

Your Baby and Newborn Screening

Dear Parents,

The Tuscany Region offers your child the opportunity to enroll in a free newborn screening program.

What is newborn screening?

As part of preventive medicine programs, all newborns undergo simple tests free of charge that allow for the early detection of certain congenital diseases. National Law No. 104 of 05/02/92 mandated screening for phenylketonuria, congenital hypothyroidism, and cystic fibrosis. Since 2004, the Tuscany Region has also introduced expanded metabolic screening for over forty metabolic diseases. National Law No. 167/2016 made such screening mandatory for all newborns in Italy. With Regional Resolution No. 909/2018, Tuscany has extended screening to include three lysosomal storage diseases and severe combined congenital immunodeficiencies, and, with Regional Resolution No. 796/2021 introduced neonatal screening for Spinal Muscular Atrophy (SMA). Regional Resolution No. 1149/2025 expanded the range of conditions eligible for neonatal screening to include other immunodeficiencies and metabolic diseases, including some lysosomal diseases.

What is the aim of newborn screening?

The purpose of newborn screening is to detect certain congenital diseases early, before the onset of symptoms, and, quickly starting specific therapies, we can prevent or limit the serious damage typical of these diseases.

How is it performed?

Blood drops collected by pricking the newborn's heel between 48 and 72 hours of life are analyzed. The blood drops are placed on special absorbent paper with a card bearing the newborn's data. Additional samples are required for certain newborn categories; for example, for newborns weighing less than 2000 grams, three samples are required: 48 hours, 14 days, and 30 days. The card is sent to the Meyer University Hospital, where tests are performed on all newborns born in Tuscany. The Meyer University Hospital retains the cards with the collected blood drops for ten years.

When will you be able to receive the results?

If the newborn tests positive for any of the diseases being investigated, the birthing center or screening center will call you back for further testing. Normal results are not communicated, so if they don't call you back, it means all the tests were negative.

Attention: if they call you back, it does not mean that the child is sick but only that further tests are necessary

Which diseases are detected through screening?

ENDOCRINOLOGICAL DISEASES

- Congenital hypothyroidism

It is caused by the lack or insufficient production of thyroid hormones, which are essential for the development and maturation of the central nervous system and for proper growth in the child. Treatment consists of oral thyroxine administration. Early diagnosis and treatment allow the child to experience normal growth and neuromotor development.

- Adrenogenital syndrome (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency)

This is a rare disease in which the adrenal glands fail to properly produce certain life-critical hormones, such as cortisol and aldosterone. In its most common form, this defect can cause mineral imbalances and excessive production of sex hormones in the first weeks of life. Early diagnosis through newborn screening allows for rapid initiation of replacement therapy with drugs that correct the defect and prevent potentially very serious complications. With proper treatment and regular checkups, children can grow up and live normal lives.

CYSTIC FIBROSIS

This disease is caused by a genetic defect that can lead, in a highly heterogeneous manner, to lung infections and impaired digestive function (maldigestion), resulting in growth disorders. One in 4,000 healthy newborns is affected. Screening is initially based on measuring trypsin (a protein with enzymatic activity) in a blood sample. During the neonatal period, it is not uncommon for abnormal trypsin levels to occur, requiring further testing to interpret. In a limited number of newborns, it is therefore advisable to undergo an in-depth genetic analysis (genetic testing), for which your consent will be obtained. Early diagnosis of the disease through neonatal screening, usually before the onset of symptoms, improves the clinical outcome, prevents many complications, and provides the family with genetic counseling for any future pregnancies. In addition to symptomatic therapy, effective drugs targeting the underlying defect of the disease are now available for an ever-increasing number of individuals with cystic fibrosis.

