UNIVERSITÄTS
KLINIKUM
HEIDELBERG

NEUGEBORENENSCREENING HEIDELBERG

PARENT INFORMATION

Dear Parents,

You are about to or have just given birth. We wish you all the best for your child. Most children are born healthy and stay that way. However, there are rare congenital diseases that exhibit no external signs in newborns. Left untreated, these diseases may seriously impair your child. Therefore, it is recommended that all newborns in Germany undergo important early detection tests (newborn screening) in the first few days of life. Participation in newborn screening is voluntary. It is necessary for you to sign the consent form (at least the signature of one of the legal guardians is required) so that these examinations can be performed on your child.

Newborn screening for congenital disorders of the metabolism, the hormonal system, the blood system, the immune system and the neuromuscular system

If left untreated, rare congenital metabolic diseases, hormonal, haematological, immune and neuromuscular disorders may lead to organ damage, physical or mental impairment, severe infections or even death. In most cases, early detection of these conditions makes it possible to prevent or alleviate the consequences of the disease by taking medication, following a diet or implementing other specific measures. The screening procedure is ideally performed on the second or third day of life, by taking a few drops of blood and placing them on a filter paper card, which is subsequently sent to a screening laboratory. The exact procedure of the examination and the individual diseases are explained on page 2.

Newborn screening for cystic fibrosis

Along with the newborn screening for congenital disorders of the metabolism, the hormonal system, the blood system, the immune system and the neuromuscular system, you have the option to have a newborn screening test for cystic fibrosis for your child performed on the same blood sample.

Children with cystic fibrosis develop viscous mucus in their lungs and other organs. This leads to permanent inflammation. As a result, the children are often underweight and do not reach their full growth potential.

In severe cases, their pulmonary function may be significantly impaired. The aim of this examination is the early diagnosis of cystic fibrosis so that treatment can be initiated as soon as possible, thus improving the quality of life and life expectancy of the affected children. In accordance with the legal requirements of the Genetic Diagnostics Act, a doctor is required to provide detailed information before newborn screening for cystic fibrosis is carried out.

Once all the tests have been completed, your child's blood spot sample will be stored for three months in accordance with the legal requirements and destroyed thereafter.

Heidelberg University Hospital
Center for Child and Adolescent Medicine
Dietmar Hopp Metabolism Center
Newborn screening
Im Neuenheimer Feld 669
69120 Heidelberg

Phone: 06221 56-8278; -8475
www.neugeborenenscreening.uni-hd.de

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NEWBORN SCREENING FOR CONGENITAL METABOLIC, HORMONAL, HAEMATOLOGICAL, IMMUNE AND NEUROMUSCULAR DISORDERS

There are rare congenital metabolic diseases, hormonal, haematological, immune and neuromuscular disorders that are not yet recognisable by external signs in newborns. These occur in approximately one in 1,000 newborns. If left untreated, these conditions, may lead to organ damage, physical or mental impairment, severe infections or even death. In order to detect these diseases, a blood test, known as newborn screening, has been recommended for all newborns as a preventive medical procedure over the past 50 years. Over the past few years, these tests have been further improved, making it possible for more treatable diseases to be included as a part of newborn screening.

Why is newborn screening performed?

These congenital metabolic, hormonal, haematological, immune and neuromuscular disorders should be detected in good time. In most cases, the consequences of a congenital disease can be avoided or alleviated by early treatment, initiated as soon as possible after birth.

When and how is the examination carried out?

During the second to third day of life (37th to 72nd hour after birth), no later than the second preventive medical check-up of your child, known as U2, a few drops of blood (from a vein or heel) are placed on a filter paper card and, once dried, immediately sent to the screening laboratory.. Once there, the samples will be analysed immediately by means of special, highly sensitive examination methods. The costs of the examination are covered by health insurance.

What diseases and conditions are screened for?

A binding directive of the Joint Federal Committee of Doctors and Health Insurance Funds (G-BA) specifies the diseases the blood spot sample may be tested for. The list includes 13 metabolic disorders, two hormonal disorders, severe combined immunodeficiency (SCID), the sickle cell disease (SCD) and spinal muscular atrophy (SMA). The consequences and symptoms of these diseases are described in detail below.

