**RETT Syndrome**

**Definition:** Progressive neurodevelopmental disorder characterized by intellectual disability, abnormal hand movements and impaired expressive language; affects mostly girls.

**Prevalence:** ~1 in 15,000 girls. About ~16,000 girls in the USA estimated to have Rett syndrome. Occurs in all races and ethnic groups.

**Etiology:** Several distinct genetic defects may lead to clinical Rett syndrome or Rett-like disorders. The cardinal form of the disorder results from mutation in the methyl cytosine binding protein-2 (*MECP2*) gene. This gene is crucial for normal nervous system development.

**Pathogenesis:** Loss of functioning MeCP2 keeps genes in the brain ‘turned on’ long after they are supposed to be ‘turned off.’ Clinically, this results in abnormal brain development and developmental arrest, autonomic nervous system dysfunction and growth failure.

**Stages of Rett Syndrome:** Early onset, rapid destructive, pseudostationary and late motor deterioration.

**Dysabilities & impairments:**

- CNS – intellectual disability, epilepsy
- Tone – hypotonia, spasticity, dystonia, parkinsonism
- Speech – absent expressive language
- RS - apnea, hyperventilation/breath holding, restrictive pulmonary disease
- CVS – long QT
- GI - drooling, dysphagia, constipation
- MSK - difficulty with ambulation, contractures, NM scoliosis, NM hip dislocation, planovalgus feet, osteoporosis, fractures
• Social – anxiety & behavioral issues

**Natural History:** 50% lose ability to walk by age 10 years. Shortened life span -- 70% survive to age 35. Most deaths are sudden & unexpected or secondary to pneumonia.

**Musculoskeletal Issues:**

• Neuromuscular deterioration results in progressive loss of walking ability, spasticity, muscle imbalance, joint contractures and bone deformities.
• Growth failure results in short stature, poor weight gain in spite of good appetite, low muscle mass and osteoporosis as a result of very low rate of bone formation (decreased bone formation; normal numbers of osteoclasts).
• Dysfunctional autonomic system results in poor circulation to hands & feet, poor pain discrimination and cardiorespiratory dysfunction.

**Prevalence of MSK Issues:** Spine deformity – 45%, Hip subluxation – 11 to 48%, foot deformity – 20 to 25%, Knee contractures – 33%, elbow contractures – 20%, fractures – 14%

**Medical Management:** No cure but focus is on symptom management. Requires a multidisciplinary team approach.

• Diagnosis & genetic counselling
• Medications – seizures, sleep, heart, breathing, tone, GI
• Feeding difficulties & nutritional support
• Drooling
• Agitation - Apnea - Hyperventilation
• Screening for Spine / hip issues
• Bone Health – Vit D, Calcium

**Osteoporosis:** Be aware that it is common
• Decreased bone mass & BMD, Vit D deficiency
• 4 times higher risk of fractures: inform parents, therapists and teacher
• Proper nutrition
• Do not add excessive calcium if levels are normal
• Treat with Vitamin D, Phosphorous and calcium
• Fosam, IV Pamidronate, teriparatide (PTH)
• Maintain muscle use and strength

Rehabilitation:

• OT / PT/ Speech Therapy - aimed at maintaining or improving ambulation and balance, maintaining full range of movement or at least functional movement, preventing deformities, promoting and improving the use of the hands, and promoting communication and choice making.
• Mobility aids
• Assistive technology
• Behavioral therapy

Tone management:

• Massage / stretching exercises
• Warm baths
• Swimming
• Medications – diazepam, clonazepam, gabapentin, trihexyphenidyl, baclofen, tizanidine
• Botox injections
• Intrathecal Baclofen

Surgical Management:

• Tone management – Intrathecal baclofen pump
• Spine deformity- Posterior spinal fusion
• Hip subluxation – Hip Reconstruction
• Planovalgus feet – foot surgery
• Contractures – soft tissue surgery

**Coping & Support:** Children need lifelong support with most activities of daily living and this can be stressful for families.

• Stress management
• Respite care
• Family support groups