SPINAL MUSCULAR ATROPHY (SMA) UPDATE IN BEST PRACTICES SUMMARY: RECOMMENDATIONS FOR DIAGNOSIS CONSIDERATIONS

Introduction

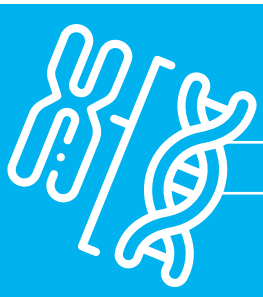
The diagnosis of SMA has improved over time. Historically, the diagnosis of SMA was based on symptoms of weakness, testing of nerve function, and a muscle biopsy. When the gene for SMA was discovered, Survivor Motor Neuron 1 (*SMN1*), the diagnosis of SMA was streamlined to a blood test for the gene that causes SMA. This testing diagnoses 95% of people with SMA. Following the approval of treatments for SMA, using this blood test for screening, babies born with SMA are diagnosed shortly after birth through nationwide testing called newborn screening.

How were the recommendations developed?

A workgroup of healthcare professionals from the U.S. and Western Europe met to review how SMA is diagnosed today compared to the last recommendations for SMA care in 2018. A workgroup of SMA community members shared their experiences on diagnosis, resources, and information that would be helpful during diagnosis to make informed decisions. The information gathered led to the following recommendations developed and published for the SMA community. The two areas ranked as high priority to update SMA diagnosis were newborn screening for SMA and diagnosing adult-onset SMA.

Core Recommendation

The workgroups strongly agreed that individuals with SMA and caregivers are essential partners in health care and must be informed and involved at all levels throughout the diagnosis, care, and treatment decision-making process.



GENETICS

SMA is caused by a mutation in the survival motor neuron gene 1 (*SMN1*). This gene produces a protein called survival motor neuron protein (SMN protein) that is critical to the function of the nerves that control our muscles. These nerve cells cannot properly function without it, leading to muscle weakness.

Most people have two copies of the *SMN1* gene. SMA occurs when both of an individual's *SMN1* copies have missing or mutated segments.

~3-5% of infants with SMA will not be identified by current usual SMA genetic testing because they have a point mutation on one *SMN1* gene. This point mutation can be found by further testing with *SMN1* gene sequencing.

What is Newborn Screening?

Newborn Screening are tests completed shortly after birth. These tests find conditions that if diagnosed and treated early, can dramatically improve a child's health and survival. Early detection of suspected SMA using newborn screening allows for prompt diagnosis, care, and treatment even before symptoms appear. With early diagnosis and treatment, infants with SMA will have the best chance for a healthier life.

During newborn screening, a small amount of blood is taken from the baby's heel and sent to a lab for testing. This blood spot is then analyzed to look for the genes that cause SMA.

What happens after Newborn Screening?

The process for SMA newborn screening includes several health care provider teams. Each team has unique responsibilities. The workgroups recommended the following responsibilities for each team of health care professionals to ensure that SMA newborn screening is as efficient as possible to identify and treat infants identified by newborn screening:

Public Health NBS Laboratories that run the tests for newborn screening should help identify the SMA specialty care centers in their state that can provide knowledgeable health care. Public health laboratories should notify the baby's primary care provider on the same day the results are available and ideally also notify the SMA specialty care provider. Public health NBS labs should check that a patient with a positive newborn screening result had additional testing to confirm the diagnosis of SMA, that they were seen in an SMA clinic, that treatment was discussed, and the family has a care plan.

The Primary Care Provider upon learning about the positive newborn screening test result for SMA should urgently notify the infant's caregivers/ family of the results, refer the infant to an SMA specialty care center and assist with scheduling the appointment to occur within 2-3 days.

The SMA specialty care center team should schedule the infant's first clinic visit to occur within 2-3 days of the positive SMA newborn screen test result.

PRENATAL TESTING

Prenatal tests are medical tests completed during pregnancy. They may be used to determine if an unborn baby has inherited a genetic disorder. After discussing with their doctor, some families may choose this type of testing if their child is known to be at risk for SMA.

