



## Opening a new horizon for children born with SMA

**Early detection of SMA by newborn screening dramatically improves the effectiveness of all available treatments for this disease.**

The **European Alliance for Newborn Screening in SMA** demands that by 2025, newborn screening programmes in Europe include a test for spinal muscular atrophy for all newborn children.

Newborn screening (NBS) is the practice of testing all babies in their first days of life for certain disorders that are treatable, but difficult or impossible to detect clinically. This allows for the identification of patients before the first symptoms emerge.

## Spinal muscular atrophy

Spinal muscular atrophy (SMA) is a rare, progressive, neuromuscular disease which leads to immobility and results in a short life expectancy for many children diagnosed with the disease.

### SMA is severe, life threatening or permanently disabling disease

- Despite being a rare disease, left untreated, SMA is the leading genetic disease cause of death in infants
- The most serious types of SMA start at an early age and severely affect motor function
- SMA involves the loss of nerve cells called motor neurons that control muscles. Once lost, motor neurons cannot be regenerated
- 50-60% of children born with SMA can never sit up independently and without treatment, do not live beyond two years of age

### Effective treatments for SMA are available

- There is no cure for SMA but as of July 2020, there are two treatments approved in the EU
- Diagnosing SMA quickly is crucial to stopping progression of the disease, which robs infants of valuable motor neurons that allow them to walk, sit and even breathe
- Early detection and diagnosis may mean the difference between life and death for an infant with a severe form of SMA

### Tests of good quality to detect SMA exist

- Being undiagnosed causes a serious and devastating psychological impact on families and patients, because of the 'missed opportunity for treatment'
- The testing is available in many states in the United States and some pilot studies are ongoing in Europe



Newborn screening involves the use of existing methods that can detect spinal muscular atrophy when the child is a few days or weeks old.

It is imperative to diagnose SMA and begin treatment, including proactive supportive care, as early as possible to halt irreversible motor neuron loss and disease progression. This is especially critical in SMA Type 1, where motor neuron degeneration starts before birth and escalates quickly.

Starting treatment at this time means the child has a chance of a reasonably normal life without developing all disease complications.

## SMA, a rare, genetic, neuromuscular disease

Spinal muscular atrophy is a rare disease linked to a biallelic deletion of the **SMN1** gene, which leads to an SMN protein deficiency. All SMA patients carry one to six **SMN2** gene copies that influence the severity of the disease. The more **SMN2** copies a patient has, the milder the disease severity.

In contrast to the **SMN1** gene, each **SMN2** gene produces only about 10% functional SMN protein. The reduced SMN protein level results in progressive and irreversible loss of motor neurons, affecting muscle functions, including breathing, swallowing and basic movement.



### European Alliance for Newborn Screening in SMA (SMA NBS Alliance)

The **SMA NBS Alliance** requests the widespread implementation of newborn screening in babies' first days of life for the biallelic deletion of the **SMN1** gene. This has to be immediately confirmed in addition to determining the number of **SMN2** copies.

There is a broad range of patients with SMA. It ranges from neonates suffering from severe problems right at the beginning of their life, up to the onset of the disease later in life with only mild motor disabilities. SMA induces not only motor restrictions, but often severe respiratory disorders, with most needing invasive ventilatory support. Most SMA type 1s and some type 2s require a tracheostomy and have severe swallowing problems.

Over the past three years, treatments for SMA have arrived on the European market. These treatments increase the production of SMN proteins and therefore prevent the death of motor neurons and the progressive loss of function. They do not however save, or repair already affected motor neurons. Neuronal turnover is very low, and therefore what is lost, is lost forever.

New treatments allow children with a severe form of SMA to survive beyond two years of age and retain some motor abilities. **It is therefore essential to treat these patients before the onset of the first symptoms.**



### **Ensuring safe and efficient treatment in the days following birth**

Various scientific studies around the world showed that treating patients before the onset of the first symptoms could preserve the nervous system and prevent the onset of functional disabilities. Some children detected and treated in the first week of life can benefit from normal functional development.



### **SMA detection in newborn screening**

Spinal muscular atrophy linked to the SMN1 gene is characterised by a biallelic deletion of SMN1 on both chromosomes 5. The detection of a biallelic deletion of SMN1 by newborn screening has to be confirmed by a second independent blood sample and a different test, which also allows the determination of the number of SMN2 copies, essential for the choice of therapy. Caveat: About 3-5% of newborns who carry SMN1 mutations other than the biallelic deletions will be missed by newborn screening.



### **Techniques to detect spinal muscular atrophy at birth**

Several large-scale pilot studies are underway, including in Belgium and Germany. Please see “One Year of Newborn Screening for SMA – Results of a German Pilot Project” and “Newborn Screening for SMA in Southern Belgium” for the initial published results. There is an ongoing pilot in Italy with further European pilots in the planning stages.

One technical and organisational solution involves the addition of one single blood spot onto the Guthrie’s testing card to be screened for SMA. This technique is already commonly used for newborn screening panels for various diseases in Europe. So far, no false positives have been detected in pilot studies using this method. These techniques do not allow for accidental findings, as it is only focusing on the SMN1 gene.



Photo by: Daniel Koston

Every day without a diagnosis of SMA results in more motor neurons lost forever, resulting in a life of significant disability or even death.



### Cost

SMA can be added to the current Guthrie test without many additional costs. This cost has to be compared to the psychological and societal impact of the death of babies in the first years of their life, and the lifetime cost of caring for a child with a serious disability.



### Ethical considerations

Adding SMA to newborn screening panels intends to identify newborn babies at risk of developing a particularly disabling disease. SMA meets the World Health Organization criteria for being added to newborn screening.

## European Alliance for Newborn Screening in SMA

In order to advocate for newborn screening for SMA in Europe, SMA Europe founded the European Alliance for Newborn Screening in SMA to bring together all stakeholders who share this vision and are willing to work together towards making it a reality.

The overarching objective of the Alliance is to decrease the time it takes for a child born with spinal muscular atrophy to be diagnosed, and to assist patient advocacy groups in their efforts to accelerate the identification of such children, given that early diagnosis and treatment of spinal muscular atrophy leads to better outcomes.

### SMA: Test at birth, save a life.



Identifying children living with SMA when pre-symptomatic through NBS allows for treatment to be started on time, preventing motor neuron death and a life with severe disabilities.

## European Alliance for Newborn Screening in SMA

Founding member



**SMA Europe**

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