

Caring for Persons with Rett Syndrome

Rett syndrome (RTT) is a severe neurodevelopmental disorder with world prevalence of ~1 in 20,000–40,000, predominantly in females (only 3-5% males.) Associated with complex medical comorbidities. Diagnosis by clinical criteria, confirmed by pathogenic variant in MECP2 gene. Over 300 mutations have been identified. MECP2 gene encodes methyl-CpG binding protein-2, an essential transcriptional regulator in the brain. Ages 0-2 note developmental delays (Stage 1 Stagnation) and hypotonia. Between 18-30 months, children show developmental regression (Stage 2). Stage 3 Pseudo-stationary ages 2-10. Stage 4 Deterioration for decades. 70% live to at least age 50.

System	Information	Follow-up
Genetics	MECP2 gene mutation on X chromosome >99% de novo, present in ~95% of typical RTT, 50-70% of atypical RTT.	Most diagnosed by gene sequencing analysis
Cognition	- Auditory/language processing delays. IQ deficit may be overestimated due to lower verbal expression. - Altered signs of pain or illness (wrinkling forehead, grinding teeth, thrashing, altered vocalization or tone, etc.) - Microcephaly (decel OFC growth 0-2 yr) more often than macrocephaly.	- Allow longer time for responses. - Ask caregivers to describe usual manifestations of illness or pain. - Consider use of DisDAT tool.
GI/Nutrition	- Oro-motor dysfunction, prolonged feeding times w/ poor weight gain. Risk for aspiration. - Constipation and upper GI sx (reflux, air swallowing, dysphagia, dysmotility, delayed gastric emptying) common. - Inc. risk volvulus, gallbladder dysfunction.	- Swallow study for sx, consider G tube. - Manage growth, nutrition, constipation. - Consider PPI for irritability. - LFTs have/poor sensitivity for gallbladder dysfxn, Use Ab US/HIDA.
Pulmonary	- Hyperventilation and breath-holding. - Sleep problems (primary insomnia 60%, sleep disordered breathing, sleep-related movement disorders, parasomnias – esp. laughing, screaming, seizures)	- Screen for breathing irregularities. - Use sleep hygiene techniques, consider melatonin trial, consider sleep study.
Neurology	- Regression, i.e. loss of purposeful hand skills and spoken language, starts at 6-18 mos and halts at 2-3 yr. - Gait abnormalities, stereotypic hand movements (hand-wringing dec. after age 10), mouthing, tapping, etc. - Early hypotonia, later hypertonia, rigidity, dystonia. - Multi-types of seizures 70-90% and non-epileptic spells.	- Surveillance for seizure-like sx. - Consider elbow splints or hand guards to aid purposeful use of hands. - Neurology for seizures.
Cardiology	Risk of prolonged QTc 7%.	- Yearly EKG and pre-anesthesia. - Caution for QT lengthening drugs.
Skin	- Pressure ulcers, irritation of skin from mouthing. - Temperature instability in extremities, likely autonomic.	Surveillance for skin pressure, wounds and early Rx.
MSK	Frequent scoliosis after age 6 w/ rapid progression, hip subluxation, contractures, osteopenia with immobility.	- Spine / hip surveillance. - Home range of motion exercises. - Prevent falls, appropriate sized equipment, screen Vit D.
Gyn	Premature adrenarche 25%. Typical age of menarche. Menses irreg w/ low weight. Watch for catamenial seizures (w/ menses).	Weigh value of menstrual suppression, consider choices re: impact on bone health.
Urology	- Urine retention d/t constipation, autonomic dysfnc. - Underhydration and seizure meds inc. kidney stone risk.	- Watch for urinary retention. - Consider UTI and/or stones for irritability.
Vision/Dental	Frequent cortical visual impairment w/ adv. disease, bruxism, thumb sucking, tongue thrusting.	Regular vision/dental care.
Mental Health	Anxiety >70%, withdrawal, inconsolable crying may be anxiety/depression.	Consider physical problems causing irritability prior to use of psych meds.
Other	- Trofinetide FDA approved 3/23. - May have increased sensitivity to anesthesia.	Consider lower anesthesia dosing, anticipate longer time to awaken.

Reference: Intl Rett Syn Foundation. Comprehensive Care Guidelines, 2024. www.rettssyndrome.org

Summary by CYACC: 2025, updated Sept 2026

