

What are “neuromuscular diseases”?

This term covers a number of disease patterns deriving primarily from neurological or muscular diseases and characterized by a variety of symptoms of different degrees of severity (such as disorders affecting posture and the locomotor system, mental disabilities, or damage to sensory perception). Many of these diseases have their onset in childhood and may, in addition to the large number of prevailing individual symptoms, lead to the development of a scoliosis over the course of the disease due to neuromuscular damage to the postural apparatus.

What are “spinal muscular atrophies” (SMA)?

The term “spinal muscular atrophy” covers diseases characterized by hereditary and progressive damage to the locomotor system. In these diseases, motor cells (motoneurons) – mainly those of the spinal cord (spinal motoneurons) – as well as motoneurons in the cerebral cortex and brain stem, are damaged or destroyed, disrupting the transmission of neural impulses from the brain to the executor muscles.

This disruption of neural impulse transmission due to destruction of motoneurons causes the following symptoms in the locomotor system:

- Muscular atrophy
- Pareses (paralyses)
- Hypotension of the muscles (reduction of muscle tension)
- Swallowing, chewing and speech dysfunctions with involvement of the motoneurons of the brain stem

What causes spinal muscular atrophies?

Spinal muscular atrophy is a hereditary disease with autosomal recessive hereditary transmission. This means that a child can only manifest spinal muscular atrophy phenotypically if both parents carry the genetic trait and if both transmit the pathological hereditary trait to the child. If only one parent transmits the genetic trait, the disease will not manifest in that child, but that child will be a carrier, i.e. he or she can transmit the trait to the next generation.

Victims of a spinal muscular atrophy or carriers of this genetic trait are missing the “survival motoneuron 1” (SMN 1). This gene produces a special protein responsible for the proper function of the motoneurons. The lack of this protein damages the motoneurons, thus disrupting the transmission of impulses in the locomotor system.

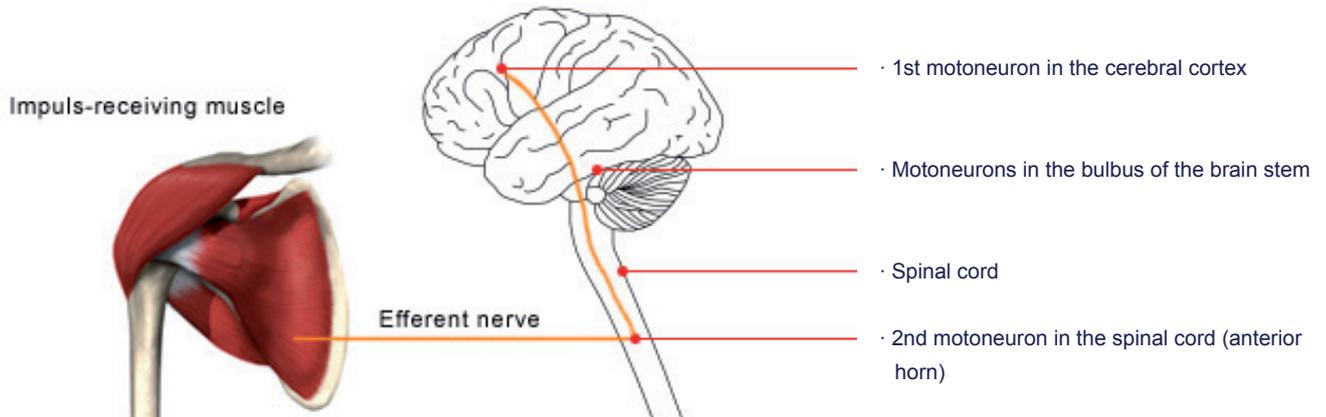
What is the “locomotor system”?

The locomotor system controls voluntary movements and supplies the muscles of the trunk, arms and legs with nerve impulses that are then translated into adequate movement patterns through the activation of the muscles. Greatly simplified, the locomotor system consists of the 1st motoneuron in the cerebral cortex and the 2nd motoneuron in the anterior horn of the spinal cord.