In total, one in 1000 newborns is affected by one of these diseases. The majority of the affected families had previously not experienced such conditions.The affected children seem perfectly healthy at birth, so that newborn screening is the only way to prevent impairments to mental and physical development. No conclusions with regard to family-related risks may be drawn from this examination alone.

Who will be informed about the test results?

In the event of abnormal test results, you will be contacted immediately. That is why you should provide your telephone number as well as the address, where you can be contacted during the first few days after the child's birth, on the test card. Please make sure that your contact details are correct and clearly legible on the dried blood spot card containing your child's blood. Early detection and treatment for affected newborns is only possible if all parties involved – parents, clinic or paediatrician and screening laboratory – collaborate without delay so that the test results can be obtained and checked in good time.

Test results that are not considered significant will only be provided to you upon request. You can also find the contact details of our laboratory in your child's yellow examination booklet.

What does the test result mean?

The result of the newborn screening is no medical diagnosis: the examined target diseases must be largely excluded or confirmed by further medical examinations. Different examinations are required for each target disease, e.g. repeated testing. However, it may also be necessary to repeat the newborn screening if the timing of the blood sample was not optimal or if the amount of blood on the card was insufficient.

Are these diseases curable?

All the metabolic diseases mentioned, immunodeficiencies, the sickle cell disease, endocrine and neuromuscular disorders are congenital and therefore cannot be cured in most cases. Furthermore, timely treatment cannot completely prevent the consequences of the disease in all medical conditions. In most cases, however, prompt treatment enables the affected child to develop normally. The treatment involves a special diet, administration of certain medications, as well as counselling and instruction for parents on how to implement preventive measures. Metabolism and hormone specialists (endocrinologists), haematologists, paediatric neurologists or immune system disorder specialists are available for advice and care in cases of suspected or actual disease.

Since the Genetic Diagnostics Act came into force in 2010, the Genetic Diagnostics Commission (GEKO) at the Robert Koch Institute has been evaluating new mass screenings for genetic diseases. The GEKO guideline of the Genetic Diagnostics Commission has endorsed the introduction of screening tests for early detection of tyrosinemia type I, severe combined immunodeficiency (SCID), the sickle cell disease and spinal muscular atrophy (SMA).

TARGET DISEASES

Adrenogenital syndrome
Endocrine disorder due to adrenal cortical defect: masculinisation in girls, may become fatal due to life-threatening salt-loss crises. Treatment with hormones, good prognosis (incidence: approx. 1/15,000 newborns).

Maple syrup urine disease
Defect in the breakdown of amino acids: mental impairment, coma, potentially fatal. Treatment involving a special diet, usually good prognosis (incidence: approx. 1/180,000 newborns).

Biotinidase deficiency
Abnormal metabolism of the vitamin biotin: skin lesions, metabolic crises, mental impairment, potentially fatal. Treatment by biotin administration, very good prognosis (incidence: approx. 1/28,000 newborns).

Carnitine metabolism defects
Defective metabolism of fatty acids: metabolic crises, coma, potentially fatal. Treatment involving a special diet, very good prognosis (incidence: approx. 1/600,000 newborns).

Galactosaemia
Defective metabolism of a lactose component (galactose): clouding of the eye lens, physical and mental impairment, liver failure, potentially fatal. Treatment involving a special diet, usually good prognosis (incidence: approx. 1/77,000 newborns).

Glutaric aciduria type I
Defect in the breakdown of amino acids: sudden metabolic crisis with permanent movement disorder. Treatment involving a special diet, usually good prognosis (incidence: approx. 1/140,000 newborns).

Hypothyroidism
Congenital hypothyroidism: Severe impairment of mental and physical development. Treatment by hormone administration, very good prognosis (incidence: approx. 1/3,000 newborns).

Isovaleric acidemia
Defect in the breakdown of amino acids: mental impairment, coma, potentially fatal. Treatment involving a special diet, very good prognosis (incidence: approx. 1/90,000 newborns).

LCHAD, VLCAD deficiency
Defective metabolism of long-chain fatty acids: metabolic crises, coma, muscle and cardiac muscle insufficiency, potentially fatal. Treatment involving a special diet, avoidance of hunger phases, generally good prognosis (incidence: approx. 1/80,000 newborns).

MCAD deficiency
Defect in terms of converting fatty acids into energy: hypoglycaemia, coma, potentially fatal. Treatment by avoiding phases of hunger, very good prognosis (incidence: approx. 1/10,000 newborns).

