About Spinal Muscular Atrophy

What is SMA?

Spinal muscular atrophy is a degenerative problem that affects the motor nerves, resulting in muscle wasting and weakness.

Spinal muscular atrophy occurs in approximately one in 6,000 -10,000 live births.

What causes spinal muscular atrophy?

SMA is an autosomal recessive disease. This means that both males and females are equally affected, and that two copies of the gene, one inherited from each parent, are necessary to have the condition.

A gene called survival motor neuron (or SMN) is found to have an abnormal area (called a deletion) in over 95 percent of cases of SMA. Symptomatic individuals of all ages can be tested through DNA studies typically done from a blood sample.

When both parents are carriers, there is a one in four, or 25 percent, chance, with each pregnancy, to have a child with SMA. Carrier testing of parents can help determine the recurrence risk in a specific family.

What are the symptoms of spinal muscular atrophy?

Spinal muscular atrophy is sometimes difficult to diagnose, as symptoms can resemble other conditions or medical problems. Each child may experience symptoms differently. There are several types of spinal muscular atrophy based on symptoms and age of onset.

SMA Type I (Werdnig-Hoffman Disease or Infantile form)
This is the most severe type of SMA, and unfortunately, the most common. Symptoms may be present at birth or develop within the first few weeks or months after birth. Infants have difficulty holding up their head, sucking, feeding,

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swallowing, and often move very little. The legs are more severely affected than the arms. The muscles of the chest which help to expand the lungs are affected, and the chest may appear small or “bell-shaped”. They have a weak cough, and are prone to respiratory infections. The tongue may demonstrate "worm-like" movements, and they may demonstrate a tendency to choke while feeding. Complications from breathing problems often lead to death or dependence on some form of respiratory support by 2 to 3 years of age.

SMA Type II (Intermediate form):

This form of SMA most commonly becomes evident in children between 6 months to 2 years of age. They may show delays in acquiring motor skills such as rolling, sitting or crawling. They are unable to walk independently without support. They typically have generalized muscle weakness and may require braces, walkers, or a wheelchair for assistance. Life-expectancy varies greatly in this group of children, since they demonstrate a very wide range in degree of weakness. However, complications commonly include weakness of chest muscles involved in breathing, resulting in a weak cough and tendency for pneumonia. Scoliosis develops in virtually all children at some point, and they are prone to bone fractures. Children who are unable to bear weight often develop hip dislocation. Contractures of the muscles and joints can limit function over time. Children in this group may also demonstrate difficulties in swallowing and chewing, and require close monitoring of nutrition. Lifespan in this group depends on the severity of respiratory muscle weakness, but many children survive well into adulthood.

SMA Type III (Kugelberg-Welander, or ambulatory form):

This form of SMA most commonly becomes evident in children between 2 and 17 years of age. These children may show delays in motor development, difficulty walking, trouble getting up from the floor, mild muscle weakness, and frequent falls. Fatigue can be a significant problem, which limits the ability to walk long distances. A tremor involving the hands is common. Scoliosis is frequent in later

childhood. Respiratory muscle involvement is much less often a problem, and difficulty swallowing is rare.

SMA Type IV (Adult-onset form)

This form of SMA includes those individuals who don't develop symptoms of weakness until they reach adulthood. Usually, this results in muscle weakness predominantly affecting the legs, and manifests as a walking disability. The symptoms of spinal muscular atrophy may resemble other problems or medical conditions, and can be confused with other muscle or nerve conditions, including muscular dystrophy, myopathy, other spinal muscular atrophy variants or even forms of amyotrophic lateral sclerosis (ALS). Another closely related condition, known as spinobulbar muscular atrophy (Kennedy's disease), can also present in late childhood or adulthood.

How is spinal muscular atrophy diagnosed?

The diagnosis of spinal muscular atrophy may be suspected if you or your child demonstrate specific symptoms or demonstrate signs on examination that are consistent with the pattern of weakness seen in this disorder. During the physical examination, your child's physician will obtain a complete medical history, and he/she may also ask if there is a family history of any medical problems.

