FACT SHEET

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Spinal Muscular Atrophy

What Is Spinal Muscular Atrophy (SMA)?

SMA is a genetic disease that results in degeneration of the anterior horn cells and muscle weakness. SMA is the leading genetic cause of death among infants and toddlers. While some symptomatic treatments are available, there is no specific treatment for the disease itself.

Disease Presentation

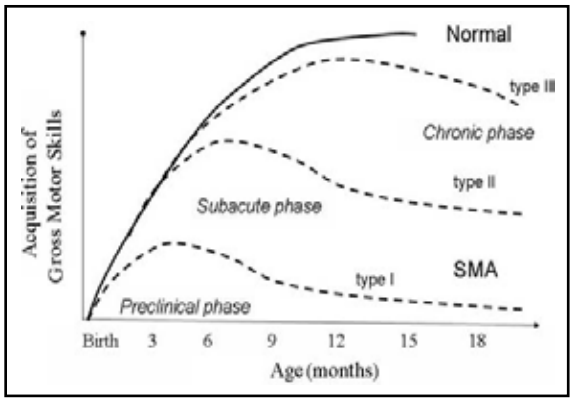
SMA can present at any age with acute onset of motor weakness and loss of function. Proximal limbs, trunk, and intercostal muscles are most affected, with the diaphragm being relatively spared. The initial period of acute weakness is followed by a prolonged plateau during which muscle strength and function may be stable. Tremor and fasciculations are often seen in the fingers and tongue. Cognitive function of children (or individuals) with SMA is typically normal. Some individuals with Type I SMA may have cognitive issues secondary to hypoxic injury. There is often a striking discrepancy between alertness and the ability to move in the more severe forms of SMA.[1-3]

Disease Classification

There are 3 types of childhood onset SMA, which are classified by the maximum motor skill attained:

- **SMA Type I (Werdnig Hoffman Syndrome, acute SMA, infantile-onset SMA)**: Most severe type; children do not attain the ability to sit without assistance. It is also the most common type of SMA; occurring in up to 60% of SMA births (ICD-9 code: 335.0)
- **SMA Type II (intermediate SMA, juvenile SMA, chronic SMA)**: Intermediate form; children achieve the ability to sit and may stand with support at an early age, but they do not walk without braces or assistance (ICD-9 code: 335.10)
- **SMA Type III (Kugelberg-Welander Syndrome)**: Mildest form; children achieve the ability to walk without bracing or assistance at some point; however, loss of motor function (including ambulation) can occur (ICD-9 code: 335.11)

Figure 1. Acquisition of Gross Motor Milestone in Controls Versus Infants With Spinal Musclar Atrophy[1]



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Characteristics

Motor (Figure 1):

Progressive weakness,[2-8] leading to:

- A paucity of overall movement in those with Type I SMA
- Decreased active movement, with limited ability for antigravity movement in those with Type II SMA
- Decreased mobility

- Motor delay
- Early hypermobility with contracture development later in disease
- Poor head control common in those with Type I and some with Type II SMA
- Muscle fatigue[9]
- Areflexia or hyporeflexia
- Axillary slippage
- Fasciculation of muscles, most common in tongue (in most cases noted visually as "polyminimyoclonus" in the tongue; may need ultrasound to visualize) and fingers

Postural Compensations:

- Common resting posture: Excessive lower-extremity abduction and external rotation with hip and knee flexion; upper-extremity pronation with ulnar drift
- Kyphotic sitting posture in those that are able to sit
- Gower's maneuver in children with Type III SMA who are able to transition from floor to standing

Cardiorespiratory:

- Restrictive lung disease and respiratory insufficiency that presents initially as nocturnal hypoventilation[10]
- At risk for cardiac involvement[3,8,10,12]

Cognitive and Sensory:

- Cognitive and Sensory systems are intact[13]

At Risk For:

- Osteopenia,[14] scoliosis,[15-18] hip dislocation,[19] falls and fractures[3]
- Issues with nutrition and weight management[8,20,21]

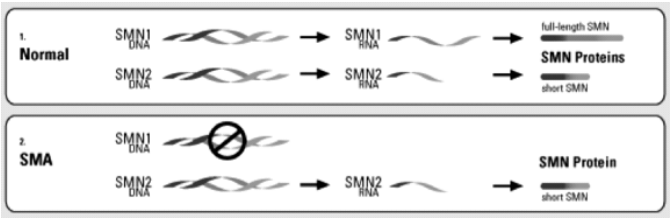
Quick Facts

- SMA is the second most common neuromuscular disease in childhood
- Recessive inheritance; parents are typically carriers and typical recurrence risk is 1 in 4
- Incidence is between 1 in 6,000 to 10,000; carrier frequency 1 in 57
- Age of onset is related to severity of phenotype[3,22]
- 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

