



## Rett Syndrome

### Alternative Names

RTT  
Autism, Dementia, Ataxia, and Loss of Purposeful Hand Use  
Rett Syndrome, Preserved Speech Variant  
Rett Syndrome, Atypical, Cdk15-Related

### WHO International Classification of Diseases

Mental and behavioural disorders

### OMIM Number

312750

### Mode of Inheritance

X-linked dominant

### Gene Map Locus

Xq28, Xp22

### Description

Rett syndrome is a neuro-developmental disorder, with slow progression, that appears to occur almost exclusively in females. Patients with RS have seemingly healthy development until about 7 to 18 months of age, after which a stage of developmental stagnation is followed by developmental regression. Regression is characterized by loss of purposeful hand skills and oral language and the development of hand stereotypies and gait dyspraxia. Other problems include breath holding and apnea during wakefulness with normal breathing during sleep, epilepsy, oral-motor dysfunction with gut motility problems (e.g., constipation, gastroesophageal reflux [GER]), scoliosis, autonomic dysfunction (cold blue extremities), and somatic growth failure.

Rett syndrome affects one in every 10,000 to 15,000 live female births. It occurs in all racial and ethnic groups worldwide. Due to lack of a biological marker associated with the disease, diagnosis is made purely on the basis of clinical features. The diagnosis is supported by a positive mutational analysis of MECP2.

However, 20% of RS patients may have no identified mutation. Since no treatment exists for the disease, treatment is palliative and supportive.

### Molecular Genetics

Rett Syndrome results from a mutation on the X chromosome that is transmitted as an X-linked trait. However, most cases are thought to represent new mutations that appear to occur sporadically. The major gene involved is the methyl CpG binding protein-2 (MECP2) gene, found on chromosome band Xq28. Multiple mutation types have been found in the three coding regions of the MECP2 gene, with most mutation types causing truncations and missense proteins.

The normal MECP2 gene encodes a protein MeCP2, which binds to methylated DNA, and activates histone deacetylase. The mutated gene produces loss of function of this protein causing unregulated expression of certain genes involved in nervous system development.

### Epidemiology in the Arab World

#### Kuwait

Eeg-Olofsson et al. (1988) investigated two girls affected with Rett Syndrome. Electron microscopy of the muscle biopsies revealed abnormally swollen and dumb-bell shaped mitochondria. Eeg-Olofsson (1998) suggested that the abnormalities in the mitochondria were due to mitochondrial mutations guided by an X-borne gene mutation. For the male zygote, this would result in a failure to implant, or an early embryonal death.

#### Saudi Arabia

Al-Jarallah et al. (1996) described five Saudi girls (age 3.5-12 years) with Rett Syndrome. The diagnosis was based on the criteria defined by the Rett Syndrome Diagnostic Criteria Work



Group (RSDWGC). None of the girls had a family history of any disease with similar clinical features. However, at least two of the girls had parents who were first cousins. The girls demonstrated gradual deterioration of mental status and loss of acquired speech, infantile autistic behavior, minimal eye contact with surrounding objects, peculiar hand-mouthing, washing and clapping movements, and episodic mouth-breathing with hyperventilation. None had evidence of intra-uterine growth retardation, visceromegaly, retinopathy, microcephaly at birth, or perinatally acquired brain damage. At least two patients showed EEG abnormalities in the form of diffused slowing, as in epilepsy. Another patient had myoclonic epilepsy, and her EEG showed generalized epileptic discharges.

### **Sudan**

Al-Jarallah et al. (1996) examined a Sudanese girl with Rett Syndrome. The diagnosis was based on the criteria defined by the Rett Syndrome Diagnostic Criteria Work Group

(RSDWGC). The patient did not have a family history of any disease with similar clinical features. The girl demonstrated gradual deterioration of mental status and loss of acquired speech, infantile autistic behavior, minimal eye contact with surrounding objects, peculiar hand-mouthing, washing and clapping movements, and episodic mouth-breathing with hyperventilation. There was no evidence of intra-uterine growth, visceromegaly, retinopathy, microcephaly at birth, or perinatally acquired brain damage.

### **References**

- Al-Jarallah AA, Salih MA, al Nasser MN, al Zamil FA, al Gethmi J. Rett syndrome in Saudi Arabia: report of six patients. *Ann Trop Paediatr.* 1996; 16(4):347-52.
- Eeg-Olofsson O, al-Zuhair AG, Teebi AS, al-Essa MM. Abnormal mitochondria in the Rett syndrome. *Brain Dev.* 1988; 10(4):260-2.

### **Contributors**

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