**Rett Syndrome (RTT)**

**Introduction**

Rett syndrome (RTT) is a progressive neurological disease predominantly affecting girls, with impairments emerging during the first year of life. While it has an incidence of 1 in 10,000-15,000 births, the prevalence is difficult to estimate secondary to the recent recognition of this disease’s existence; specifically, RTT wasn’t formally identified until the late 1960’s and the pathophysiology wasn’t recognized until the late 1990’s.1,2 Despite this young history has resulted in a shallow pool of evidence, numerous case and cohort studies exist. The effects of these studies are threefold as they: 1) paint a picture of the girl with RTT, 2) provide guiding information for the therapist, and 3) suggest areas for further research. The purpose of this paper is to provide a thorough review of RTT as interpreted by the ICF model to serve as a template for patient exam, evaluation, and plan of care.

**Pathophysiology**

*Current Understanding*

Research on RTT pathophysiology has identified spontaneous genetic mutation at the methyl CpG binding protein 2 (MECP2).1,3 It is because this is an X-linked gene that RTT presents almost exclusively in girls. Furthermore, this gene is responsible for protein production and expression of other genes; thus, mutation results in faulty brain development.1 Specifically, mutation of MECP2 causes hypofunction of the midbrain and brainstem’s aminergic neuronal systems. Decreased noradrenaline and serotonin is believed to produce impairments in locomotion while dysfunction of dopamine in the basal ganglia produces the characteristic bilateral hand wringing and clenching.4 MECP2 is also believed to have an effect on higher cortical function, which could be responsible for the cognitive and communication impairments as well as apraxia.3-5

*Future Research*

While the current understanding of RTT’s pathophysiology provides a general foundation for its associated impairments, there is still a lot that is unknown. Both researchers and clinicians have several questions about RTT that cannot yet be explained by current understanding of pathophysiology. For example, intrauterine development appears to be fairly typical, as does development during the first few months of life; in fact, most girls will meet initial developmental milestones. However, this period is then followed first by regression of skills then subsequent progressive developmental delay. While this could be secondary to the increasing impact of aminergic hypofunction, most scholars acknowledge the need for further research as there could also be effects of the MECP2 gene that are not yet understood.4,5

Lack of confidence in pathophysiology is further emphasized by actual incidence of MECP2 mutation. Barrera et al. found that only 84% of subjects tested positively for MCEP2 mutation whereas Neul et al. suggest a lower incidence, with this specific mutation only occurring in 50-80% of patients with RTT.6,7.6 Genetic testing is further complicated by the occurrence of MECP2 mutation without typical RTT impairment resulting in a diagnosis such as autism or Angelman Syndrome.6 Currently, researchers are trying to identify other possible genetic mutations, with a transformation of the CDKL5 gene being a possibility.6,7

*Clinical Application*

Despite all that is unknown, the continued research to determine RTT’s pathophysiology should be considered a triumph, as a cure cannot be found without this effort. The more we know about the disease, the more equipped therapists can be for effectively working in this population. Research thus far has helped with the development of a Rett classification system for diagnosis as well as well as a staging system for tracking disease progression. Each are valuable tools that should be used by therapists for educating families and developing appropriate reactive as well as preventative plans of care.

**Pathology**

*Making a Diagnosis*

Making a clear RTT diagnosis is complicated by a limited understanding of the disease’s pathophysiology in combination with its initial similarity to cerebral palsy and autism as well as quick neurological progression.6 Proper diagnosis is vital as this progressive nature benefits from early education and intervention. The following Rett Syndrome Classification System is utilized by physicians and clinicians:

Main Criteria—1) loss of purposeful hand skills, 2) loss of spoken language, 3) gait abnormalities, 4) stereotypical hand movements (wringing, clapping, tapping, rubbing, etc.)6,8

Exclusion Criteria—1) a history of traumatic brain injury, metabolic disease, or severe infection, 2) Gross psychomotor development delays from 0-6mos.3,6,8

Supportive Criteria—1) breathing disturbances, 2) teeth grinding, 3) impaired sleep habits, 4) abnormal muscle tone, 5) peripheral vasomotor disturbances, 6) scoliosis/kyphosis, 7) slowed growth, 8) small hands/feet, 9) inappropriate laughing/yelling, 10) diminished pain response, and 11) intense eye contact3,6,8

*Staging Classification*

Ideally, the aforementioned criteria will lead to quick diagnosis; however, this may be delayed based on the individual’s specific presentation. Presentation will varies with disease progression, but typically four stages of RTT are seen over the course of the lifespan.3 Stage 1 is identified typically occurs from 6-18 months and is referred to as the Early Onset Stage. Presentation during this stage generally includes hypotonia, developmental regression and delay, microcephaly, and limited interest in the environment. Stage 2 is the Rapid Regression Stage and occurs in girls 1-4y.o. During this period, families will begin to identify cognitive and motor delays, unusual hand movements and positioning such as wringing and fisting, a loss in spoken communication, and respiratory impairment including apnea, hyperventilation, and breath holding. This stage can last for a few weeks, months, or years before progression to the third stage. Stage 3 is the Plateau Stage; all previous impairments will continue to progress and are often further complicated by autonomic dysfunction, anxious behavior, scoliosis, and epilepsy. While it is possible to remain in the Plateau Stage, a portion of girls will progress to Stage 4, called the Late Motor Deterioration Stage. This progression is identified by the loss of ambulation.1,2,7

**Impact of Pathology on Systems**

**Anticipated Impairments**

The following list represents common impairments associated with RTT. It is important to note that while all of these impairments will affect activity/participation and *can be* addressed by a physical therapist, there are times that it will be in the best interest of the patient to refer to another discipline such as occupational therapy, speech language pathology, or respiratory therapy. Furthermore, level of delay will vary based on the patient’s RTT stage and previous treatment. All impairments have the potential to influence therapy and choosing appropriate therapeutic activities.

