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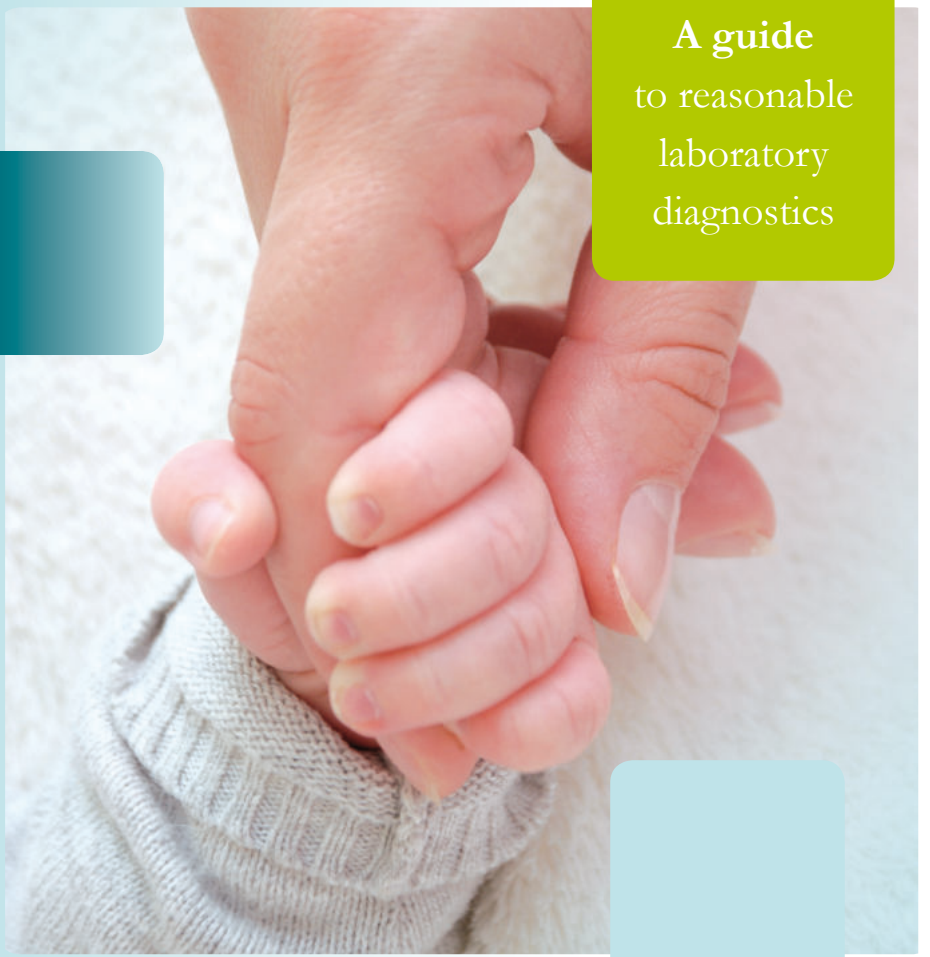
Medical Care Centre for Laboratory Medicine,
Microbiology, Hygienics and Human Genetics

Planning a family and prenatal care

A guide
to reasonable
laboratory
diagnostics



Stand: 06/2022

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Preface

Already 100 years ago, women were cared for by a midwife during pregnancy.

Today, prenatal care is defined and regulated according to the German maternity guidelines established by the German Federal Committee (GBA). This ensues a regular monitoring of the expectant mother's health as well as of the developmental status of the unborn child. Should problems occur, timely advice and treatment can thus be performed.

At present, care and support for expectant mothers is provided by gynaecologists and midwives.

Contents

1. Necessary Prenatal Care

Some infectious diseases may be transmitted to the unborn child during pregnancy. The resulting complications are varied and may lead to harming the development of the foetal organs as well as to miscarriages, premature birth or stillbirth.

Women who wish to have children should see their attending physician and check their vaccination card or, as appropriate, other health documents in order to detect any vaccination gaps. This check-up is recommended several months before an intended pregnancy to enable a timely booster dose (approx. 3 months before an intended pregnancy) in case of insufficient immune protection, e. g. against rubella or chicken pox.