Even when prenatal testing is completed, a child will be tested after birth to confirm the diagnosis of SMA and the number of *SMN1* and *SMN2* gene copies.

What happens at the first clinic visit to a SMA Specialty Care Center?

The workgroups recommended that during the first clinic visit after a positive SMA newborn screening test result, healthcare providers should determine whether the child has any symptoms of SMA. This will include asking questions about the infant's birth and development, including any signs of weakness such as decreased or difficulty moving arms or legs, difficulty feeding, or difficulty breathing, and examining the child for early signs or symptoms of SMA. The health care team will share their findings with the family. Information about SMA will be provided, including resources both written and online. Key takeaways include understanding that SMA is a severe disease, treatment options are available, and treatment is not a cure.

The health care team will discuss treatment options, including each treatment's description, how it helps, the risks and benefits, and any additional tests to check for side effects over time. Tests will be ordered (blood work) to confirm the diagnosis of SMA and other tests that may be needed before prescribing a medication or treatment. The provider may prescribe treatment at this visit. Several health care providers may be involved in the first visit. See below. The health care team will work with the patient and family to develop the care plan and goals for follow up clinic visits. The family is encouraged to ask questions. The clinic team should provide contact information for additional questions and a person who will help coordinate and schedule clinic visits and tests. A follow up clinic visit should be scheduled before leaving the clinic.

What's next?

The follow-up visit at the SMA specialty clinic generally includes asking more questions and examining the child for their progress and any changes since the last visit. Tests to assess motor function and strength may be completed and available test results will be reviewed. Information about SMA will be discussed again to answer any questions. SMA specialty care centers may also order medication to treat SMA.

When the SMA diagnosis is confirmed, what will care look like?

The family and care team will determine a treatment plan. This plan should include:

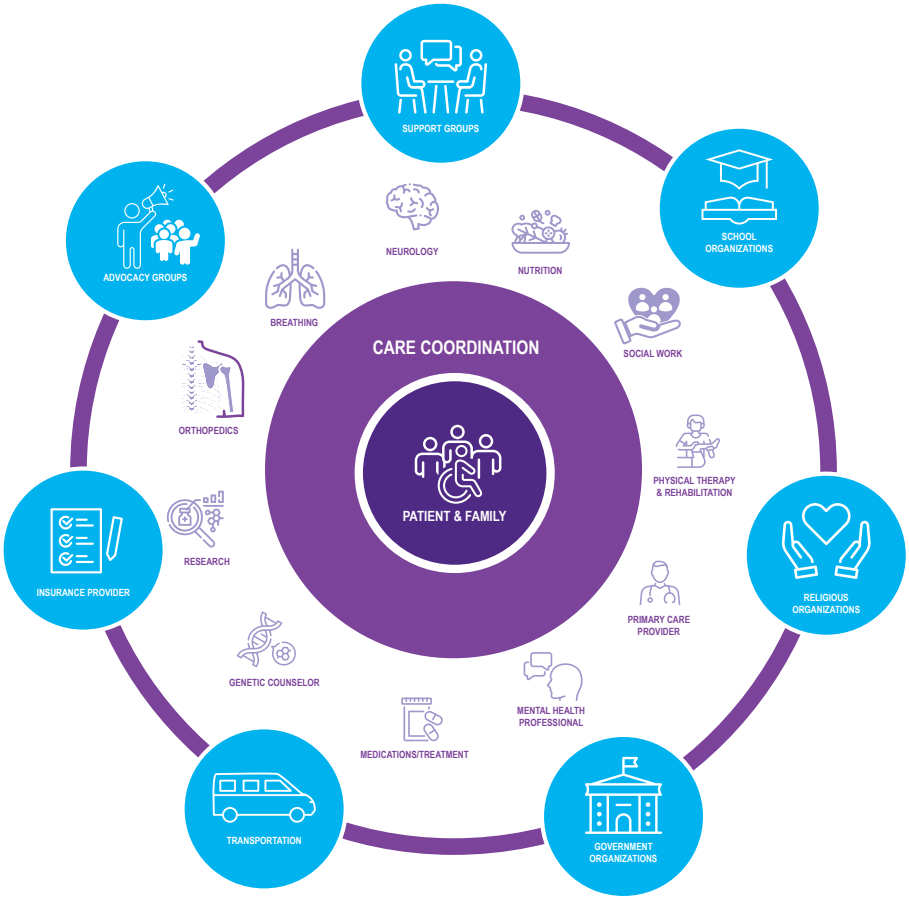
- Checking the child's motor skills and development;
- Discussing different treatment options available, including how they are given, how long they are given, and any side effects;
- Checking insurance and writing any materials needed for medical approval of treatment;
- Providing written information about SMA, including resources about different treatment options discussed;
- Community resources including advocacy groups, community resources, and support groups; and
- Making sure the family and child are at the center of all care coordination and decision-making regarding care and treatment.