Survival

- SMA is a result of homozygous deletion of what is called the Survival of Motor Neuron (SMN) 1 protein (Figure 2)

Figure 2. Model of Normal and SMA Survival of Motor Neuron (SMN)1 Protein



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- In the typically developing child, both SMN1 and SMN2 genes are present on chromosome 5q13 and produce SMN protein.
- SMN protein is ubiquitously expressed and considered essential to life. It has been identified as a critical component of the RNA spliceosome and may have other cellular functions.
- In the child with SMA, the SMN1 gene is mutated and does not produce functional SMN protein.

- The SMN2 gene is a modulator of disease severity in SMA, and the child with SMA relies on the SMN2 gene to produce SMN protein. 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.

- The biological reason for motor neuron sensitivity to SMN protein depletion is still unknown.

Survival Is Dependent on Severity and Age of Presentation as Well as Treatment Choices[3]:

SMA Type I:

- Survival is typically limited to 18 months with rare exceptions

- With mechanical ventilation (BiPAP, tracheostomy) and gastrostomy feeding, life expectancy can be extended[23]

SMA Type II:

- Variable survival that is dependent on respiratory compromise and support provided

SMA Type III:

- Normal life expectancy

SMA Is Not to Be Confused With:

- Muscular dystrophies and myopathies

- Congenital hypotonia

- Other diseases of the peripheral nerves

Diagnostic Criteria

- **Genetic testing (blood test)**: Homozygous deletion of exon 7 of the SMN1 gene[3]

- **EMG**: Diminished compound motor action potential (CMAP), normal nerve conduction velocity (NCV)[3]

- **Muscle biopsy**: Grouped atrophy (not required for diagnosis)[2]

Tests and Measures[3,8]

Tests of Body Functions and Structure:

- Manual Muscle Test[24]

- Myometry[25,26]

- Goniometry[27]

- Pulmonary function tests[10]

Tests of Activity and Participation:

- Hammersmith Functional Motor Scale (HFMS)[28,29]

- Modified Hammersmith Functional Motor Scale-Extend (MHFMS-Extend)[30-33]

- Expanded Hammersmith Functional Motor Scale[33,34]

- The Test of Infant Motor Performance Screening Items (TIMPSI)[35]

- The CHOP Infant Test of Neuromuscular Disorders (CHOP Intend)[35-36]

- Gross Motor Function Measure (GMFM)[38,39]

- Timed tests of function (time to walk/run 30 feet or 10 meters; time to rise to standing from the floor; time to climb steps)[39,40]

- North Star Ambulatory Assessment for SMA (NSAA-SMA)[42]

- Motor-Function Measure (MFM)[43,44]

- EK Scale[45]

- 6-Minute-Walk Test[46,47]

- Activlim[48,49]

- Pediatric Inventory of Disability Evaluation (PEDI)[50]

- Children's Assessment of Participation and Preferences for Activities (CAPE-PAC)[51]

- PedsQL©[52-55]

- PedsQL Neuromuscular Module©[56]

Intervention

Why Is It Important for Children Diagnosed With SMA to Receive Intervention?[3,8]

To 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.

Intervention Strategies

- Gait training for ambulatory patients to minimize safety risks and optimize energy expenditure[57]
- An assistive technology evaluation to maximize activity and participation. This may include:
    - ¤ Manual or power wheelchairs or scooters as early as 18 months to 2 years[58]
    - ¤ Standers or long leg braces to initiate standing in the second year for patients with SMA Type II[59]
    - ¤ Adapted computer access or switch toys as appropriate
    - ¤ Equipment for ADLs, including environmental adaptations, bath equipment, and mechanical lifts
- Patient/caregiver education regarding handling, positioning, optimizing potential and safety, and preparing for changes with aging.[60]
- The maintainence of strength and the conservation of energy through exercise and activity (this includes play, aquatic therapy,[61] hippotherapy, and developmental exercises).
- The maintainence of flexibility through range of motion/stretching, positioning, bracing, splinting, standing programs, and serial casting.
- The faciliation of good posture, with appropriate seating to optimize alignment.
- The promotion of weight-bearing exercises to optimize bone health.

Helpful Websites

- **Families of SMA (FSMA)**: www.fsma.org
- **SMA Foundation**: www.smafoundation.org
- **Muscular Dystrophy Association (MDA)**: www.mdausa.org
- **SMA outcomes**: www.smaoutcomes.org
- **TREAT NMD Registry of Outcome Measures (ROM)**: www.researchrom.com/masterlist

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