Overview of Rett Syndrome

The clinical features of Rett syndrome were first described in 1966 by Dr. Andreas Rett. Patients with these clinical features were subsequently given the designation of Rett syndrome in 1983 in recognition of Dr. Rett’s original report. Rett syndrome is still considered a clinical diagnosis based on specific developmental history and clinical criteria. These clinical criteria were last revised in 2010.

Initially, Rett syndrome was recognized only in females. It was hypothesized that Rett syndrome was lethal in males. This suggested that Rett syndrome was a sex-linked genetic disorder with the gene being localized on the X chromosome.

In 1999 it was reported that mutations in the MECP2 gene, located on the X chromosome, were associated with the clinical presentation of Rett syndrome. Since the ability to test the MECP2 gene has been available, there have been over 60 males reported with mutations in the MECP2 gene. A few of these males had a clinical picture consistent with the clinical criteria for Rett syndrome; however, most of these males presented with a different clinical presentation. Most males with mutations in MECP2 gene present with an earlier onset of symptoms, typically with significant problems beginning at or shortly after birth.

The diagnosis of Rett syndrome is still based on clinical criteria and the clinical presentation. Over 95% of females with classic Rett syndrome will have a mutation in the MECP2 gene. Mutations in the MECP2 gene by themselves are not sufficient to make a diagnosis of Rett syndrome. Patients with mutations in the MECP2 gene that do not meet the clinical criteria for Rett syndrome are given the designation of MECP2-related disorders.