Phenylketonuria
Defect in the metabolism of the amino acid phenylalanine: leads to mental impairment if left untreated. Successful treatment based on a special diet, very good prognosis (incidence: approx. 1/10,000 newborns).

Tyrosinaemia type I
Impaired breakdown of the amino acid tyrosine, which may lead to severe liver impairment with jaundice and increased tendency of bleeding, impaired kidney function and neurological crises in the absence of treatment from the first days of life. Treatment based on medication (Nitisinone) and protein-restricted diet, good prognosis (incidence: approx. 1/135,000 newborns).

Severe combined immunodeficiency (SCID)
Total absence of immune defence: high susceptibility to infections along with infectious complications, starting already during infancy. Treatment by strict hygienic precautions. Therapy with bone marrow or stem cell transplantation, enzyme replacement therapy. Abstention from breastfeeding, live vaccinations or transfusion of untreated blood products. In the absence of treatment, most affected children die within one to two years (incidence: approx. 1/32,500 newborns).

Sickle cell disease (SCD)
Deformation of red blood cells (sickle cells) leading to anaemia, increased blood viscosity and reduced oxygen supply to organs. Long-term organ damage. Acute complications including cerebral infarction, kidney failure, spleen infarction, sepsis and anaemia. Treatment approach includes patient counselling and instructions on behavioural measures, infection prophylaxis (e.g. vaccinations), administration of hydroxyurea, blood transfusions if necessary, and stem cell transplantation in some cases as additional treatment approach. Without treatment, symptoms may occur from around the third month of life (incidence: approx. 1/6,000 newborns).

Spinal muscular atrophy (SMA)
Deficiency of a certain protein (survival motor neuron (SMN) protein) leads to progressive muscle weakness associated with a decline in motor skills and impaired lung function. Treatment is medication-based and symptomatic (physiotherapy, rehabilitation, orthopaedics, psychology). First symptoms of the disease in children with infantile SMA (the most common and most severe form) appear by the age of six months. In the absence of treatment, these children die within one to two years (incidence: approx. 1/6,700 newborns).

NEWBORN SCREENING FOR CYSTIC FIBROSIS

Along with the newborn screening for congenital metabolic diseases, hormonal, haematological, immune and neuromuscular disorders, you will also have the option to have your child screened for cystic fibrosis. The purpose of this examination is to diagnose cystic fibrosis at an early stage so that treatment can be initiated as soon as possible, thus improving the quality of life and life expectancy of children with cystic fibrosis. Screening for cystic fibrosis is subject to the special regulations of the Genetic Diagnostics Act. The following information is intended to help you prepare for a consultation with your doctor.

What is cystic fibrosis?

Cystic fibrosis is a hereditary disease that affects approximately one in 3,300 children. A genetic mutation in the so-called CFTR gene leading to impaired salt exchange in glandular cells. This in turn stimulates the formation of viscous mucus in the respiratory tract and other organs, resulting in permanent inflammation. The severity of the symptoms may vary depending on the type of the genetic mutation. Often, the function of the pancreas is restricted. Consequently, affected children are often underweight and do not reach their full growth potential. In severe cases, recurrent severe pneumonia episodes may result in significant lung function impairment.

What are the treatment options for cystic fibrosis?

Currently, there is no curative treatment for cystic fibrosis. However, the symptoms of the disease can be improved or alleviated by various therapeutic approaches, so that the life expectancy of patients with cystic fibrosis has been continuously increasing. Treatment for cystic fibrosis involves inhalation therapy and physiotherapy, high-calorie nutrition and medication. Furthermore, regular check-ups at specialised cystic fibrosis clinics are necessary to ensure that treatment can be initiated in good time to counteract even early changes.

Why is cystic fibrosis screening important?

Screening for cystic fibrosis is subject to the special regulations of the Genetic Diagnostics Act. If treatment is initiated at an early stage, the physical development of the affected children can be improved. Thus, the chnances of a longer and healthier life are also increased.

How is screening for cystic fibrosis carried out?

No additional blood sample is required for screening for cystic fibrosis. The screening for cystic fibrosis is performed at the same time and using the same blood sample which is taken for the newborn screening for congenital metabolic diseases, hormonal, haematological, immune and neuromuscular disorders in your child.

