Spinal Muscular Atrophy Information Sheet for Health Care Providers

What is Spinal Muscular Atrophy?

Spinal muscular atrophy (SMA) is a rare genetic disease affecting about one in every 10,000 babies. SMA results in muscle weakness and atrophy. The 4 main types of SMA are defined by the age of symptom onset and the highest level of motor skills (for example sitting, crawling, walking) that the baby or child is able to achieve.

- Babies with SMA type 1 are weak and are unable to sit unassisted. They have symptoms apparent in the first 6 months of life and rarely survive beyond 2 years of age.
- Children with SMA type 2 can sit independently but do not walk. They have symptoms apparent from 6-18 months old.
- Children with SMA type 3 can walk and sit independently but start having muscle weakness and wasting (atrophy) in childhood, after 18 months of age.
- People with SMA type 4 do not have symptoms until adulthood

How is SMA inherited?

- SMA is caused by alterations to the SMN1 (survival motor neuron 1) gene and is inherited in an autosomal recessive manner.
    - When a baby is born with no working copies of the SMN1 gene then they can develop SMA
    - In the majority (~97%) of cases, SMA is caused by deletions in the SMN1 gene; in the remainder of cases, it is caused by other types of genetic variants in the SMN1 gene.
- The type of SMA depends upon the number of copies of another gene, SMN2. People can have 1 to 6 copies of the SMN2 gene. The higher number of SMN2 copy numbers, the less severe the symptoms.
- The table below gives the chance of having each type of SMA depending upon the SMN2 copy number. For example, a baby found to have 1 copy of SMN2 has a 96% chance of having SMA type 1 and a 4% chance of having SMA type 2.

SMA type	SMN2 copy number			
	1	2	3	4
SMA type 1	96%	79%	15%	1%
SMA type 2	4%	16%	54%	11%
SMA type 3	0%	5%	31%	88%*

***Note that 88% includes SMA types 3 and 4.**

How does NSO screen for SMA?

- To detect SMA, NSO screens the dried blood sample for deletions in the SMN1 gene. This means newborn screening in Ontario is not able to detect forms of SMA caused by other genetic variants in the SMN1 gene.
- By testing for SMN1 gene deletions, >99% of SMA type 1 and 2 cases and >97% of SMA type 3 cases can be detected through newborn screening. SMA type 4 will also be detected if caused by SMN2 copy numbers of 4 or less.
- It is expected that approximately 15 babies with SMA will be identified through newborn screening each year in Ontario.

What does a screen positive result for SMA mean?

- NSO reports out samples as screen positive when both copies of the SMN1 gene have a deletion and 1, 2, 3 or 4 copies of the SMN2 gene are detected.
- The likelihood is very high that an infant with a screen positive result will be confirmed to have a form of SMA.

- NSO refers infants with screen positive results to their closest newborn screening Regional Treatment Centre for follow-up.
- Confirmatory testing for SMA involves blood tests, a physical exam and an appointment with specialists, including a pediatric neurologist, who will likely discuss management and treatment options.

How is SMA managed and treated?

- In Ontario, treatment with the medication Nusinersen (Spinraza) is approved for patients with SMA who have 1, 2 or 3 copies of the SMN2 gene as these infants are expected to have SMA types 1, 2 or 3.
    - Nursinersen is provided at a medical facility or hospital by a physician
    - Treatment with Nusinersen is administered through a lumbar puncture
    - In the first year of life, six treatments are required. After the first year, treatment is given 3 times per year, for life.
    - Nusinersen can stop the progression of SMA if started early. Without treatment, the more severe, early onset forms of SMA (particularly type 1) will lead to death in the first year or two of life.
- Gene therapy (Zolgensma) for SMA is being developed but is not yet approved for use in Canada. It may be available on a compassionate basis through Global Access Program, however this cannot be guaranteed.
- Infants with 4 or more copies of the SMN2 gene will be monitored regularly for symptoms. Individuals with SMN2 copy numbers of 4 or more are expected to have SMA types 3 or 4, but some children may develop type 2. If symptoms develop, your child's specialist will discuss treatment options available.

How do I get screening results?

- From mid-January to late July 2020, infants with screen positive results were referred to a Newborn Screening Regional Treatment Centre for follow-up and screen negative results were available by request from NSO.
- Starting in late July 2020, screen negative results for SMA will be reported out as part of the routine newborn screening report that NSO issues to the ordering healthcare provider and/or submitting institution.
- Negative screening results do not provide information regarding a child's carrier status for SMA; such information is considered incidental to the newborn screen. If you (or parents) are interested in obtaining carrier status for SMA for a child in your care, please contact NSO directly with these requests.

More questions?

- Please contact NSO at newbornscreening@cheo.on.ca or 613-738-3222 if you have additional questions regarding newborn screening for SMA.