Spinal Muscular Atrophy
Carrier Screening and Prenatal Diagnosis

The Most Common Inherited Cause of Early Childhood Mortality

Accurate, Fast Testing for SMA

- Approximately 95% detection rate, varies by ethnicity² (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

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>A Priori Carrier Risk</th>
<th>Reduced Carrier Risk for 2 Copy Result</th>
<th>Reduced Carrier Risk for ≥ 3 Copy Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pan-ethnic</td>
<td>1:54</td>
<td>1:527</td>
<td>1:5400</td>
</tr>
<tr>
<td>Caucasian</td>
<td>1:47</td>
<td>1:834</td>
<td>1:5600</td>
</tr>
<tr>
<td>Ashkenazi Jewish</td>
<td>1:67</td>
<td>1:611</td>
<td>1:5400</td>
</tr>
<tr>
<td>Asian</td>
<td>1:59</td>
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</tr>
<tr>
<td>Hispanic</td>
<td>1:68</td>
<td>1:579</td>
<td>1:5400</td>
</tr>
<tr>
<td>Asian Indian</td>
<td>1:52</td>
<td>1:443</td>
<td>1:5400</td>
</tr>
<tr>
<td>African American</td>
<td>1:72</td>
<td>1:130</td>
<td>1:4200</td>
</tr>
<tr>
<td>Mixed Ethnicities</td>
<td>For counseling purposes, consider using the ethnic background with the most conservative risk.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

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

REFERENCES:

LabCorp Client Services 800-345-GENE (4363)
Spinal Muscular Atrophy
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. 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).

Clinical Characteristics

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

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.

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."

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%.

Clinical Characteristics

SMA Type | Age of Onset | Typical Life Span | Key Clinical Characteristics/Milestones
--- | --- | --- | ---
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

SMA type I
- No milestones achieved
- Severe weakness
- Joint contractures
- Early respiratory failure

SMA type II
- Most severe form of childhood SMA
- Sit with support only
- Early respiratory failure

SMA type III
- Independent sitting when placed, with loss of this ability by the mid-teens

SMA type IV
- Ambulation, with loss of this ability as disease progresses

Carrier Screening

If both parents are carriers there is a 25% chance for each child to be affected. 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.

Carriers of SMA have decreased SMN1 allele copy numbers that can be detected and quantitated using laboratory techniques.

From data included in reference 5.
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SMA Type | Age of Onset | Typical Life Span | Key Clinical Characteristics/Milestones
--- | --- | --- | ---
I | Birth – 6 months | <2 years | Most severe form of childhood SMA
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
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- Prenatal
- Type I: Severe weakness, Joint contractures, Early respiratory failure
- Type II: Most severe form of childhood SMA, Sit with support only, Early respiratory failure
- Type III: Independent sitting when placed, with loss of this ability by the mid-teens
- Type IV: Ambulation, with loss of this ability as disease progresses

Derived from data included in reference 5.
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