The procedure involves placing a few drops of blood (from vein or heel) on a filter paper card and sending it to a screening laboratory. There, first the enzyme immunoreactive trypsin (IRT) is determined . If the result indicates an increased value, a second examination for pancreatitis-associated protein (PAP) is carried out with the same blood sample. In case the second test result is also abnormal, a DNA test (genetic test) is carried out with the same sample to identify the most common genetic mutations that occur in cystic fibrosis. If one or two gene mutations are found, the screening result requires further examination. However, if the first test result (IRT) proves to be highly abnormal, the screening result alone requires verification and no further tests are carried out. All testing steps are combined to ensure the greatest possible accuracy and reliability of the results. In very rare cases, it is possible that cystic fibrosis is present in a child, whileit is not detected by this early screening test. In accordance with the legal requirements of the Genetic Diagnostics Act, it is mandatory that a doctor discusses the matter with you before your newborn child is screened for cystic fibrosis. If a midwife or obstetric nurse is present at birth, the screening for cystic fibrosis in your child can be carried out by a doctor (for example as part of the U2 check-up) up to the age of four weeks. In this case, an additional blood sample is required. In contrast to screening for cystic fibrosis, newborn screening for congenital metabolic diseases, hormonal, haematological, immune and neuromuscular disorders should ideally take place within the 37th to 72nd hour of life, since, unlike cystic fibrosis screening, immediate initiation of treatment is crucial for the majority of the diseases tested.

Your child's blood sample will be stored for three months after the test and destroyed thereafter.

Who will inform you about the result of the screening and what is the follow-up procedure?

The laboratory will inform you within 14 days if the findings require any further action. If the result is normal, no information will be provided, unless you explicitely request it. In the case of results that require further examination, a doctor will refer you to a specialised institution where you can have a follow-up examination with your child. A result requiring further diagnostic examination does not mean that your child has cystic fibrosis. Merely one in five children whose results require further diagnostic examination actually suffers from cystic fibrosis. However, the probability of a so-called genetic predisposition is increased. The genetic carriers are healthy, but can pass this trait on to their offspring. Whatever the case, genetic counselling will be offered to you so that you can be fully informed about the significance of this result. The first step at the Cystic Fibrosis Centre is a confirming examination, usually a sweat test, and all further steps will be discussed with you. The sweat test is safe and painless and does not put any strain on your child. You will be informed of the result immediately after the examination. Further investigation may be required.

You make the decision regarding your child.

Participation in cystic fibrosis screening is voluntary. The costs of the examination are covered by statutory health insurance. The results of the examination are subject to medical confidentiality and may not be passed on to third parties without your consent. In the event of abnormal test results, you will be contacted immediately. That is why you should provide your telephone number as well as the address, where you can be contacted during the first few days after the child's birth, on the test card. You have the right to withdraw your consent to cystic fibrosis screening at any time. A decision in favour of or against cystic fibrosis screening should be made after thorough and informed consideration. You are always welcome to discuss your concerns with the doctors. This genetic screening for cystic fibrosis is endorsed by the Genetic Diagnostics Commission at the Robert Koch Institute.

DATA COLLECTION / PROCESSING

Personal data related to the contact details of the legal guardians and health data of the newborns are processed for the purpose of conducting the extended newborn screening according to the Children's Directive (G-BA) under Art. 9 para. 2 lit. a GDPR. Additional processing purposes such as invoicing, documentation of laboratory services and quality assurance are carried out in accordance with Art. 9 para. 2 lit. b GDPR. Apart from the blood sample for the screening test, the following information is included on the test card: your child's name (to ensure correct assignment of the sample), birth information (to assess validity or medical validation), and your name and contact information (for the purpose of contacting you in the event of abnormal findings, sending test results, invoicing, and management of reminders). The test card including all the data mentioned above is sent to the contracted laboratory, which carries out the extended newborn screening and/or the screening for cystic fibrosis. The data on the test card is processed and stored in the laboratory's IT system. The examination results are medical findings that are stored in pseudonymised form for a period of 10 years. The test cards with residual blood are destroyed three months after completion of the procedure. Your data and your child's data will not be processed for purposes other than those stated and will not be disclosed to unauthorised third parties.