The following infectious agents may pose a risk to the unborn child:

Agent	Disease
Treponema pallidum	syphilis (lues)
Rubella virus	rubella (German measles)
Varicella zoster virus (VZV)	varicella (chicken pox), herpes zoster (shingles)
Hepatitis B virus	liver inflammation (hepatitis or jaundice)
Toxoplasma gondii	toxoplasmosis
Cytomegalovirus (CMV)	cytomegaly
Parvovirus B19	fifth disease
Chlamydia trachomatis	sexually transmitted disease
Human immunodeficiency virus (HIV)	AIDS

To clarify immunity against the above-mentioned agents, the mother's blood is tested for antibodies and antigens, except for Chlamydia trachomatis (PCR).

Furthermore, it should be checked whether any necessary and regular medication can be taken during pregnancy (e. g. embryotox.de).

In the following you will find the necessary prenatal care screenings which are carried out during the early stages of pregnancy, with the exception of Hepatitis B (after 32nd week of pregnancy), and which are covered by health insurance.

a) Treponema pallidum as cause for syphilis (lues)

Syphilis is an infectious disease developing in several stages which is sexually transmitted.

Approximately 9-90 days after infection a painless ulceration and swellings of the lymph nodes in the area of infection (usually genitals) and, later, non-specific skin and mucosal alterations are noticed. After years without complaints, disorders of the nervous system, the heart, the bones and other internal organs may occur.

An infection of the unborn child is possible by transfer of the agents via the placenta or during birth due to a skin or mucosal defect.

Generally, a high infection rate of the foetus can be expected if the initial infection took place during the two previous years. Without appropriate treatment of the expectant mother there is an increased risk for severe malformations of the child or miscarriages, premature or stillbirths. Infected live births have syphilis in different stages of the disease.

In most cases, an early treatment of the mother prevents this serious infection of the unborn child. Therefore, the maternal blood is usually tested during early pregnancy. For data protection reasons the screening result will not be entered into the pregnancy record (Mutterpass), it is merely noted that the screening was performed.

b) Rubella virus
as cause for rubella (German measles)

A rubella virus infection in children usually occurs as a harmless illness with fever and rashes. A human-to-human transmission takes place by droplets which are spread by sneezing or coughing.

An initial infection during the early stages of pregnancy does not only affect the mother but also the unborn child. Usually there are grave consequences for the child. Deformations of the heart, the inner ear (hardness of hearing), the eyes (cataract) and mental development disorders are possible. These developmental disorders are referred to as rubella embryopathy (congenital rubella syndrome). The risk for abnormal embryonic developments is greatest for an infection during the first trimester (1st-6th week ca. 55 %, 7th-12th week ca. 25 %, 13th-17th week ca. 10-15 %). An infection after the 17th week of pregnancy usually does not lead to any defects of the unborn child.

There is a risk for pregnant women who do not have any protective antibodies. According to the maternity guidelines an antibody test of the maternal blood is mandatory during early pregnancy. This screening can be omitted if the attending gynaecologist has medical findings on hand e. g. from a previous pregnancy or two vaccinations documented in the vaccination card. An existing immunity is then assumed.

The screening result will be entered into the pregnancy record (Mutterpass).

c) Varicella zoster virus
as cause for varicella (chicken pox) or herpes zoster (shingles)

The Varicella zoster virus causes a disease in children which is generally called “chicken pox”. Clinical symptoms occur within 8-28 days after contact with the virus. These are manifested by fever and blister-like changes of the skin, the scalp and the oral mucosa occurring in several phases. These blisters eventually scab over, usually without leaving scars. The virus remaining in the body throughout life, a second manifestation often occurs later in life which is called shingles or herpes zoster. This so-called reactivation is characterised by local, sometimes very painful, belt-shaped skin rashes, primarily on the back. Other parts of the body may be affected, e. g. the forehead and the eyes.

