Regione Toscana

Servizio Sanitario della Toscana

Meyer Azienda Ospedaliero Universitaria

Newborn Screening for Spinal Muscular Atrophy in Tuscany

Further information

In Tuscany, the Regional Council Deliberation N° 796 of 2/8/2021 has made neonatal screening available for Spinal Muscular Atrophy (SMA).
Neonatal screening for SMA is aimed at identifying affected infants in the pre-symptomatic phase, i.e. at a very early stage, in which clinical signs have not manifested yet. The effectiveness of newborn screening for SMA has been demonstrated by pilot projects carried out around the world and by the two-year project conducted in Lazio and Tuscany since September 2019.

What is SMA?

SMA is a rare genetic neuromuscular disease characterized by progressive muscle weakness and atrophy. Intellectual development is normal. Based on the severity and age at onset of symptoms, SMA is classified into 3 forms:

- Type 1 (about 50-60% of patients) is the most severe form of SMA, with symptoms beginning within the first six months of life. Many children do not live past age 2. The cause of death is generally due to respiratory failure, caused by muscle weakness.

- Type 2 (about 30% of patients) is an intermediate form of SMA with symptoms starting within 18 months of life. The ability to walk without support is not acquired. Life expectancy is slightly reduced but causes significant disability.

- Type 3 is the rarest and mildest form of SMA. Symptoms begin after 18 months of age and the course of disease is highly variable. Patients may or may not lose the ability to walk and have a normal life expectancy.

SMA is caused by an autosomal recessive inherited genetic defect, which means that both parents of an SMA patient are healthy carriers of the genetic defect causing the condition, which occurs only if they both pass it on to their children. It is estimated that one child with SMA is born for every 6,000-10,000 newborns.
In 95-98% of cases, the disease is caused by specific mutations in the SMN1 gene, essential for the production of the SMN (Survival Motor Neuron) protein, which is crucial for the survival and normal functioning of motor neurons. Patients with SMA have a variable number of copies of a second gene, SMN2, which encodes a shortened form of the SMN protein. Such shortened form has a reduced function compared to the full SMN protein (that encoded by the healthy SMN1 gene).
The number of copies of the SMN2 gene (usually 1-4 copies) hence underlies the great variability of the disease, with more or less severe forms.

What therapies are available for SMA today?
Until a few years ago, the treatment of SMA was symptomatic, based on multidisciplinary approaches and aimed at improving the quality of life of patients. Today, specific therapies are available in Italy: antisense oligonucleotides and gene therapy.

Antisense oligonucleotides (ASOs) act on the SMN2 gene allowing the production of a complete and functional SMN protein. Intrathecal and oral formulations are available. Gene therapy uses a viral vector that penetrates the neuronal cell and transfers the missing SMN1 gene, without integrating into the human genome, continuously producing the SMN protein.
The great advantage of SMA neonatal screening is that affected children treated in the pre-symptomatic phase show stages of development similar to those of children who do not have the disease.

How is newborn screening for SMA carried out?
In all newborns, a small blood spot sample is taken from the heel for the so-called "mandatory neonatal screening", provided for by Italian law.
In Tuscany, with the Regional Council Deliberation N° 796 of 2/8/2021, the panel of pathologies subject to mandatory neonatal screening has added spinal muscular atrophy (SMA).
The screening test consists of a molecular genetic analysis of the SMN1 gene (presence / absence of the gene in homozygosity) on DNA extracted from the blood absorbed on the neonatal card. You will be asked to sign a consent form.

What will happen to your child's biological sample?
The genetic test for SMA will be performed at Meyer University Hospital Laboratory for Neonatal Screening, Biochemistry and Pharmacology. In a first transitional phase, the newborn's blood sample will be sent to the Department of Life Sciences and Public Health, Disciplinary-Scientific Sector of Medical Genetics of Università Cattolica del Sacro Cuore in Rome, where the genetic test for SMA will be performed.
The extracted DNA will be destroyed at the end of the analysis while the blood sample will be stored for ten years.

How will you be informed of the results of the genetic test for SMA?
Genetic test results will be available within seven workdays of collection, subject to exceptions.
If the genetic test turns out negative (normal), there won't be direct notice, as already happens with mandatory newborn screenings. Since genetic testing can identify approximately 98% of SMA patients, there is a small, residual risk (<1 / 300,000) that your child will still have SMA. This risk cannot be further reduced, unless there are clinical signs that suggest the presence of it. If the test turns out positive, indicative of a genetic diagnosis of SMA, you will be called to carry out an evaluation at the Metabolic and Hereditary Diseases Ward of Meyer University Hospital, where your child will be clinically evaluated and you will be informed of the test result. A blood sample will then be taken from him/her to confirm the results. You will be provided with all the information related to SMA, available therapeutic opportunities, and the reproductive risk for you and your family members. As for the results obtained from the confirmation test, a written report with the specific diagnosis will be issued.

What to do if your child has SMA?
The genetic tests available to us (absence of SMN1 and determination of the number of copies of SMN2) allow us to establish the severity of SMA, with a reliability of approximately 80%. Therefore, these data will allow you to establish the most appropriate care plan for your child at Meyer University Hospital Inherited Metabolic and Muscular Diseases Ward in Florence, where SMA patients are treated according to internationally shared standards of care.

Possible Risks of Participating in SMA Newborn Screening
There are no additional risks as your child's blood sample will be taken along with that to be used for mandatory neonatal screenings. Since genetic testing will be performed only for the diagnosis of SMA, there is no risk of obtaining unsolicited, incidental information.