Diagnostic tests which can help to confirm the diagnosis of spinal muscular atrophy include:

Blood tests: Genetic testing via a blood test can confirm a suspected diagnosis in most cases**.** Sometimes the initial genetic test is negative, and additional genetic testing or other testing may be needed to confirm a suspected diagnosis.

Electromyogram (EMG): EMG is a test that measures the electrical activity of a muscle or a group of muscles. An EMG can detect abnormal electrical muscle activity due to diseases and neuromuscular conditions.

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Muscle biopsy: A small sample of the muscle is removed and examined to determine and confirm a diagnosis or condition.

MRI or imaging studies: Imaging studies of the brain or spine are sometimes performed to help rule out other conditions.

Management and Treatment

While there are as yet no specific pharmaceutical therapies which have been confirmed which can either extend lifespan or increase strength in SMA subjects, the identification of compounds that can increase SMN protein in cells from SMA subjects and in genetic animal models of SMA is promising. Moreover, proactive management strategies to optimize lung function, physical mobility and nutrition can help preserve motor function, improve quality of life and extend survival, particularly in more severely affected SMA infants and young children.

Following diagnosis in children with milder forms of SMA, including the infant with an as yet uncertain prognosis, it is important to work closely with parents in order to anticipate problems and pursue management aggressively to optimize outcomes. Because of the tremendous variability in severity of muscle weakness, an individualized approach is often necessary. Far too often, respiratory, nutritional and even physical rehabilitation interventions are reactive rather than proactive.

Treatment for the intermediate or milder forms of SMA should be focused

on preserving mobility and minimizing respiratory complications, particularly restrictive pulmonary disease or respiratory compromise due to progressive scoliosis. Specific interventions can be helpful in optimizing the individual's health and helping to maintain motor function.

Respiratory Management

Since respiratory management can impact lifespan considerably, physicians should support families in implementing a proactive approach. While .pulmonary management is often demanding, it is also the therapeutic modality that will most likely enhance quality of life and prolong lifespan. To maintain lung capacity, breathing exercises and supplementary aids may be helpful. Incentive spirometry and “breath-stacking” can be implemented at an early age but require discipline to perform on a daily basis. Aerosol therapy with nebulizers may be helpful in some settings and can be initiated at the onset of respiratory symptoms. Benefit from the routine use of mucolytics, bronchodilaters or steroid treatments is unclear and should be dictated by individual circumstances. Cough assist devices such as the Emerson In-Exsufflator, along with postural drainage and percussion, are essential when ineffective cough inhibits adequate removal of bronchial secretions in the lower airways. Regular use of such therapies can help prevent a mild upper respiratory infection from evolving into pneumonia or a collapsed lung resulting in

respiratory crisis. Even when children are well, daily use of such a regimen can help minimize atelectasis and chest wall contractures and deformity. In many children and young adults, nocturnal hypoventilation with and without obstructive apnea necessitates assisted ventilation. BiPAP can be initiated when the vital capacity falls to < 40%. Recurrent nocturnal awakenings are often an indication that patients may benefit from institution of nocturnal BiPAP, and a sleep study may prove helpful in determining whether or not there is an obstructive component, or whether nocturnal hypoventilation is present. BiPAP is often instituted for use only at night but can be invaluable whenever an upper respiratory infection or other illness resulting in increased fatigue is present.

Flu prophylaxis is recommended annually. In younger infants and children with significant intercostal weakness (all type I and weak type II subjects), prophylaxis for respiratory syncytial virus (RSV) is also recommended. Pulmonary medicine consultation is recommended to assist in making decisions regarding long-term respiratory management. Aggressive treatment of respiratory infection is essential. Antibiotic use is of value when symptoms arising from a presumed viral upper respiratory infection persist longer than expected or new fever or altered secretions appear in the midst of an apparent viral illness. Since recurrent or prolonged antibiotic treatment can predispose patients to yeast infections or even enterocolitis, a balanced approach is needed. In the severely compromised infant or child, a lower threshold for administering antibiotics

may be warranted. If illness results in persistent hypoxemia below 93%, the need for hospitalization and potential intubation should be discussed, although many such patients can be managed effectively in hospital using a non-invasive respiratory protocol. Oxygen therapy should only be used in conjunction with assisted ventilation in such patients as it can suppress respiratory drive, resulting in atelectasis and hypercarbia.