The child and family will meet many healthcare professionals focused on addressing their unique medical needs. The health care team may include the following people:

- Neurologist
- Pulmonologist
- Nutritionist/dietitian
- Respiratory therapist
- Care manager or care coordinator
- Social worker

Who else is involved in care?

The individual with SMA's care involves many people in addition to the SMA specialty care team, such as an insurance provider, pharmacist, and primary care provider. It also includes community support groups, advocacy groups, and local state resources that may include transportation services or home health staff. The individual with SMA and their family are at the core of this team, and it is important to have someone coordinating all aspects of care.



How should SMA be described today?

Historically, and before disease modifying treatment being available, SMA was described and divided into types of SMA based on the age that symptoms began, and the highest physical milestone achieved. With the introduction of SMA treatments and newborn screening, the workgroup determined that SMA infants diagnosed by newborn screening and before treatment starts should be described by *SMN2* copy number, current motor function, age when symptoms start, if present, and severity of symptoms.

Adult-Onset 5q SMA Diagnosis

Adult-onset or SMA type 4 represents a small proportion of people diagnosed with SMA. The symptoms of Adult-onset SMA are like many diseases of muscle weakness, and this has resulted in delays with diagnosis.

Adult-onset SMA symptoms often start in late adolescence or adulthood and include:

- Weakness of the upper arms and thigh muscles
- Walking independently but with frequent falling
- Muscle pain, cramping or twitching
- Muscle stiffness
- Difficulty taking part in sports due to becoming more tired and not able to keep up with others (decreased endurance)

Diagnostic studies:

- Creatinine Kinase (CK) may be high
- Electromyography (EMG) may show non-specific nerve changes
- Definitive diagnosis is made by testing for the *SMN1* gene and *SMN2* gene
    - If only one copy of *SMN1*, an *SMN1* single nucleotide variant or point mutation may be present and additional testing with *SMN1* gene sequencing will help with diagnosis
    - Often 4-6 *SMN2* copies

Someone having the above symptoms and EMG with neurogenic findings may have SMA and genetic testing should be completed.

Further studies assessing the natural history of adult-onset SMA are needed.

Further Resources

Have you or someone you know been diagnosed with SMA? Please email infopack@curesma.org and provide your name and mailing address so we can send an unbiased, comprehensive information packet on SMA right to your door. The information packet includes our SMA Care Series Booklets that cover a range of topics and information needed to make decisions on treatment and care. They also cover genetics and testing, current research updates, managing daily life, and more. Upon emailing a member of our team will reach out to provide you with resources and support as you navigate the diagnosis."

For more information, please check out these additional resources.

Resources Guide Request Form

Understanding SMA

Care Series Booklets

To review the published manuscript on Diagnosis recommendations:

Spinal Muscular Atrophy Update in Best Practices: Recommendations for Diagnosis Considerations

2018 Guidelines:

Diagnosis and management of spinal muscular atrophy: Part 1: Recommendations for diagnosis, rehabilitation, orthopedic and nutritional care

Diagnosis and management of spinal muscular atrophy: Part 2: Pulmonary and acute care; medications, supplements and immunizations; other organ systems; and ethics