Patients who have overcome chicken pox as children, possess protective antibodies preventing an infection following renewed contact. Only approximately 6 % of adults have no protection against varicella zoster viruses. Especially in non-protected, pregnant women a severe course of the disease and complications may occur which also affect the unborn child. So, if an initial infection occurs until the 20th week of pregnancy, foetal malformations occur in 1-2 % of cases. Frequently, scarring of the skin, ocular anomalies, disorders of the nervous system and underdeveloped extremities are observed. An initial infection during late pregnancy may lead to a life-threatening pneumonia of the mother or a severe, life-threatening varicella infection of the newborn.

Varicella is highly infectious as it is transmitted from human to human by droplets which occur among other things by sneezing or coughing. These droplets are inhaled and subsequently, the virus is taken in via the mucous membranes of the respiratory tracts. There is a risk of infection from one to two days before blisters occur until the scab falls off. Herpes zoster blisters are less infectious. However, if a non-protected person comes into contact with it, they may contract chicken pox.

Please avoid contact to all persons with chicken pox or herpes zoster.

If you are planning a pregnancy and you know that you do not have protective antibodies, you can get vaccinated (please consult your gynaecologist). Vaccination should take place at least 3 months before an intended pregnancy.

If you do not have protective antibodies or you do not know your immune status and had contact to infected persons, you should immediately consult your attending gynaecologist. They will decide whether an immunisation with antibodies is possible to prevent the disease.

This screening can take place before an intended pregnancy (as part of birth control counselling) or if an infection during pregnancy is suspected. In both cases health insurance covers the costs.

d) Hepatitis B-Virus as cause for liver inflammation

Hepatitis B is a liver inflammation caused by viruses. The viruses are transmitted by blood/blood products, by sexual intercourse with an infected partner or during birth from mother to child. To rule out an infection of the mother, a laboratory test (HBsAG) is performed only at the end of pregnancy (after the 32nd week of pregnancy) and is entered into the pregnancy record (Mutterpass). The new guideline on prophylaxis, diagnosis and therapy of hepatitis B virus infection of 2021 recommends therapy after the first trimester and before the 28th week of pregnancy. Accordingly, we recommend testing for HBs antigen as early as possible in the first trimester.

Immediately after birth, the newborn baby of a Hepatitis B infected mother is vaccinated against this virus. This will be an active and passive immunisation. The child's immune system will be actively induced to produce antibodies with the regular Hepatitis B vaccine and, additionally, (passively) receives antibodies against Hepatitis B which destroy the viruses in the child's blood. The regular Hepatitis B vaccine will be administered again after one and six months.

An infection with Hepatitis B viruses in newborn babies often becomes chronic and life-threatening consequences may be expected, and this so-called serovaccination prevents an infection in newborns in 95 % of all cases.

e) Chlamydia trachomatis as cause for a sexually transmitted disease

The bacterium Chlamydia trachomatis is transmitted by sexual intercourse or by smear infection of contaminated objects. It causes diseases of the urinary tract or the genitals with varying symptoms. A distinction is made between an asymptomatic disease progression and diseases with severe complaints, e. g. discharge, bleeding disorders, lower abdomen pain, inflammation of the uterus and the Fallopian tubes possibly leading to infertility.

An infection with Chlamydia trachomatis carries an increased risk for premature births, a premature rupture of membranes, conjunctivitis or pneumonia of the newborn. Therefore, a Chlamydia infection should be treated with a suitable antibiotic even during pregnancy. The simultaneous treatment of the partner is also recommended to avoid a re-infection of the mother. The antibody detection for an infection with Chlamydia trachomatis is not very conclusive. Therefore, the direct pathogen detection (detection of the genome or the DNA) from at least 10 ml of the first void urine of the first morning urine is recommended.

f) Human immunodeficiency virus (HIV) as cause for AIDS

Based on estimations of the Robert Koch Institute, currently 91,400 people are infected with the HI virus in Germany, approximately 6 % are women of child-bearing age between 20 and 40 years. The risk of infection for the child during pregnancy is approximately 7 %, during birth the probability increases to 18 %. A transmission through breastfeeding is also possible in 7-22 % of all cases.

Therefore, it is very important to know about an HIV infection of the pregnant woman.

By implementing specific measures, there is a high probability that an infection of the newborn can be prevented, e. g. a treatment of the pregnant woman before the presumed date of birth, a planned Caesarean section, an early prophylactic treatment of the newborn and not breastfeeding.

