

FACT SHEET

Spinal Muscular Atrophy

INTRODUCTION

This fact sheet is intended to provide an overview of Spinal Muscular Atrophy including common presentations, diagnosis, prognosis, pharmacological management, and physical therapy management of the condition. The information provided can help the physical therapist or physical therapist assistant better understand the complex nature of this condition and plan appropriate examination and intervention activities.

WHAT IS SPINAL MUSCULAR ATROPHY (SMA)?

SMA is a genetic condition that results in degeneration of the anterior horn cells and muscle weakness. SMA is the leading genetic cause of death among infants and toddlers.

QUICK FACTS

- SMA is inherited in an autosomal recessive pattern, meaning that both parents are typically genetic carriers of the condition
- Incidence is 1 in 11,000 live births, carrier frequency is 1 in 40¹⁻³, and the typical recurrence risk for siblings born of the same parents is 1 in 4
- Age of symptom onset is related to severity of phenotype:
 - Type I typically presents in infancy (0-3 months)
 - Type II after the onset of sitting (6-18 months)
 - Type III (after 18 months) after the onset of walking

ETIOLOGY OF SMA

In typically developing children, both SMN1 and SMN2 genes are present on chromosome 5q13 and produce SMN protein.² SMN protein has been identified as a critical component of the RNA spliceosome functioning in the nuclear production of a group of other proteins⁴ and is considered critical to normal development and postnatal maintenance of the motor unit (see FIGURE 1)⁵ SMN is critical in axonal transport and neuromuscular junction function and development, and also plays a role in muscle sarcomeric structure possessing critical binding partners at the M band and I band in the muscle.⁶ The SMN protein is found throughout the body, but is most prevalent in concentration in the spinal cord.

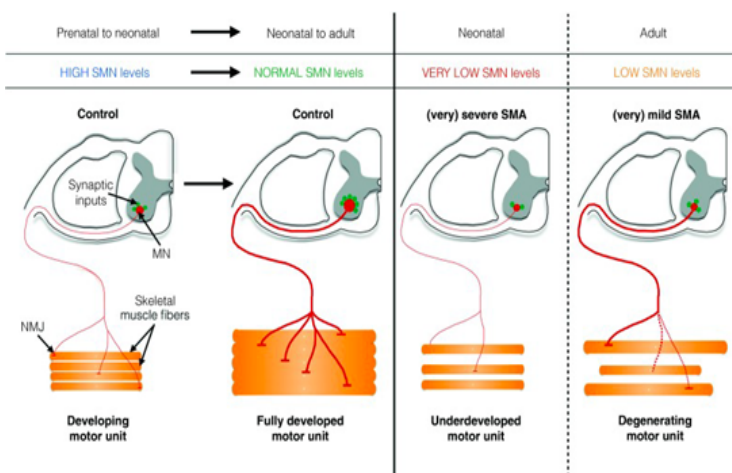
In children with SMA, the SMN 1 gene is mutated and does not produce functional SMN protein² Only the SMN2 gene produces SMN protein, therefore it becomes a modulator of condition severity in SMA. While additional copies of SMN2 may allow for greater ability to compensate for the absence of SMN1, the relationship does not fully predict prognosis or outcome^{7,8} Motor neuron degeneration and atypical development are hallmarks of SMA but the root cause of motor neuron sensitivity to SMN protein depletion is still unknown.

PRESENTATION OF SMA

The natural history of SMA includes presentation at any age, with acute onset of motor weakness and loss of function. Since the approval of several SMN modulating therapies, a new natural history has begun to emerge. In some cases, this includes the hallmark characteristic of proximal weakness, while other presentations include subclinical strength limitations and/or development that appears entirely normal. Newborn screening⁹ or prenatal genetic testing may allow pre-symptomatic treatment; however, often treatment follows symptomatic presentation. Those with more copies of SMN2 and earlier treatment have better motor outcomes.¹⁰⁻¹²

In the untreated natural history, proximal extremity and trunk muscles are most affected, with the diaphragm being relatively spared, even in the most severely affected children. The initial period of acute progressive weakness is followed by a prolonged plateau during which muscle strength and function may be stable. The degree of severity is related to age of onset of weakness, which can range from weakness at birth to adult onset. Minipolymyoclonus, a fine tremor, is often seen in the fingers and fasciculations and tremor are often seen in the tongue. Cognitive function of individuals with SMA is typically unaffected. There is often a striking discrepancy between alertness and cognitive ability and the ability to move in the most severe forms of SMA.¹³

FIGURE 1: Survival Motor Neuron (SMN) Protein may be crucial for normal development and postnatal maintenance of the motor unit⁵