Insert PDFs for acute respiratory management here

Insert link to DVD on daily respiratory management strategies

Nutrition

Nutrition is critically important for maintaining muscle mass and strength and minimizing fatigue in SMA patients. Intermittent monitoring of dietary intake in consultation with a dietician experienced in management of patients with neuromuscular conditions or metabolic disorders can be extremely helpful. Children may be deficient in carnitine due to decreased intake of meat related to jaw contractures interfering with chewing. Swallowing problems sometimes be difficult to detect, and in weaker children or in those with borderline nutritional status or frequent respiratory illness, swallowing studies should be performed on a regular basis to ensure that silent aspiration isn't contributing to respiratory problems. Maintenance of appropriate nutrition is especially critical during illness. SMA subjects have diminished lean body mass and a secondary defect in

fatty acid oxidation that limits their reserve in the setting of prolonged fasting. Thus, when concerns regarding the ability to safely administer oral feeds develop, alternative forms of nutrition should be considered. Options include temporary nasogastric or nasojejunal feeds, or peripheral or total parenteral nutrition (PPN or TPN).

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Exercise and maintenance of mobility

Physical therapy on a daily basis, performed by parents with appropriate direction from a physical therapist, can help to minimize joint contractures and maintain mobility. The use of standing devices, appropriate orthotics, bracing, and facilitated ambulation can help significantly in this regard. Weight bearing on a daily basis, instituted as early as possible in non-ambulatory children for a minimum of 2 hours per day, can help to delay onset of scoliosis, limit contractures, and improve circulation and gastrointestinal motility. Daily exercise should be encouraged, to include the upper extremities in those children with severely impaired lower extremity function, to help maintain motor function and promote cardiovascular health. A daily exercise program could include part-time use of manually propelled mobility devices. The major orthopedic problems these children face include scoliosis, hip dislocation; and an increased risk of fracture due to decreased bone density and propensity

for falls. The age of onset and rate of progression of such complications are directly related to the severity of muscle weakness, but early intervention can minimize the impact and severity of such problems. Contractures can develop quite rapidly in the setting of illness, excessive time spent in a wheelchair, decreased activity, or recovery after scoliosis surgery or other orthopedic procedures. Daily range of motion and early return to supported weight-bearing can help maintain function in these children.

Scoliosis

Scoliosis almost invariably begins in the first decade of life in SMA type II and in a substantial proportion of children with SMA type III. The curves progress over time, sometimes quite rapidly during transition to increased wheelchair use or in conjunction with a growth spurt. In non-ambulatory patients, spinal bracing may improve sitting stability, as long as care is taken not to compromise abdominal movement in those with intercostal muscle weakness. However, continuous use of such bracing should be limited if possible in order to maintain trunk strength and mobility. Periodic pulmonary function studies help to establish a profile for the individual patient, allowing design of the most appropriate care plan surrounding respiratory care in the post-surgical period. Since worsening is invariable, once the curve reaches 40 degrees a decision to intervene may be

warranted. When very young patients develop scoliosis, bracing can sometimes help to defer surgery for variable periods of time, and “growth rods” or other means of accommodating growth may be indicated.

Proximal muscle weakness predisposes patients to progressive subluxation and dislocation of the hip. Subsequent hip degeneration can result in significant chronic pain. In non-ambulatory patients, it is important to prevent the hips from dislocating for reasons of comfort, good sitting balance, and maintenance of pelvic alignment. To achieve an optimal result, operative intervention may be required in some cases. Patients who have type III SMA and are still able to walk present a difficult management problem. These patients are also prone to subluxation of the hip due to significant proximal muscle weakness. However, because surgical intervention with proximal femoral varus osteotomy may result in additional weakening of the abductor muscles, the physician should be cautious in recommending such surgical procedures in an ambulatory patient. Since these patients rely to a great extent on lumbar lordosis and a side-to-side waddle to walk, bracing or spinal arthrodesis may worsen their gait. It is not uncommon for SMA type III patients to become non-ambulatory following spinal surgery, particularly if a rehabilitation plan is not instituted immediately in the post-operative period. Joint contractures can progress quite rapidly in this setting without dedicated prevention. In a subset of cases in which ambulatory status is considered at risk,

postponement of surgery may be the best choice. Special consideration of nutritional support in the perioperative period can help ensure a good outcome.