The development of a required movement pattern, such as raising a leg in order to climb a stair, can be expressed in simplified terms as follows:

The 1st motoneuron in the cerebral cortex produces the “blueprint” for the movement sequence and sends the necessary impulses along the spinal cord to the 2nd motoneuron in the anterior horn of the spinal cord. The 2nd motoneuron is connected to the muscles via nerves and passes the impulses on to the muscles, which can then carry out the required movement sequence. The motoneurons in the brain stem are also part of the locomotor system. They are responsible for the muscles used to swallow, speak and chew.

- Simplified depiction of the locomotor system



How are the muscular atrophies classified?

Spinal muscular atrophies are classified in 4 groups (SMA type I-IV) that vary as to symptoms, progression, and prognosis. All of the muscles in the body may be affected, where the muscle groups close to the trunk such as the shoulder, back and pelvic muscles are usually affected the most. Muscle atrophy is usually more pronounced in the legs than in the arms.

Type I SMA, also known as Werdnig-Hoffmann disease or acute infantile SMA, shows the following symptoms:

- Disease onset in the womb
- Autosomal recessive heredity
- Diagnosis prior to 6th month of life
- Limited movement of fetus in uterus
- Muscle tone greatly reduced (“floppy infant”)
- Frog-leg position
- Weakness or absence of proprioceptive muscular reflexes
- Notable fasciculations (“quivering”) of the tongue
- Muscle atrophy, mainly in the trunk
- Onset usually around the pelvic girdle and thighs
- Child incapable of learning to sit and walk
- Suckling and swallowing disorders with risk of aspiration (“choking”) of food, liquids, or saliva into the lungs, potentially causing pneumonia.
- Respiratory dysfunctions up to and including respiratory paralysis due to weakening of the intercostal muscles responsible for moving the ribcage during breathing.
- Formation of a bell-shaped thorax (bell-shaped deformation of the ribcage)
- Deformities of the bony skeleton with formation of scoliosis, hyperlordosis, and foot deformities and malpositions
- Decubitus (“bedsores”)
- Frequent lung infections
- Low life expectancy, about 90% of these children do not survive to the age of 10 due to respiratory insufficiency.

Type II SMA, chronic infantile or intermediate SMA exhibits the following symptoms:

- Autosomal recessive heredity
- Disease onset usually in the 1st year of life
- Child can learn to sit unsupported
- Walking only possible with help or walking devices
- Tongue fasciculations and slight quivering of the fingers
- Development of a scoliotic spinal deformity
- Deformity of the ribcage
- Swallowing disorders, rare
- Disrupted food uptake
- Atrophy of intercostal muscles with respiratory insufficiency
- Pulmonary infections
- Approx. 30% of these children live to the age of 10, few live longer than 20 years

Type III SMA, also known as juvenile SMA or Kugelberg-Welander disease, is characterized by:

- In most cases autosomal recessive heredity, occasionally occurs as new mutation
- Variable disease onset (between the first year of life and late adolescence)
- Disease onset usually in the muscles of the pelvic and shoulder girdles
- No significant shortening of life expectancy
- It is possible to walk without help, though the ability to stand or walk may be reduced once again by the progression of the disease.
- Foot deformities
- Joint contractures

Type IV SMA, adult SMA, exhibits the following symptoms:

- As a rule, gradual onset after age 30
- Varying levels of muscular weakness
- Respiratory and glutitonal muscles only rarely affected
- Life expectancy not shortened

How is spinal muscular atrophy diagnosed?

- Molecular genetic blood analysis to detect absence of the SMN 1 gene
- Clinical and neurological examination to determine muscular and reflex status and to distinguish it from other organic diseases
- Muscle biopsy, a procedure in which tissue is removed from a muscle under local anesthesia. This tissue sample is examined under a microscope and can thus rule out other muscular diseases with different causes.
- Determination of velocity of nerve conduction and an electromyogram (EMG) are used to measure the electrical impulses carried by a nerve, the conduction velocity of the impulse, and the level of muscle receptivity to the impulse.
- Measurement of creatine kinase (CK) levels, a muscle enzyme, is not very informative when confirming a diagnosis, since its levels may be either within the normal range or slightly elevated in a variety of forms of spinal muscular atrophy.

How is spinal muscular atrophy treated?