The following are independently responsible for data protection:

- your obstetrician for information, data collection, obtaining consent
- as the recipient, the laboratory commissioned to carry out the newborn screening, transfer of findings, contact and reminder management
- in the event of abnormal findings, a specialised institution of your choice for the implementation of clarification diagnostics
- and possibly the attending physician for the care of your child

You have the right to request information about the personal data stored about you and your child from any data controller. You can also request the correction of inaccurate data or the restriction of processing. For questions or concerns regarding data protection in relation to newborn screening, please contact:

Heidelberg University Hospital (UKHD)
Center for Child and Adolescent Medicine
Dietmar Hopp Metabolism Center
Newborn screening
Im Neuenheimer Feld 669
69120 Heidelberg
Phone: 06221 56-8278, -8475
Fax: 06221 56-4069
E-mail: neugeborenenscreening@uni-hd.de
Web: www.ukhd.de/ngs

or confidentially the data protection officer of Heidelberg University Hospital:

E-mail: datenschutz@med.uni-heidelberg.de

You also have the right to lodge a complaint with a data protection supervisory authority, if you believe that the processing of your personal data violates d the ata protection act. The responsible data protection supervisory authority for Heidelberg University Hospital is:

The State Commissioner for Data Protection and Freedom of Information (Landesbeauftragte für den Datenschutz und die Informationsfreiheit) Baden-Württemberg
Postal address: Postfach 10 29 32, 70025 Stuttgart
Königstraße 10a, 70173 Stuttgart, Germany
Phone: 0711 615541-0
Fax: 0711 615541-15
Email: poststelle@lfdi.bwl.de
Internet: www.baden-wuerttemberg.datenschutz.de

If your data protection concerns relate to information, data collection, consent, care or clarification diagnostics, please contact the person responsible for you.

Right of withdrawal

The extended newborn screening and the screening for cystic fibrosis are voluntary. You don't have to accept these offers and you can revoke them at any time either in whole or in part with effect for the future. The legitimacy of data processing that has already taken place remains unaffected by revocation. Please send your revocation to the contact details of the Dietmar Hopp Metabolic Centre (UKHD) - Newborn Screening mentioned above.

DECLARATION OF CONSENT TO NEWBORN SCREENING

Name of the child: _____

Date of birth: _____
(or adhesive label)

I/we have been informed in detail about the newborn screening for congenital metabolic diseases, hormonal, immune, haematological, neuromuscular disorders and newborn screening for cystic fibrosis. I/we have been informed of the possible negative consequences for my/our child if individual parts of the newborn screening are rejected.

My/our consent includes the performance of the extended newborn screening for the above-mentioned target diseases and/or the performance of the screening for cystic fibrosis. The consent includes in each case:

- ✓ transfer of the test card (contact details, birth data and blood sample) from your obstetrician to the contracted laboratory for the purpose of performing newborn screening.
- ✓ in the event of a test result requiring further examination: contact between the laboratory and you to request a second test card/second blood sample for further examination, including reminder management.
- ✓ in the event of an abnormal test result: contact between the laboratory and you for the purpose of providing information on further procedures and choice of a specialised institution for the diagnostic investigation, as well as
  - transfer of the test results and your contact details to the selected specialised institution for the purpose of timely and uncomplicated booking of an appointment for the diagnostic investigation.
  - transfer of the test results from the laboratory to the attending physician at the hospital for the purpose of coordinated provision of medical care, provided that your child is still in hospital at the time of screening.
  - contact between the laboratory and you for the purpose of reminder management if you do not attend the clarifying examination.
  - transfer of the results of the clarifying examination from the specialised institution to the laboratory for quality assurance purposes.

Consent

I/we consent to the execution of the following examinations, including any data transfers and third-party contacts intended for this purpose (please tick the appropriate box):

○ Newborn screening for the target diseases listed (page 3)

○ Screening for cystic fibrosis (page 5)

The consent is **voluntary** and can be refused or withdrawn at any time without giving reasons. Further information on data protection can be found on page 6.

Date, names in block letters, signatures of the legal guardians in accordance with Art. 9 para. 2 lit. a GDPR (at least of one legal guardian)

Date, name in block letters, signature of the doctor providing information in accordance with § 8 para. 1 GenD

This declaration of consent remains with the sender of the sample.
Consent to newborn screening or refusal of a part of the screening programme must be noted on the filter paper card for newborn screening in the fields provided.