Spinal Muscular Atrophy (SMA)

Definition:

Spinal Muscular Atrophy (SMA) is a genetic disorder that affects the control of muscle movement due to the loss of specialized nerve cells called motor neurons. This loss of motor neurons causes weakness and atrophy resulting from progressive degeneration. SMA affects muscles used for activities such as crawling, walking, sitting up, and controlling head movements. Severe cases of SMA affect the muscles used for breathing and swallowing.

Diagnosis:

Confirmatory genetic testing of *SMN1* and *SMN2* genes will be offered by the Newborn Screening Program. To establish the extent of disease and needs of an individual diagnosed with SMA, the specialty care center may perform additional nutrition and respiratory assessments.

How is it inherited:

SMA is inherited in an autosomal recessive manner.

A couple who already has a child with SMA has an approximately 25% chance of having another affected child, a 50% chance of having a child who is an asymptomatic carrier, and an approximately 25% chance of having a child unaffected by SMA and who is not a carrier.

However, about 2% of affected individuals have a *de novo SMN1* variant on one allele. This means that only one parent is a carrier of the *SMN1* variant., and therefore future pregnancies are not at a 25% risk for SMA.

Newborn screening:

- **Incidence**: The overall incidence of SMA in NYS is approximately 20-30 per 235,000 births a year.
- **New York State Method of Screening (First Tier)**: Screening for SMA is accomplished by performing *SMN1* exon 7 deletion analysis. Homozygous deletion of exon 7 is the most common cause of SMA. Parents should not be told that a negative screen rules out SMA. This testing does not identify other types of mutations.
- **Second Tier Screening**: All specimens which are found to be homozygous for the exon 7 deletion will then undergo *SMN2* dosage

analysis. This testing aids in prediction of age at onset and disease course.

- **Testing can be affected by**: N/A
- **Interpretation/reporting of data**: Results are reported as within acceptable limits, repeat specimen required, or as a referral. Prompt consultations with specialists are required for each referral. When homozygous *SMN1* exon 7 deletions are identified, it is usually consistent with a diagnosis of SMA and the baby must be referred to an accredited Neuromuscular Specialty Care Center. Individuals with higher *SMN2* copy numbers may have a milder phenotype.
- **Referral to Specialty Care Center**: Patients with an abnormal newborn screen for SMA are referred to a Specialty Care Center for evaluation by a neuromuscular specialist trained in the diagnosis and treatment of SMA.

Prognosis:

Prognosis is variable and dependent on multiple factors, including the subtype of disease.

Symptoms:

The symptoms of SMA vary in terms of age of onset and severity.

Type 1: Diagnosed within the first 6 months of life. This type is considered the most severe and common, occurring in about 60% of cases. Symptoms include: muscle weakness, difficulty breathing, coughing, and swallowing. Without treatment, survival beyond two years of age is rare.

Type 2: Diagnosed after 6 months of age, usually following failure to achieve motor function milestones. This type affects about 30% of SMA cases. Those with type 2 are able to sit up (may need assistance sitting), but are unable to walk and require a wheelchair for mobility.

Type 3: Diagnosed after 18 months of age up into late teenage years. It affects about 10% of SMA cases. Those affected may initially be able to walk, but this can deteriorate over time, making the use of a wheelchair common.

Type 4: Diagnosed in adulthood after age 18. This type is very rare, only affecting less than 1% of SMA cases. Those affected usually have mild motor impairment.

Symptoms in carriers:

Carriers of SMA do not have symptoms. Carriers of SMA will not be detected by the newborn screen.

Treatment:

At this time the only FDA-approved treatment for SMA is the medication Spinraza (nusinersen). This medication improves SMN protein expression using synthetic genetic material to fix splicing errors. Other clinical trials investigating additional treatments, including gene therapy, are ongoing.

Educational materials:

More information:

http://www.curesma.org/documents/advocacy-documents/ny-state-fact-sheet.pdf

https://ghr.nlm.nih.gov/condition/spinal-muscular-atrophy

https://www.ncbi.nlm.nih.gov/books/NBK1352/