In order to check for a possible infection, a blood sample is taken and tested in the laboratory for the simultaneous presence of antibodies and antigen (p24) against HIV. For data protection reasons the screening result will not be entered into the pregnancy record (Mutterpass).

2. Other recommended diagnostics as part of prenatal care

Apart from the already mentioned infectious agents, there are further pathogens which are significant during pregnancy. Additional screenings are offered by your attending physician and can improve the medical care. So, if pregnant women know their immune status, it is possible to prevent an infection with e.g. toxoplasmosis or cytomegaly during pregnancy.

a) Toxoplasma gondii as cause for toxoplasmosis

Toxoplasma gondii is a protozoan (single-cell) parasite which settles in the muscles and the central nervous system (e. g. brain) after oral intake and forms cysts which do not usually cause any diseases. An initial infection of healthy persons usually proceeds undetected or shows flu-like symptoms such as headaches and limb pains, fever and swellings of the lymph nodes in the throat or neck.

But an initial infection during pregnancy may have grave consequences for the unborn child. These are, e. g. enlargement of the liver and the spleen, eye damage possibly leading to blindness, calcification of the brain, hydrocephalus with seizures or mental development disorders as well as miscarriages or premature births.

With increasing gestational age, the transmission rate increases (10-100 %), while the severity of the illness of the child decreases (from 40 to <5 %).

In order to avoid an initial infection during pregnancy a number of preventive measures should be observed:

- only eat sufficiently heated or roasted meat, if possible wear gloves when processing and handling meat
- thoroughly wash your hands after contact with cats
- wear gloves when cleaning the cat toilet and rinse with hot water, if possible assign the cleaning to another person
- thoroughly clean vegetables and fruits

An early diagnosed initial infection during pregnancy can be treated with suitable antibiotics to decrease the probability for a transmission of the infection.
The screening result will be entered into the pregnancy record (Mutterpass).

b) Parvovirus B19 as cause for fifth disease

Parvovirus B19, as pathogen for fifth disease, causes a feverish condition, usually during childhood, which is associated with rashes and proceeds without complications. In adults, the disease progression is more severe and subsequently may lead to joint pains (arthritis), inflammations of the liver, the brain or the heart. Additionally, acute infections in pregnant women who do not possess protective antibodies may lead to foetal malformations in approximately 20-30 % of cases due to oedema in the head and body cavities (hydrops fetalis), to anaemia or to miscarriages or stillbirths.

Parvovirus B19 is also transmitted from human to human by droplets due to sneezing or coughing. The risk of infection is highest before rashes occur and an infection is then difficult to prevent.

Additionally, fifth disease is currently considered to be a childhood disease, so that contact to toddlers and schoolchildren presents an increased infection risk.

c) Cytomegaly virus (CMV) as cause for cytomegaly

Cytomegaly infection is the most common infection leading to foetal malformations with 0.2-2 %. In Germany, an estimated 40-50 % of women of childbearing age do not have protective antibodies against this virus. Approximately 1-3 % of these seronegative women are infected during pregnancy, an initial infection proceeding undetected in 80 % of cases. Only few women observe non-specific, flu-like symptoms such as fever, swelling of the lymph nodes, headache and limb pains.

In approx. 40 % of cases the virus is transmitted to the unborn child. Possible consequences of a CMV infection are growth retardation, calcification of the brain, liver and spleen enlargements, hardness of hearing, eye damages as well as miscarriages and stillbirth. Even if the children of infected women appear healthy at birth, deafness, inflammations of the retina or mental development disorders may occur months or even years later.

CMV is transmitted by exposure to body fluids, e. g. saliva, urine, tears, sperm, vaginal secretion, blood transfusions or breast milk and so enters the body via the mucous membranes. CMV is particularly often excreted in urine and saliva by asymptomatic toddlers who were infected in childcare facilities. Therefore, women who are often in contact with toddlers, privately or at work, are especially at risk. Unfortunately, there is no CMV vaccine yet.