From: D'Ydewall and Sumner, 2015, Neurotherapeutics©

CLASSIFICATION OF SMA

Traditionally childhood onset forms of SMA are classified as one of 3 types with each defined by the maximum motor skill attained (see FIGURE 2). However, with the advent of SMN modulating therapies, often current motor function ability (non-sitter, sitter, and walker) is used as a classification.¹³

- SMA type I: (Werdnig Hoffman Syndrome, acute SMA, infantile-onset SMA): Most severe type; typically presents prior to 6 months; children typically do not attain the ability to sit without assistance. Most common type of SMA, occurring in up to 60% of SMA births
- SMA type II: (Intermediate SMA, juvenile SMA, chronic SMA) Intermediate form; typically presents between 6 and 18 months of age; children achieve the ability to sit and may stand with support at an early age, but never walk without braces or assistance
- SMA type III: (Kugelberg-Welander Syndrome): Mildest form; typically presents after onset of ambulation and after 18 months of age. Children achieve the ability to walk without bracing or assistance at some point; however, loss of motor function (including ambulation) can occur
- Some also describe a type IV (adult onset) and a type 0 with onset at birth

DIAGNOSIS

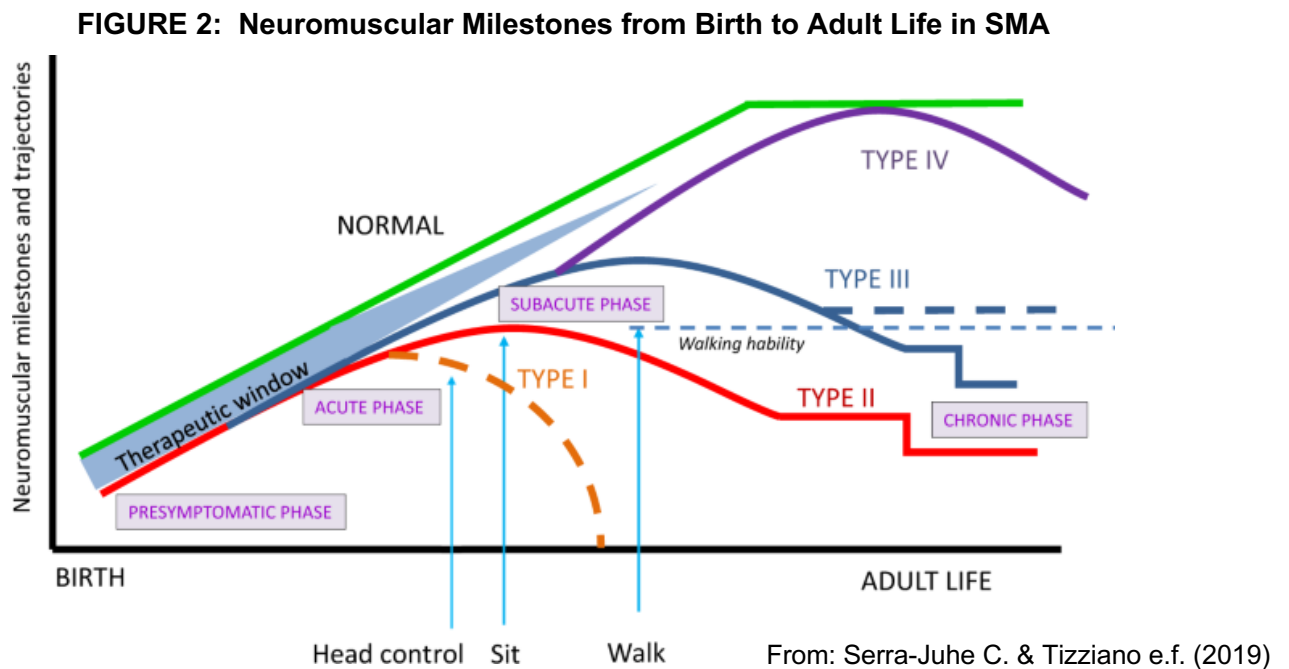
Newborn screening for SMA¹⁴

- SMA was added to the federal Recommended Uniform Screening Panel (RUSP) for newborn screening in 2018. Screening for SMA is now available on Newborn Screening panels in 36 states, and 74% of infants are screened for the disorder in the United States.¹⁴

- Newborn screening allows for early access to treatments which are known to have a greater effect at younger ages.¹⁵

Diagnostic testing findings:

- Genetic testing (blood test): Homozygous mutation typically of exon 7 of the survival Motor Neuron 1 (SMN1) gene on chromosome 5q13, 95% sensitivity with the remaining 5% having undetected uncommon mutations identifiable on follow up testing¹⁶
- EMG: Diminished compound muscle action potential (CMAP), fibrillation potentials, normal nerve conduction velocity (NCV), diminished motor unit number estimation (MUNE), polyphasic potentials
- Muscle ultrasound: fasciculations can be visualized within the muscle¹⁷
- Muscle biopsy: Grouped atrophy (not required for diagnosis)



