Rett syndrome (RTT) is a severe X-linked neurodevelopmental disorder affecting almost exclusively girls. It belongs to autistic spectrum disorders and it is characterized especially by psychomotor regression, loss of acquired speech, microcephaly, repetitive stereotypic hand movements, and seizures. Most of RTT cases are caused by de novo mutations in the gene for the methyl-CpG-binding protein 2 (MECP2) and familial cases are extremely rare. The MECP2 gene product plays an important role in chromatin remodeling, regulation of gene expression and is also involved in RNA splicing. Some atypical RTT cases are caused by mutations in other genes, such as CDKL5, FOXG1 or NTNG1. In this paper we give an overview of RTT, its clinical aspects, molecular basis, diagnostic criteria, medical management and DNA diagnosis.