PDF for perioperative nutritional management here

Special considerations in SMA type I infants

Before and after confirmatory genetic testing is completed in an obviously severely affected infant, it is essential to work closely with parents to ensure that they understand what they may face in the months following the diagnosis, fully reviewing their options regarding supportive nutritional and respiratory interventions. This is particularly important to address early, since these infants are often diagnosed in the setting of an initial respiratory event and may already have bulbar insufficiency and respiratory insufficiency. It is important that families be presented with a range of options and that quality of life for the entire family be preserved as much as possible. Many parents, when presented with options, choose to forgo invasive diagnostic and therapeutic procedures. However, others are anxious and willing to embrace a very proactive care plan if it means extending the life of their child. It is vital to maintain open communication so that all caregivers are aware of choices already made as well as areas of continuing uncertainty regarding interventions to be considered.

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Proper positioning, daily passive range of motion, and use of alternative mattress systems or seating devices can enhance quality life. A flat car bed rather than a car seat is advisable for infants who rely primarily on abdominal breathing. If swallowing problems are mild, thickening the formula and positioning the infant properly can help to avoid aspiration of formula into the lungs. However, families of Type I infants will almost certainly need to consider some alternative means of providing nutrition at some point. A nasogastric or nasojejunal tube (a slender tube which goes through the nose and down to the stomach or to the first part of the intestine) is often sufficient for prolonged periods of time, allowing the family time to consider the range of options. More permanent options include gastrostomy or a combined Nissan/gastrostomy procedure. While surgery and general anesthesia clearly carry some potential risks, laparoscopic techniques are available that allow a more rapid recovery. In severely weak infants in whom general anesthesia is a concern, percutaneous gastrostomy with local anesthesia is an option. Given the SMA child's need to eat regularly, limiting fasting prior to such procedures and providing nutritional support immediately afterward will help to enhance recovery.

Respiratory management is a challenge, presenting the greatest risk of death or serious disability in the weakest infants and children. The most aggressive approach, including tracheostomy and mechanical ventilation,

does nothing to prevent disease progression. Complications such as tracheitis (infection involving the windpipe), sepsis (life-threatening infection in the blood) and ongoing respiratory complications can compromise quality of life. Families may be pressured to make quick long-term decisions without adequate preparation when infants are intubated emergently due to respiratory crisis. However, the increasing availability of noninvasive ventilation techniques including bilevel positive pressure support (BiPaP), inexsufflator treatments (cough assist machine), percussion, postural drainage and suction can help allow such infants to be extubated more readily than in the past, providing an intermediary between tracheostomy and withdrawal of support. Perhaps more important, however, it offers families additional options for ongoing respiratory support on a daily basis at home, thus minimizing emergency room and hospital visits, and potentially extending lifespan in more moderately affected infants. An individualized approach to respiratory infection or compromise should be developed with the child's family and updated regularly with regard to choices surrounding a need for intubation. If the family chooses palliative care, hospice provides compassionate support for such families. The use of narcotic medication in this setting to reduce discomfort, along with proper positioning and a less aggressive respiratory support regimen, in concert with the family's wishes can minimize discomfort for the infant. It may be beneficial to have the family communicate with others who have experienced the loss of an

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infant with SMA type I during this difficult period.

Future Treatment Directions

Proven treatments for SMA may soon become a reality as we gain a better understanding of disease pathogenesis. Clinical trials to assess compounds that increase SMN protein levels in cell and animal models have begun. In the meantime, a proactive management strategy can help to limit disease progression and optimize outcome. Undoubtedly, intervening as early as possible in the disease process will prove most effective as additional therapeutic strategies are identified. Participation in clinical trials can provide patients and families with additional clinical care and monitoring that can help to ensure that proactive care is the rule, rather than the exception. Participation is also vital to the community to help demonstrate the effectiveness of potential treatments, as . However, a careful consideration of the potential risks as well as the time commitment involved should be carefully considered in each case. For a listing of clinical trials on SMA involving the University of Utah or the Project Cure SMA Investigators Network, **click here**

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