# Your child and newborn screening

*Dear parents,*

*the Region of Tuscany offers your child the opportunity to be included in a newborn screening programme free of charge.*

**What is newborn screening?**

As part of preventive medicine programmes, all newborn babies undergo, free of charge, simple examinations that allow the early detection of certain congenital diseases.

National law no.104 of 05/02/92 provides for screening for phenylketonuria, congenital hypothyroidism and cystic fibrosis.

Since 2004, the Region of Tuscany has also introduced expanded metabolic screening for over forty metabolic diseases.

National law 167/2016 made such screening mandatory for all those born in Italy.

Tuscany with the regional resolution n° 909/2018 extended screening also to three lysosomal storage diseases and to severe combined congenital immunodeficiencies and, with the regional resolution n° 796/2021, included neonatal screening for Spinal Muscular Atrophy (SMA).

**Why newborn screening?**

The aim of newborn screening is to detect certain congenital diseases early, before symptoms appear, and with the rapid initiation of specific therapies, to prevent or limit the serious damage typical of these diseases.

**How is it carried out?**

Blood drops collected through a small puncture in the heel of the newborn baby between 48 and 72 hours of life are analysed.

The blood drops are placed on a special absorbent paper attached to a card with the newborn's details on it.

Additional blood samples are taken in particular categories of newborn babies, for example, if the newborn baby weighs less than 2,000 grams, three samples are taken at 48 hours, 14 and 30 days.

The card is sent to the Meyer University Hospital (AOU), where the tests are carried out for all those born in Tuscany.

The Meyer AOU keeps the cards with the blood drops collected for ten years

**When will you know the results?**

If the newborn baby tests positive to one of the tests for the diseases under investigation, he/she will be called back to the birth centre or screening centre for further investigations.

Normal results are not reported, so if you are not recalled it means that all the tests have come back negative.

**Attention: recall does not mean that the child is ill, but only that further investigations are necessary**

**What diseases are detected by screening?**

**Congenital hypothyroidism**

Congenital hypothyroidism is due to the lack or insufficient production of thyroid hormones, which are essential for the development and maturation of the central nervous system and for normal growth of the child.

It is treated by administering oral thyroxine. Early diagnosis and treatment allow normal development of the child.

**Phenylketonuria and other metabolic diseases**

Phenylketonuria was the first metabolic disease to be screened in newborns.

It is due to a congenital defect in an enzyme that causes the body to accumulate phenylalanine, one of the components of proteins. The accumulation of phenylalanine is toxic to the brain. Treatment consists of a diet low in this substance and allows normal mental development and growth. In some cases, drug therapy is possible.

In addition to phenylketonuria, screening can identify more than forty metabolic diseases with a complex instrumentation called mass spectrometry (LC-MS/MS). Metabolic diseases are a large group of genetic diseases caused by defects in metabolism. Symptoms can occur as early as the first days of life, but often during the first year or later, even in adulthood. The diseases, if not properly treated, can affect various organs and systems such as the central nervous system, heart, liver, kidneys, skin, etc. In some cases they can cause sudden death. Early diagnosis allows early initiation of dietary and/or drug therapy with improved prognosis and quality of life.

The metabolic diseases screened for in newborns are: **defects in amino acid metabolism, defects in organic acid metabolism, defects in the urea cycle, defects in the beta-oxidation of fatty acids** (about 1 in every 2,000 newborns is affected).

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**Biotinidase defect**

This is a congenital defect in the metabolism of a vitamin, biotin, leading to a multiple carboxylase defect. Symptoms are varied and may include psychomotor retardation, convulsions, immune defect and skin alterations.

Screening assesses the activity of the enzyme biotinidase. Treatment consists of the oral administration of biotin.

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**Galactosemia**

This is due to a genetic defect that causes the body to accumulate galactose, which is derived from the metabolism of carbohydrates, with toxic effects on various organs such as the liver and eye. Treatment consists of a galactose-free diet.

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**Cystic fibrosis**

This disease is caused by a genetic defect that can lead, in a very heterogeneous way, to lung infections and impaired digestive function (digestive malfunctioning), resulting in growth disturbances. It affects 1 in every 4,000 healthy newborns.