If you know that you do not have protective antibodies, you should observe the following preventive hygiene measures:

- clean and disinfect all surfaces that have come into contact with the toddler's saliva or urine
- thoroughly wash your hands with hot water and soap after changing diapers or feeding, cleaning the nose, contact with your child's tears or saliva
- do not share towels, dishes or cutlery, cups or pacifiers

d) Group B streptococci

Group B streptococci are bacteria which can be detected in the vagina or the stools in up to 40 % of pregnant women. The women are not sick, but only asymptomatic carriers of this pathogen. One in two newborns of mothers with a positive B streptococci detection is colonised by these bacteria. They can be detected on the skin or the mucous membranes even without any symptoms. Only approx. 1-2 % of these newborns are infected. The disease only occurs several days or even weeks after birth and is manifested by meningitis, pneumonia or blood poisoning.

Therefore, the medical societies of gynaecologists and paediatricians recommend a microbiological test for group B streptococci at the end of the pregnancy (approx. 35th-37th week of pregnancy). For this, a smear test of the vaginal entrance and the rectum is done.

By administering a suitable antibiotic from the first contractions or the bursting of the amniotic sac, the risk of transmission can be significantly reduced and an infection of the newborn can be prevented.

group B streptococci on Columbia blood agar

3. Diabetes during pregnancy (gestational diabetes)

Diabetes mellitus is a disease in which the sugar metabolism (carbohydrate metabolism) is impaired. This disease is caused by the lack of or insufficient effectiveness of the body's own hormone insulin which regulates the glucose transport to the body cells (e. g. muscles) and reduces blood sugar levels. Insulin is produced in the pancreas and released depending on the blood sugar level.

There are two types of diabetes mellitus, congenital diabetes mellitus type 1 which leads to an absolute insulin deficiency due to the destruction of insulin-producing cells and diabetes mellitus type 2 which is characterised by a reduced insulin efficiency and usually occurs at an advanced age or in obese people.

Gestational diabetes is a special type and occurs during pregnancy for the first time. This is caused, among other things, by pregnancy hormones which lead to a reduced insulin efficiency and therefore to increased blood sugar levels. The oversupply of carbohydrates (sugar) reaches the unborn child via the placenta reacting with an increased insulin production. This leads to a significant increase in height and weight and to an increased urine production of the child. Due to the higher levels of amniotic fluid, there is an increased risk for premature births or miscarriages. Furthermore, birth complications may occur possibly requiring a Caesarean section. Newborns are monitored after birth to recognise low blood sugar levels requiring treatment at an early stage.

How is gestational diabetes diagnosed?

The maternity guidelines envisage urine tests for sugar which are, however, very unreliable to make a diagnosis. Therefore, a glucose tolerance test (oral glucose tolerance test = OGTT) is recommended to every pregnant woman between the 24th-28th week of pregnancy.

Usually, the shortened version is performed as screening test for which the expectant mother does not have to fast prior to the test. For the screening test an oral dose of 50 g glucose solution must be taken. After one hour blood sugar is measured by taking a blood sample. If the blood sugar level is more than 135 mg/dl or 7.5 mmol/l, a longer version of the glucose tolerance test is performed. The pregnant woman is instructed to fast from 10 p. m. the night before. The next morning a blood sample is drawn on an empty stomach. Then, a 75 g glucose solution is taken orally. After one and two hours further blood samples are drawn to determine the blood sugar levels.