No causal treatment has yet been devised capable of curing spinal muscular atrophies. For this reason, it is important to make intensive use of those therapeutic measures that can enhance muscle strength or slow the progression of muscular weakness. Depending on the individual findings in each case, the following therapies can be effectively used within the framework of a therapy schedule formulated in cooperation with the parents, the patient, the physicians in charge of treatment and the therapists involved:

- Physiotherapy to improve and preserve muscle function and for the treatment and prevention of muscle contractures (foreshortening)
- Physical therapeutic applications (massages, cold/heat applications)
- Electrotherapy (TENS, interferential current)
- Ultrasonic treatments
- Ergotherapy
- Logopedic treatment, especially for treatment of swallowing disorders
- Psychological care
- Pain therapy
- In cases of swallowing dysfunctions with insufficient food intake, the patient may have to be fed with a gastric tube. In most cases, a PEG (percutaneous endoscopic gastronomy) tube is implanted. In this method, a thin tube is inserted through the abdominal wall into the stomach under optical gastroscopic control, through which food can then be administered.
- Treatment of respiratory dysfunctions
 Due to the atrophy of the thoracic wall muscles, the secondary respiratory muscles, the diaphragm, and the weakness of the abdominal wall, respiratory function is more or less restricted. This may lead to oxygen deficiency. The limited mobility of the ribcage also results in insufficient physiological removal of secretions and mucus from the lungs, potentially resulting in repeated pulmonary infections.
 For these reasons, it is important to monitor the pulmonary function parameters, improve mucus drainage from the lungs by means of specific respiratory and positioning therapy, and to treat existing lung infections with antibiotics. In cases of severe respiratory disorders, particular in children with type I SMA, mechanical support of respiratory function may become necessary.
- Orthopedic aids such as special sitting, standing, and walking aids and an environment adapted to the patient's handicap can improve and facilitate the individual situation, patient independence, and make caring for the patient easier.

Surgical treatment of a scoliosis

Due to the existing muscular atrophies of the trunk muscles, the body statics change drastically, which is why patients with spinal muscular atrophy who are confined to a wheelchair often develop scoliosis. Since the conservative treatment of neuromuscular scolioses is of limited success, early surgery, before the respiratory and circulatory functions worsen, may be advisable.

What other neuromuscular diseases are there?

The best-known neuromuscular diseases are:

- **Meningomyelocele**
- **Infantile Cerebralparese**
- **Duchenne Muskeldystrophie**

These terms describe a progressive muscle disease beginning in the first two years of life with a weakness of the pelvic muscles that then spreads to the shoulder girdle muscles and develops into a generalized muscular weakness. The relevant trait is carried on the X chromosome, meaning that only boys are affected. Life expectancy is about 20 years. Patients suffering from this condition die of cardiac or respiratory insufficiency due to affected heart or respiratory muscles with repeated bouts of severe pneumonia.

- **Syringomyelia, syringobulbia**

Syringomyelia is a disease of the spinal cord affecting mainly the cervical and thoracic spine, while syringobulbia affects the extended spinal cord (medulla oblongata). Cavities (syringes) containing no nerve cells form in the spinal cord, resulting in dysfunctions of varying severity (disturbance of depth perception, sense of position, uncertain gait, muscular atrophy with altered body statics and the development of scoliosis).

The causes leading to formation of these cavities may be both congenital (Arnold Chiari malformation, spina bifida and other primary diseases) and acquired (tumors or infections of the spinal cord).

- **Poliomyelitis**

Polio is caused by RNA viruses from the group of the picorna viruses.

After it attacks the central nervous system, poliomyelitis damages the second motor neurons in the spinal cord, causing paralyzes and meningitis.

No antiviral therapy has been developed as yet. The best protection is preventive vaccination.

- **Spinocerebellar ataxia (Friedreich's ataxia)**

Friedreich's ataxia is an inherited spinal locomotor system disorder, characterized by poor locomotor coordination with uncertain stance and gait (stance and gait ataxia). The disease is progressive. A possible cause is iron oversaturation of the mitochondria, resulting in the formation of free radicals, which then damage the nerve cells. In addition to other complications, such as cardiac muscle enlargement (cardiomyopathy), this ataxia may also cause the development of scoliosis.

- **Arthrogryposis multiplex congenita (AMC)**

This is a congenital disorder of the connective tissues and nervous system resulting in the disruption of the development of muscles (muscle weakness, missing muscle groups) and therefore in poorly developed joints with rigidification. The disease may be associated with malpositions of the spinal column and severe anomalies in the central nervous system.