The screening test is based in the first instance on the trypsin (a protein with enzymatic activity) dosage on a drop of blood. In the neonatal period it is not uncommon for there to be an alteration in trypsin values, the interpretation of which requires further tests. In a limited number of newborns, it is therefore advisable to proceed to an in-depth genetic analysis (genetic test) for which your consent will be sought.

Early diagnosis of the disease by screening in the neonatal period, usually before the onset of symptoms, can improve the clinical course, prevent many complications and provide the family with genetic counselling for possible future pregnancies.

In addition to symptomatic therapy, in an increasing number of people with cystic fibrosis, drugs effective against the underlying defect of the disease are now available.

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**Lysosomal storage diseases (LSD)**

LSDs are due to genetic defects of lysosomal enzymes with accumulation of substances in the lysosomes of organs and tissues. They are progressive diseases and can lead to severe disability or death at a more or less early stage. They are characterised by extreme variability in age of onset, symptoms, clinical course and severity, even within the same disease.

Three diseases are included in the neonatal screening in Tuscany, by means of enzymatic dosage on a drop of blood: **Pompe disease, Fabry disease, mucopolysaccharidosis type I**.

Enzyme replacement therapy is available for these diseases, which has changed their natural history and modified the quality and life expectancy of patients.

In case of diagnosis by neonatal screening, the time of initiation of therapy may vary depending on the enzymatic/genetic defect and the clinical phenotype.

**Pompe disease**

It is caused by a deficiency in the enzyme lysosomal acid α-glucosidase, which leads to a build-up of glycogen, particularly in cardiac and skeletal muscle tissue. The manifestations of Pompe disease vary in age of onset (infantile, juvenile or adult), type of progression and severity of muscle involvement.

**Fabry disease**

It is caused by deficiency of the enzyme α-galactosidase leading to an accumulation of glycosphingolipids, particularly in the kidneys, heart and nervous system with renal failure, cardiomyopathy or stroke. Neonatal screening generally does not allow diagnosis in females.

**Mucopolysaccharidosis type I**

It is caused by a deficiency in the enzyme α-hyduronidase, which leads to the accumulation of mucopolysaccharides, particularly in the liver, bones, eye and nervous system. In some cases, early transplantation of haematopoietic stem cells may be indicated.

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**Severe combined congenital immunodeficiencies (SCID)**

Severe immunodeficiencies are a large group of rare diseases (over three hundred are known today), all characterised by a defect in the immune system.

Children with severe combined congenital immunodeficiency (SCID) are apparently born healthy. However, due to the severe defect in their immune system, which does not allow them to defend themselves against infectious diseases, they may suffer serious, irreversible damage at an early age or even die from infections that are trivial for children with a normal immune system.

Neonatal screening makes it possible to diagnose SCIDs in the first days of a child's life and then, if an immune defect is suspected, to activate therapy to heal the immune system while protecting the child against all possible infections. In many cases the therapies are able to make the child perfectly healthy again.

Screening is done by looking for molecules called TRECs in a drop of blood from the newborn. TRECs (T *cell receptor excision circles*) are small molecules that are produced during the development and maturation of T cells, which are very important in the function of the immune system. If the immune system is normal it will produce lots of TRECs; conversely, low or absent levels of TRECs are a warning sign and suggest that the immune system is not functioning properly.

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## Spinal Muscular Atrophy (SMA)

Spinal muscular atrophy (SMA) is a genetic disorder (approximately 1 in every 6,000-10,000 infants is affected) characterised by progressive muscle weakness and atrophy. Among the different forms of the disease, SMA type I is the most severe and manifests itself in the first months of life, with the failure to acquire motor skills such as head control and sitting; the course is progressive with exitus on average at 8-9 months of life in the absence of supportive therapies. Specific therapy (antisense oligonucleotides and gene therapy) is more effective the earlier it is introduced; therapy started in the pre-symptomatic phase can allow motor development stages to be reached that are comparable to those of unaffected children.
The screening test consists of molecular genetic analysis of the SMN1 gene (presence/absence in homozygosity of the gene) on DNA extracted from blood drops on the card.

For information on how the data is processed, please consult the Information Notice on the Hospital Company's website www.meyer.it/screeningneonatale.

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**In the event of a positive neonatal screening and confirmed diagnosis, you will be guaranteed a course of care and treatment coordinated by the AOU Meyer in collaboration with the regional birth point, the family paediatrician and the specialised clinical centres for the treatment of the specific pathology diagnosed.**

For further information
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