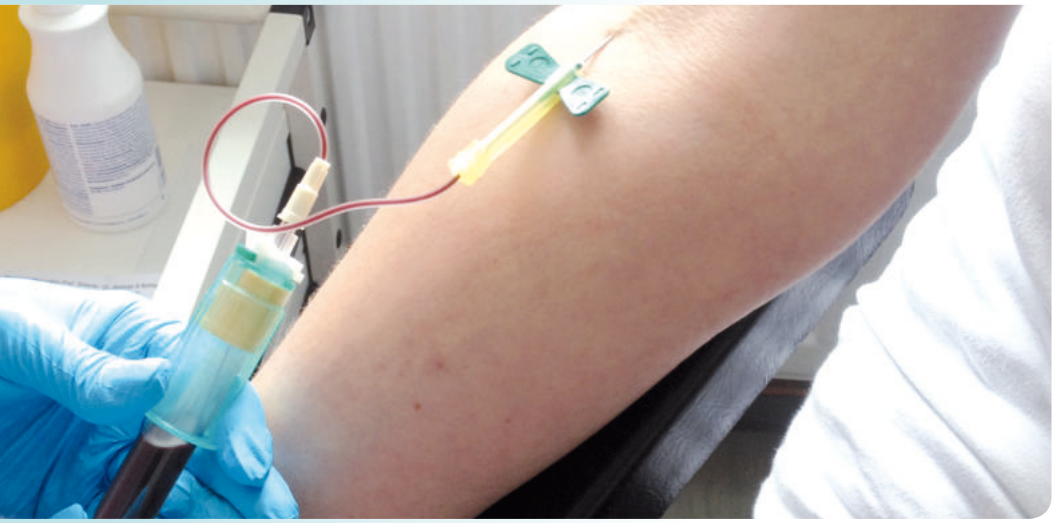
screening time	blood sugar threshold value in venous plasma
prior glucose consumption (empty stomach)	92 mg/dl bzw. 5.1 mmol/l
after 1 hour	180 mg/dl bzw. 10 mmol/l
after 2 hours	153 mg/dl bzw. 8.5 mmol/l

Following recommendations of the German Diabetes Association (Deutsche Diabetes Gesellschaft, DDG) 2011, a gestational diabetes is diagnosed if at least one of the three threshold values is exceeded.

Which treatment is recommended?

In approx. 85 % of pregnant women a change of diet and light physical activity are sufficient to improve blood sugar levels. In the remaining cases an insulin therapy is necessary.

The attending gynaecologist or midwife should be informed about the diagnosis, as additional screenings (CTG or ultrasound) may be necessary during the pregnancy.



4. Blood typing and Rhesus incompatibility

The blood group system describes characteristics of the red blood cells (erythrocytes). The AB0 system is the principal classification system with the blood groups 0 (zero), A, B and AB.

In 1937, another important blood group system – the Rhesus system with the types C, D, E, c, d and e was discovered. During pregnancy, the Rhesus factor D plays a significant role. If a person has the Rhesus or Rh factor D, they are referred to as RhD-positive. Carriers of type d are RhD-negative.

Antibodies against blood types may occur in the blood. These antibodies, however, are never directed against the body's own but always against foreign erythrocytes, e. g. after blood transfusion. The laboratory method for antibody detection is called antiglobulin or Coomb's test.

When a pregnancy is detected, blood group and Rhesus factor are determined. Additionally, an antiglobulin test is performed at the beginning of the pregnancy and between the 24th and 27th week of pregnancy in order to detect blood group incompatibilities between mother and child at an early stage.

If a pregnant woman is RhD-negative and her partner is RhD-positive, the child can be RhD-positive according to hereditary rules. Then, if small amounts of the baby's blood pass into the mother's bloodstream (possible from the 28th week of pregnancy, but often not until birth), the mother produces antibodies against the child's RhD-positive blood cells. The produced maternal antibodies recognise the baby's cells as "foreign" and this is referred to as blood group incompatibility.

In case of a transfer of the child's cells during birth, the anti D antibodies produced by the mother can no longer harm the newborn. Then, there is a risk for a subsequent pregnancy, if the second, unborn child is also RhD-positive. Now, if the foetal cells transfer to the mother, antibodies are produced immediately which are released via the placenta into the child's blood stream and destroy the child's blood cells possibly leading to severe damages or the child's death.

In order to prevent these severe consequences, a Rh prophylaxis (anti D prophylaxis) is performed: RhD-negative mothers get an injection of an antibody (anti D) between the 28th and 30th week of pregnancy and in the first 72 hours after birth. A similar immunisation is done after amniocentesis (amniotic fluid test), premature births or miscarriages and in case of bleedings (particularly after abortion). The administered antibody neutralises the transferred blood cells of the child and prevents the permanent production of maternal antibodies against the Rhesus factor. Due to the low dose of the injected antibody there is no danger for the child. After this early anti D prophylaxis, the routine second antiglobulin test between the 24th and 27th week of pregnancy is positive.