Decline in Oromotor Skills: feeding, chewing, swallowing, and drinking. Therapist should discuss use of food and drink with family or SLP prior to utilizing in clinic.9

Breathing Abnormalities: tends to be most prevalent in adolescents and young adults9

* + Hyperventilation
  + Breath holding

Delayed an decline motor skills: mobility and transitions deteriorate with progression through RTT staging9

Hypotonia: associated with initial regression and subsequent delays in developmental milestones; most prevalent before the age of 5, later replaced by hypertonia and rigidity9

* Apraxia: difficulty following direction as well as mirroring motor skills; possibly associated with cognitive and communication delays
* Declines in balance: both static and dynamic

Postural malalignment: tight gastrocs resulting in toe walking, scapular retracting leading to kyphosis, pelvic asymmetry which tends to increase with age9

Scoliosis: found in a majority of girls by stage 3; right rib hump more commonly seen (67.3% in a study by Cass et al.)9

Seizure activity: 2/3 of girls had a history of epilepsy in the study by Cass et al.9

Abnormal hand use: described as reaching, grasping, scratching, rubbing, wringing, tapping, plucking, and complex finger movements; limits ability to participated in ADLs such as self-feeding, dressing, toileting9

**APTA Guide Patterns:**

The *APTA Guide to Physical Therapist Practice* has several practice patterns that are appropriate when treating a patient with RTT. This should come as no surprise, especially after seeing the vast number of effects RTT can have on multiple systems of the body. Selection of a pattern(s) will likely depend on stage, level of progression, and prior exposure to therapy. Patterns that therapists should consider include:

* Pattern 4B: Impaired Posture
* Pattern 4C: Impaired Muscle Performance
* Pattern 4D: Impaired Joint Mobility, Motor Function, Muscle Performance, and Range of Motion Associated With Connective Tissue Dysfunction
* Pattern 4F: Impaired Joint Mobility, Motor Function, Muscle Performance, Range of Motion, and Reflex Integrity Associated With Spinal Disorders
* Pattern 5A: Primary Prevention/Risk Reduction for Loss of Balance and Falling
* Pattern 5E: Impaired Motor Function and Sensory Integrity Associated With Progressive Disorders of the Central Nervous System
* Pattern 6B: Impaired Aerobic Capacity/Endurance Associated With Deconditioning
* Pattern 6F: Impaired Ventilation and Respiration/Gas Exchange Associated With Respiratory Failure

**Activity**

**Participation**

Intervention Examples

Importance of Interdisciplinary Care

Tests and Measures

WeeFim

Walk test

Sitting Balance

Dynamic Balance

Fear of Falling

Family Assessment of the patient

Something NonVerbal…

Smiley face visual analogue skill

Something cardiorespiratory esque…

Functional…

Speech…

Parent interview

Scoliosis Assessment

Muscle Tone

ROM/MET

Postural Assessment

SOMA (cass)

Look at Cass Article

Chailey Sitting Levels (cass)

**Assignment: In Depth Review of a Neurological Diagnosis or Clinical Problem**

Select a neuromuscular diagnosis/clinical problem that you wish to learn more about in depth (this was negotiated at the beginning of the course with Karen – **your topic is ‘assigned’ in the assignment spreadsheet posted under the assignment tab**). This topic will be approved (and possibly narrowed) via input from Karen. We will attempt to have a range of problems with minimal duplication of topics so that you can learn from your classmates.

Do a literature search on your topic to identify articles that will help you:

1. Describe the pathology and pathophysiology on the systems (nervous, musculoskeletal, pulmonary, cardiac, etc.) the disorder affects.
2. Identify impairments that result from the pathology.
3. Describe activity and participation limitations that commonly occur in the population.
4. Identify key environmental and individual factors that may influence outcomes for individuals with this disorder.
5. As you read in these areas, collect information that you will synthesize in the assignment for Module 5 (developing a toolbox of assessments).
6. Identify interventions that effectively address impairments, activity, participation OR quality of life for this disorder. You may limit your reading to a part of this continuum for the purposes of the assignment (pick what interests you the most – see examples below).

Organize the information you gather in a format that will be useful to you for future clinical use or presentation to your colleagues. Consider following the Guide to PT Practice format, since the components of the Guide following a similar train of thought. This assignment is an ideal foundation for publishing a case report in the future – you just need a case to which you apply the concepts….

You will post parts of this work to a practice centered discussion group (pediatrics, musculoskeletal and adult neurorehab) during the weeks of Module 4 and 5…. you can build the components of your final assignment, sharing parts that you need feedback on with your classmates on the discussion board – then integrate that feedback into your final project you turn in at the end of the semester.