Spinal Muscular Atrophy

Carrier Screening and Prenatal Diagnosis

Integrated GENETICS
LabCorp Specialty Testing Group

Your Partner for Genetic Testing

Integrated Genetics offers carrier screening and prenatal diagnosis for spinal muscular atrophy (SMA), the most common inherited cause of early childhood mortality.

This test enables couples who are planning a pregnancy, or who are already pregnant, to determine if they are carriers and at risk of having a baby with SMA.

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Carrier Screening and Prenatal Diagnosis

2nd Most Common Lethal Autosomal Recessive Disease After CF

Spinal Muscular Atrophy (SMA) is the most common inherited cause of early childhood mortality. It is the second most common lethal autosomal recessive disease in the U.S. after cystic fibrosis.[1]

SMA has been known as congenital axonal neuropathy, arthrogryposis multiplex congenita (prenatal SMA), Werdnig-Hoffman disease (SMA type I), Dubowitz disease (SMA type II) and Kugelberg-Welander disease (SMA type III).

Spinal Muscular Atrophy	
Inheritance	If both parents are carriers there is a 25% chance for each child to be affected.
Carrier Frequency	■ SMA has an ~1 in 54 carrier frequency ■ Affects all racial and ethnic groups, and as with most genetic diseases, there is some ethnic variability in carrier frequencies ■ SMA carrier risk in people with no family history of SMA ● Caucasian 1 in 47 ● Asian Indian 1 in 52 ● Asian 1 in 59 ● Ashkenazi Jewish 1 in 67 ● Hispanic 1 in 68 ● African American 1 in 72
Incidence	Has an estimated incidence of 1 in 11,000 births

Carrier frequencies/detection rates are calculated based on analysis of allele frequencies among >72,000 individuals.[2]

Clinical Characteristics

SMA is characterized by the progressive degeneration of the lower motor neurons, muscle weakness and, in the most common type, ***respiratory failure by age two***. The disease most severely affects the muscles responsible for crawling, walking, swallowing and head and neck control. Given the severity and overall frequency of this disease, the American College of Medical Genetics (ACMG) recommends SMA carrier screening be offered before conception or early in pregnancy to everyone.[3]

Every day a child who will develop SMA is born in the United States.

ACMG Guidelines for Spinal Muscular Atrophy

"Because SMA is present in all populations, carrier testing should be offered to all couples regardless of race or ethnicity. Ideally, the testing should be offered before conception or early in pregnancy. The primary goal is to allow carriers to make informed reproductive choices."[3]

Clinical Classification

Testing of the disease-causing gene, *SMN1*, does not provide information about the clinical severity (SMA type) for which the fetus is at risk. The clinical classification system below is useful for prognosis and management. Of the types of SMA with childhood onset, type I is the most severe and most frequent, affecting 60–70%.[4]

SMA Type	Age of Onset	Typical Life Span	Key Clinical Characteristics/Milestones
Prenatal	Prenatal	<6 months	■ No milestones achieved ■ Severe weakness ■ Joint contractures ■ Early respiratory failure
I	Birth – 6 months	<2 years	■ Most severe form of childhood SMA ■ Sit with support only ■ Early respiratory failure
II	6 – 12 months	70% alive at 25 years	■ Independent sitting when placed, with loss of this ability by the mid-teens
III	After 12 months	Normal	■ Ambulation, with loss of this ability as disease progresses
IV	Adulthood	Normal	■ Ambulation, with loss of this ability as disease progresses

Derived from data included in reference 5.

The Most Common Inherited Cause of Early Childhood Mortality

Accurate, Fast Testing for SMA

- Approximately 95% detection rate, varies by ethnicity[2] (see table below)
- Fast 5–8 day turnaround time
- Prenatal diagnosis by CVS or amniocentesis
- Expert geneticists available for physician consultation

Risk Reduction for Individuals with No Family History of SMA

Ethnicity	Detection Rate	*A Priori* Carrier Risk	Reduced Carrier Risk for 2 Copy Result	Reduced Carrier Risk for ≥ 3 Copy Result
Caucasian	94.8%	1:47	1:834	1:5,600
Ashkenazi Jewish	90.5%	1:67	1:611	1:5,400
Asian	93.3%	1:59	1:806	1:5,600
Hispanic	90.0%	1:68	1:579	1:5,400
Asian Indian	90.2%	1:52	1:443	1:5,400
African American	70.5%	1:72	1:130	1:4,200
Mixed Ethnicities	For counseling purposes, consider using the ethnic background with the most conservative risk.			

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To learn more about SMA testing, please visit www.mytestingoptions.com and www.integratedgenetics.com or call (800) 848-4436.

Additional SMA Resources:

- GeneTests: geneclinics.org/profiles/sma
- Claire Altman Heine Foundation: www.preventsma.org
- Families of Spinal Muscular Atrophy: www.fsma.org

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1) Smith, M. et al., Population screening and cascade testing for carriers of SMA. *Euro J Hum Genet* 2007; 15:759-766.
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3) Prior, T.W., ACMG Practice Guidelines: Carrier screening for spinal muscular atrophy. *Genet Med* 2008; 10:840-842.
4) Meldrum, C. et al., Spinal muscular atrophy genetic counseling access and genetic knowledge: Parents' Perspectives. *J Child Neurol* 2007; 22:1019-1026.
5) Prior, T.W. and Russman, B.S., Spinal Muscular Atrophy. www.ncbi.nlm.nih.gov/books/NBK1352/

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