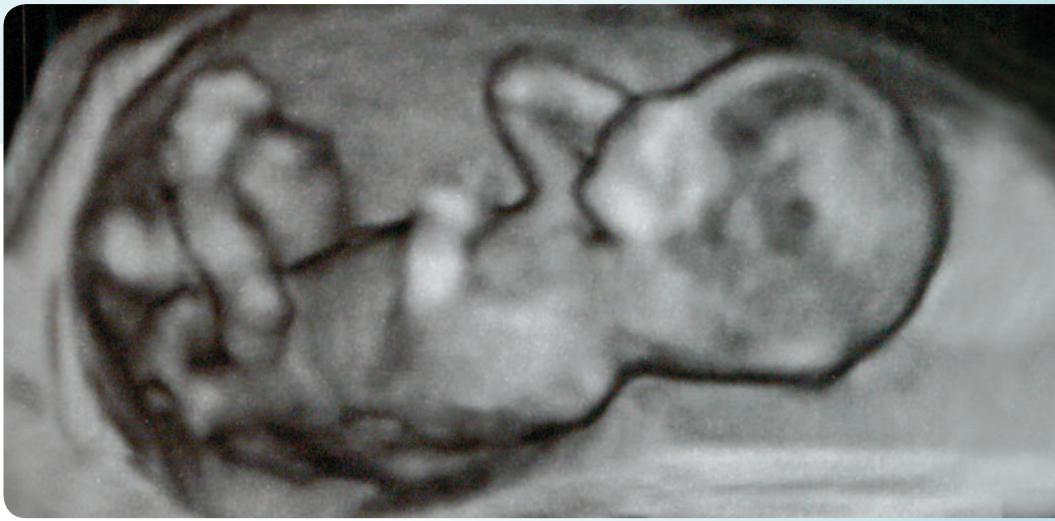
So far, RhD prophylaxis has been given to all RhD-negative pregnant women. Since immunization of the mother can only take place with an RhD-positive fetus, there is the possibility to determine the RhD factor of the unborn child from the blood of the mother. In this case, DNA released by the fetal cells into the maternal blood is detected. If the genetic information for the RhD-positive trait is detected, the mother can be immunized and rhesus prophylaxis must be administered. In case of detection of fetal RhD-negative trait in the maternal blood, rhesus prophylaxis can be omitted. The costs for this examination are covered by health insurance in singleton pregnancies. Since this is a genetic test, the mother must be informed in accordance with the Genetic Diagnostics Act and the mother‘s written consent must be obtained.

5. Screening for genetic defects (Down syndrome, spina bifida)

Prenatal diagnostics comprehend screenings which are performed from the time of the fertilisation of the egg until the birth of the child to recognise possible future or existing damages of the child. Non-invasive (without tissue injury) methods include ultrasound screenings, screening tests for risk calculation or hormone testing of the blood. Invasive screenings are chorionic villus sampling and amniocentesis.

Screening tests for risk calculation:

By combining different data, such as the mother's age, ultrasonic measurements and lab markers, risks for certain congenital disorders can be assessed. These screenings do not help to establish a diagnosis, but to measure an increased (statistical) probability to expect a child with chromosomal defects. Most available screenings calculate the risk for trisomy 21 (Down syndrome) and can provide indications for a few other chromosomal defects (e. g. trisomy 18).



In this brochure, the two most frequent tests (first trimester screening and triple test) are explained. There are several, non-invasive diagnostic methods your attending gynaecologist can inform you about (e. g. combinations of these two tests (integrated screening), extended second trimester test with 4 lab markers (quadruple screen) and recently a molecular-genetic blood test (non-invasive prenatal blood test), based on the presence of foetal DNA in the mother's blood.

What is Trisomy 21 (Down syndrome)?

