Understanding Spinal Muscular Atrophy (SMA)

Fast Facts

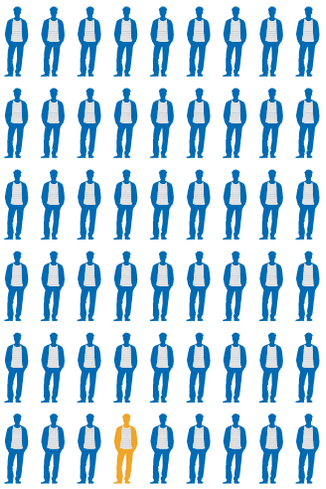
SMA affects approximately

1 in 10,000

live births worldwide[1]

SMA can affect

Any Race or Sex



~1 in 54

People carry the genetic defect[2]

When both parents are carriers, their baby has a **25% chance** of having SMA[1]

Spinal Muscular Atrophy

SMA is a rare and devastating genetic disease that leads to progressive muscle weakness, paralysis and, when left untreated in one of its most severe forms, death. It is caused by a lack of a functional *survival motor neuron 1* (*SMN1)* gene, which leads to an insufficient amount of SMA protein resulting in the rapid and irreversible loss of motor neurons, affecting all muscle functions, including breathing, swallowing and basic movement.[1,3]

Many primary care physicians are unfamiliar with SMA, which leads to delays in diagnosis and treatment due to a "wait and see" approach when patients present with initial symptoms or exhibit lack of motor milestone achievement. For this reason, SMA experts recommend universal newborn screening to facilitate identification, diagnosis, treatment and supportive care as early as possible to halt irreversible motor neuron loss and disease progression.[4]

The severity of SMA varies across a spectrum of types that correspond to the number of copies *SMN2* gene, the "backup gene" that produces a small fraction (~10%) of functional SMN protein compared with *SMN1*. [5]

Disease Incidence: [6,7]

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Type 1

Typically have 1-2 copies of *SMN2*

If left untreated, SMA Type 1 leads to death or the need for permanent ventilation by the age of two in more than **90% of cases**.[8]

Degeneration and loss of motor neurons start shortly before birth and escalate quickly, with **>95% loss by 6 months of age**.[3,13,14]

Untreated infants with SMA Type 1 will never be able to achieve normal developmental milestones, like sitting without support.[9]

They also experience:

- Difficulty breathing and swallowing[10]
- Poor head control[11]
- Worsening muscle weakness and poor muscle tone (hypotonia or "floppy baby"), and “frog-leg” position.[9,10,12]

Type 2

Typically have 3-4 copies of *SMN2*

Signs are disabling and appear between **6 and 18 months of age**.[9]

More than 30% will die by age 25.[15]

Untreated children with SMA Type 2 will never walk without support and need a wheelchair.[11]

Additionally:

- They will not be able to stand without support[9]
- They may be able to sit independently early in development, but often lose this ability by their mid-teens[16]
- They may experience trembling in their fingers[15,16]
- They may experience skeletal abnormalities, such as scoliosis and hip dislocation[15,16]
- Difficulty with feeding and breathing often develop later in the course[15,16]

Type 3

Typically have 3-4 copies of *SMN2*

Signs and symptoms typically appear **in early childhood to early adulthood**.[9]

Untreated individuals with SMA Type 3 have difficulty walking, running and going up and down stairs.[17]

Additionally:

- They may lose the ability to stand or walk without support over time[9]
- Their legs are more severely affected than their arms[17]

1.National Organization for Rare Disorders (NORD). Spinal muscular atrophy. http://rarediseases.org/rarediseases/spinal-muscular-atrophy/. Accessed January 31, 2022. **2.** Mendell JR, et al. Single-dose gene replacement therapy for spinal muscular atrophy. New Eng J Med. 2017;377(18)1713-1722. **3.** Anderton RS and Mastaglia FL. Advances and challenges in developing a therapy for spinal muscular atrophy. Expert Rev Neurother. 2015;15(8):895-908. **4.** Lin CW, et al. Delay in diagnosis of spinal muscular atrophy: A systematic literature review. Pediatr Neurol. 2015 Oct;53(4):293-300. **5.** Lorson CL, et al. Spinal muscular atrophy: mechanisms and therapeutic strategies. Hum Mol Genet. 2010; 19(R1): R111-8. **6.** Verhaart IEC, Robertson A, Wilson IJ, et al. Prevalence, incidence and carrier frequency of 5q–linked spinal muscular atrophy – a literature review. Orphanet J Rre Dis. 2017;4;12(1):124. **7.** Data on file. **8.** Finkel RS, McDermott MP, Kaufmann P. et al. Observational study of spinal muscular atrophy type I and implications for clinical trials. Neurology. 2014;83(9):810-7. **9.** Farrar MA, et al. Emerging therapies and challenges in spinal muscular atrophy. Ann Neurol. 2017;81(3):355-368. **10.** Spinal muscular atrophy 1. National Center for Advancing Translational Sciences. Genetic and Rare Diseases Information Center. https://rarediseases.info.nih.gov/diseases/7883/spinal-muscularatrophy-1. Accessed January 31, 2022. **11.** d'Ydewalle C, Sumner C. Spinal muscular atrophy therapeutics: where do we stand? 2015;12:303-316. **12.** Arnold WD, et al. Spinal muscular atrophy: diagnosis and management in a new therapeutic era. Muscle Nerve. 2015;51(2):157-67. **13.** Swoboda K, et al. Perspectives on clinical trials in spinal muscular atrophy. J Child Neurol. 2017;22(8):957-966. **14.** Bromberg MB. Updating motor unit number estimation (MUNE). Clin Neurophysiol. 2007;118(1):1-8. **15.** Darras BT, Finkel RS. Spinal muscular atrophy. Chapter 25 - Natural history of spinal muscular atrophy. October 2016. **16.** Spinal muscular atrophy 2. National Center for Advancing Translational Sciences. Genetic and Rare Diseases Information Center. https://rarediseases.info.nih.gov/diseases/4945/spinal-muscular-atrophy-type-2. Accessed January 31, 2022. **17.** Spinal muscular atrophy 3. National Center for Advancing Translational Sciences. Genetic and Rare Diseases Information Center. https://rarediseases.info.nih.gov/diseases/198/spinal-muscular-atrophy-type-3 Accessed January 31, 2022.

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