of the rest of the world’s medical community. Even after Dr. Rett published a description of the disease in English in 1977, Rett syndrome remained in the backwaters of medical concern: The pre-internet world lacked the electronic information highways taken for granted in the 21st Century.

But in 1983 an article on Rett syndrome appeared in the mainstream, English-language journal, Annals of Neurology. Written by none other than Dr. Hagberg and his colleagues, the report finally raised the profile of Rett syndrome and put it on the radar screen of many more investigators. This article was a breakthrough in communicating details of the disease to a wide audience, and the authors honored its pioneering researcher by naming it Rett syndrome.

As investigators continued to chip away at the shell of mystery surrounding Rett syndrome, increased research funding ensured that the work would continue. A team of scientists from Baylor University (Houston, TX) and Stanford University (Palo Alto, CA), toiled in the labs and clinics trying to pinpoint the cause of Rett syndrome.

A major breakthrough occurred in 1999, when a research fellow at Baylor named Ruthie Amir discovered MECP2, the gene that, when mutated, causes Rett syndrome. The discovery of the gene, located at the Xq28 site on the X chromosome was a triumph for the Baylor team, led by Huda Y. Zoghbi, MD, a professor in the departments of pediatrics, neurology, neuroscience, and molecular human genetics at the Howard Hughes Medical Institute.

The discovery that MECP2 is on the X chromosome proved that Rett syndrome is an X-linked disorder. And because only one of the two X chromosomes need have the mutation in order for it to cause the disorder, this is a dominant disorder as well. The fact that Rett syndrome is an X-linked dominant disorder also helps explain why it is usually found only in girls.