CHARACTERISTICS OF SMA

Motor:

Progressive weakness, leading to:

- A paucity of overall movement in those who are non-sitters (Type I SMA)
- Decreased active movement, with limited antigravity movement in those who are sitters (Type 2 SMA)
- Decreased mobility
- Typical motor development prior to symptom onset followed by motor delay
- Early hypermobility with contracture development later in disease
- Poor head control common in non-sitters and some weaker sitters
- Muscle fatigue²
- Areflexia or hyporeflexia
- Axillary slip through
- Fasciculation of muscles, most common in tongue
- “Polyminimyoclonus” in the fingers
- Difficulty swallowing and chewing

Postural compensations:¹⁸

- Common resting posture: Excessive lower extremity abduction and external rotation with hip and knee flexion, use of 'stacking maneuvers' to maintain head and trunk control, asymmetric weightbearing, upper extremity pronation with ulnar drift
- Kyphotic sitting posture in those who sit, with scoliosis over time
- Gower's maneuver in children with Type III SMA who transition from the floor to standing

For a more detailed list of biomechanical and compensatory behaviors please see the [Best Practices Toolkit for PTs and Clinical Evaluators in SMA](#)

Cardiorespiratory:

- Restrictive lung disease and respiratory insufficiency which presents initially as nocturnal hypoventilation
- Increased risk for cardiac involvement and in the most severe cases congenital heart disease

Cognitive and sensory:

- Cognitive and sensory systems are typically intact,⁵ though more recently it has become apparent that cognitive delay may be a characteristic of some individuals with SMA type I.¹⁹

At risk for:

- Contractures, osteopenia, scoliosis, kyphosis, hip dislocation, falls and fractures
- Issues with nutrition and weight management

PROGNOSIS

Survival is dependent on severity, age of presentation, management using standard care guidelines, and treatment with disease modifying therapy¹³

SMA type I (non-sitters):

- Survival is typically limited to 18 months with rare exceptions without SMN modulating therapies
- With mechanical ventilation (BiPAP, tracheostomy) and gastrostomy feeding this can be extended²⁰

SMA type II (sitters):

- Variable survival without disease modifying therapy. This is dependent on respiratory compromise and support provided

SMA type III (standers/walkers):

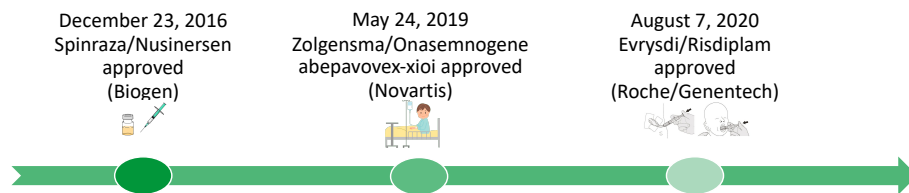
- Typical life expectancy

CHANGING PHENOTYPES WITH PHARMACOTHERAPEUTICS

Decision-making about which SMN modulating therapy is indicated takes place as a part of family-centered specialized care between the child, their caregivers, and the medical team. As of 2020 there are 3 SMN modulating therapy options with FDA approval for SMA (see FIGURE 3).

- Spinraza (Nusinersen) approved for all types of 5q SMA; intrathecal administration three times per year after initial loading doses
- Zolgensma (AVXS101) approved for patients <2 years of age with 5q SMA; one time IV infusion
- Evrysdi (Risdiplam) approved for patients 2 months and older with 5q SMA; daily oral administration

FIGURE 3: FDA Approval Timeline of SMN Modulating Therapies



TESTS AND MEASURES

Consideration of an individual and family’s goals, concerns, and needs, as well as SMA type and current functional level (non-sitter, sitter walker) should guide the selection of outcome measures for those with SMA across the various levels of the ICF (see FIGURE 4).^{18,21}

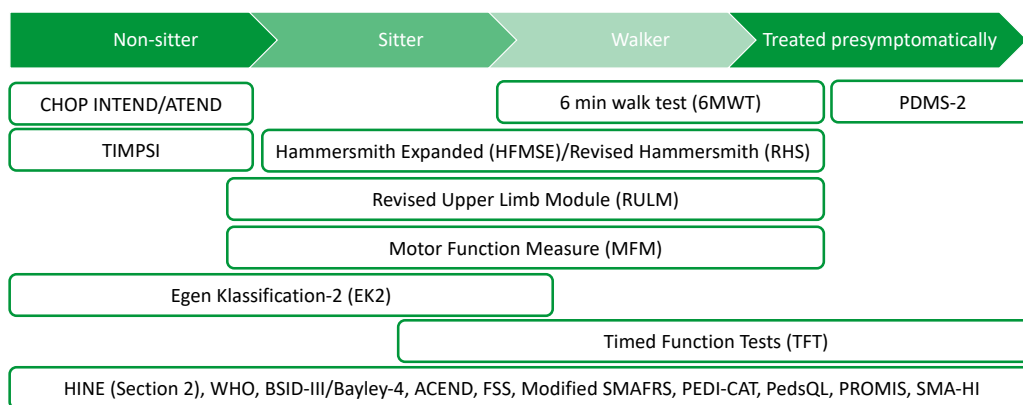
Tests of body functions and structure:

- Manual Muscle Test
- Myometry
- Goniometry
- Pulmonary function tests

Tests of activity and participation:^{18,22}

- Hammersmith Functional Motor Scale-Expanded (HFMS-E)
- Modified Hammersmith Functional Motor Scale (HFMS)
- Revised Hammersmith Scale (RHS)
- The CHOP Infant Test of Neuromuscular Disorders (CHOP-Intend)
- The Test of Infant Motor Performance Screening Items (TIMPSI)
- Hammersmith Infant Neurologic Examination (HINE) Motor Section 2
- Revised Upper Limb Module (RULM)
- Timed tests of function (TFT) (time to walk/run 10m, time to rise to standing from supine on the floor, time to climb 4 steps)
- Activlim
- Adult Test of Neuromuscular Disorders (ATEND)
- Egen Klassifikation-2
- Motor-Function Measure (MFM)
- The 6-minute-walk test (6MWT)
- PedsQL®/PedsQL Neuromuscular Module®
- Assessment of Caregiver Experience with Neuromuscular Disease (ACEND)
- Pediatric Inventory of Disability Evaluation (PEDI/PEDI-CAT)
- Fatigue Severity Scale (FSS)
- Modified SMA-Functional Rating Scale (Modified SMA-FRS)
- Children’s Assessment of Participation and Enjoyment and Preferences for Activities (CAPE-PAC)²³
- Bayley Scales of Infant Motor Development (III)®/Bayley-4®
- Peabody Motor Scales-2®

FIGURE 4: Most Commonly Used Outcomes by SMA Functional Level/Phenotype



PHYSICAL THERAPY INTERVENTIONS²⁴

- Recommended intervention plans should follow SMA standard of care guidelines for stretching, strengthening, aerobic exercise, standing, bracing, and balance^{21,20}
- Maintain flexibility through range of motion/stretching, positioning, bracing, splinting, standing²⁵ programs, and serial casting²¹
- Maintain strength and conserve energy through exercise and activity (this includes play, aquatics, hippotherapy, and developmental exercises)²⁶⁻³²
- Foster good posture, with appropriate seating to optimize alignment³³
- Promotion of weight-bearing to promote bone health^{13,21}
- Foster and maintain movement and mobility to allow for independence, and environmental exploration at younger ages as well as to foster overall health and wellness and participation in activity, adapted sports, and recreation at all ages
- Educate patient and caregivers on the role of assistive technology to maximize activity and participation including:
 - Manual or power wheelchairs or scooters as early as 12 months to 2 years³⁴
 - Stenders or long leg braces to initiate standing for patients with SMA who cannot stand on their own²⁵
 - Adapted computer access or switch toys as appropriate
 - Equipment for ADLs, including: environmental adaptations, bath equipment and mechanical lifts
- Educate patient and caregivers regarding handling, positioning, optimizing potential and safety and preparing for changes during growth

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HELPFUL WEBSITES

- Best Practices Toolkit for Physical Therapists and Clinical Evaluators in SMA. Available at: <https://www.curesma.org/clinical-trial-readiness-toolkits/>
- Cure SMA. Available at: www.curesma.org
- SMA Foundation. Available at: www.smafoundation.org
- Muscular Dystrophy Association. Available at: www.mdaua.org
- SMA Outcomes. Available at: www.smaoutcomes.org
- SMA Common Data Elements (NINDS). Available at: <https://www.commondataelements.ninds.nih.gov/Spinal%20Muscular%20Atrophy>
- STEP IN SMA: Teaching and Excellence for Physiotherapists. Available at: www.STEPINSMA.org
- TREAT NMD Spinal Muscular Atrophy Core Dataset. Available at: <https://treat-nmd.org/patient-registries/treat-nmd-core-datasets/sma-core-dataset/#1596626402330-3004fec9-c9a6>

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Developed by expert contributors Kristin J Krossschell, PT, DPT, MA, Board-Certified Pediatric Clinical Specialist & Allan Glanzman PT, DPT, Board-Certified Pediatric Clinical Specialist. Special thanks to Shree Pandya, PT for her contribution to the previous version of this fact sheet. Supported by the Fact Sheet Committee of APTA Pediatrics.

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