INBIRTH DEFECTS OF IMMUNITY (INBD)

Inborn errors of immunity (INBD) are a large group of rare diseases (over five hundred are known today), all characterized by a defect in the immune system. Children with an inborn error of the immune system are born apparently healthy. However, precisely because of the serious defect that prevents them from defending themselves against infectious diseases, they can suffer serious and irreversible damage early on or even die from infections that are otherwise common in children with normal immune systems. Newborn screening allows us to diagnose most inborn errors of the immune system in the first few days of a child's life and therefore initiate the most appropriate treatments to protect them against all possible infections. In many cases, these treatments are able to restore the child to perfect health. Screening is done by looking for molecules called TRECs and KRECs in a drop of a newborn's blood. A normal immune system will produce large numbers of TRECs and

KRECs; conversely, a low or absent level of these molecules is a warning sign and suggests that the immune system is not functioning properly. Severe combined immunodeficiencies (SCID) are the most severe form of inborn errors of the immune system. Stem cell transplantation or gene therapy can treat SCID, resulting in a successful outcome for the child. The transplant is most successful when the child is only a few months old and has not had previous infections. This is why screening is so important, as it detects SCIDs in the first few days of life. Screening can also identify many other immune system defects which, although less serious than SCIDs, still require immediate treatment and early management of the child to avoid serious infections and other complications. In some of these cases, the immune system defect is associated with other clinical manifestations (for example, heart, kidney, and intestinal diseases). In other cases, the defect is associated with the child's inability to produce antibodies, and children can develop serious infections such as pneumonia or meningitis if they don't receive antibody therapy early. Before screening, these diseases were diagnosed late, when the child had already suffered serious infections and complications. Screening, however, allows for early diagnosis and prompt implementation of all necessary treatments.

HEREDITARY METABOLIC DISEASES

Hereditary metabolic diseases are a large group of genetic disorders. Symptoms can appear in the first days of life, but often during the first year or later, even in adulthood. If not properly treated, hereditary metabolic diseases can affect various organs and systems, such as the central nervous system, heart, liver, kidneys, skin, and so on, and in some cases can cause sudden death. Early diagnosis allows for early initiation of dietary and/or pharmacological therapy, improving prognosis and quality of life.

Over 50 inherited metabolic diseases are screened for newborns in Tuscany, including:

- amino acid metabolism disorders (e.g., phenylketonuria)
- organic acidurias
- urea cycle disorders
- fatty acid beta-oxidation disorders
- biotinidase deficiency
- galactosemia
- aromatic L-amino acid carboxylase (AADC) deficiency
- pyridoxine-dependent epilepsy
- X-linked adrenoleukodystrophy
- Lysosomal storage diseases (LSDs): LSDs are caused by genetic defects in lysosomal enzymes, resulting in the accumulation of substances in the lysosomes of organs and tissues. They are progressive diseases and can cause severe disability or death at a later or earlier age. They are characterized by extreme variability in age of onset, symptoms, clinical course, and severity, even within the same disease. Six of these diseases are included in newborn screening in Tuscany, using enzyme assays in a blood sample: **Pompe**

disease, Fabry disease, mucopolysaccharidosis type 1, metachromatic leukodystrophy (MLD), Gaucher disease, and acid sphingomyelinase deficiency (ASMD). Treatment is available for all of these diseases, which has changed their natural history and modified the quality and life expectancy of patients. If diagnosed through newborn screening, the time to initiate therapy may vary based on the enzyme/genetic defect and the clinical phenotype. Newborn screening for Fabry disease may miss the diagnosis in females.

SPINAL MUSCULAR ATROPHY (SMA)

Spinal muscular atrophy (SMA) is a genetic disease (affecting approximately 1 in 6,000–10,000 newborns) characterized by progressive muscle weakness and atrophy. Of the various forms of the disease, SMA type I is the most severe and manifests in the first months of life, with a failure to acquire motor skills such as head control and maintaining a sitting position. The course of the disease is progressive, leading to death on average at 8–9 months of age without supportive care. Specific therapy (antisense oligonucleotides and gene therapy) is more effective the earlier it is started; treatment started in the pre-symptomatic phase can allow motor development milestones comparable to those of unaffected children. The screening test consists of a molecular genetic analysis of the SMN1 gene on DNA extracted from blood drops on the card. The presence of variants in the gene may suggest the presence of the disease.

If your newborn screens positive and your diagnosis is confirmed, you will be provided with a comprehensive care and treatment plan coordinated by the Meyer Children's Hospital in collaboration with the regional birth center, your family pediatrician, and specialized clinical centers for the treatment of your specific diagnosed condition.

For further information
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The information on data processing is available at: www.meyer.it/screeningneonatale