Trisomy 21 (or Down syndrome) is a genetic disease caused by a chromosomal defect. The chromosome 21 occurs not twice but three times (trisomy 21) in the genome. The affected persons have a limited mental and physical development. Additionally, there is an increased risk for a congenital heart disease or malformations of the intestines as well as impaired vision and hearing. The individual risk to have a child with Down syndrome is 1:1100 in pregnant women aged 20, at the age of 35 1:380 and at 40 years approx. 1:68. Therefore, pregnant women aged 35 or older are generally recommended an amniotic fluid test and a screening test is forgone.

What is a first trimester screening?

The first trimester screening can be offered already during early pregnancy (10th to 14th week of pregnancy). For the screening an ultrasound examination of the child is performed, including the nuchal translucent measurement and the crown-rump length (CRL) measurement.

Nuchal translucency (NT) presents a physiological accumulation of fluid (lymph) behind the neck between the foetus' skin and spinal column. In the ultrasound, this appears as a low echo intensity area (black) and transparent. Due to the not yet fully developed lymphatic system and the immature foetal kidneys, the lymph cannot be drained away immediately at that time and the fluid accumulates in the neck area. During the pregnancy, the accumulation of lymph recedes. In case of certain chromosomal defects (such as trisomy 21) or organ defects (e. g. heart defects, kidney malformations) nuchal translucency is often increased as an early indication of anomalies. The size of nuchal translucency depends on the size of the foetus (CRL).

In addition to the ultrasound scan two lab markers are measured in the mother's blood: PAPP-A (pregnancy-associated plasma protein A) and free ß-HCG (human chorionic gonadotropin). The software calculates the biochemical risk (without NT) and an individual risk (with NT) for the unborn child to have a chromosomal defect (trisomy 21 and trisomy 18). Other diseases/defects cannot be detected with this test.

What is a triple test?

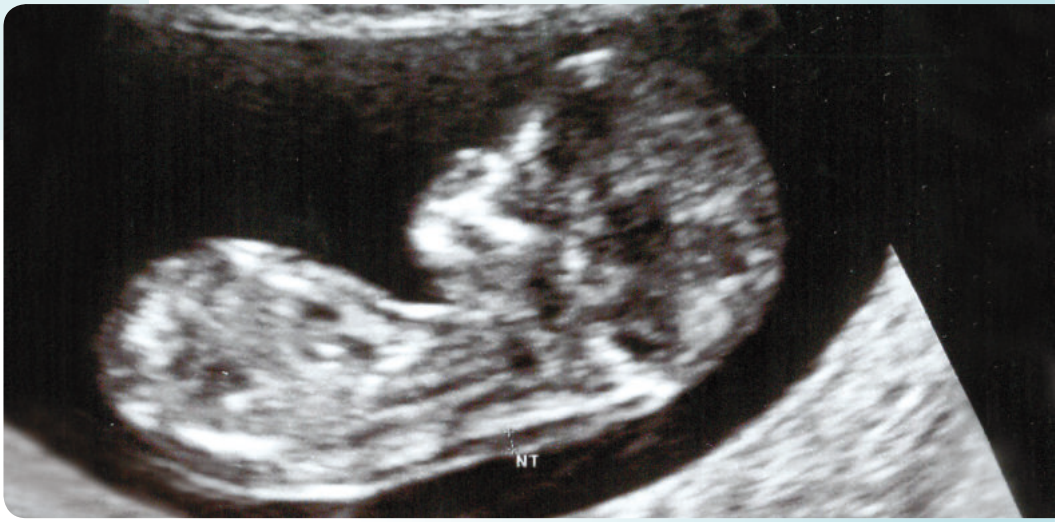
The triple test is one of the oldest screenings to perform a risk calculation for the unborn child. As early as 1988, scientific studies found a connection between a change in concentration of certain lab markers and different chromosomal defects of the foetus. For the risk calculation of trisomy 21 the exact week of pregnancy as measured by CRL and biparietal diameter (diameter of the foetal head; BPD) via ultrasound and three biochemical markers (triple test) are needed. AFP (Alpha-fetoprotein), HCG (human chorionic gonadotropin) and estriol are measured in the mother's blood. Due to the higher significance of these markers in the second trimester, this screening is not used for calculation until the 14th to 19th week of pregnancy.

In contrast to the first trimester screening, the triple test also measures the risk for a neural tube defect ("open back").

What does neural tube defect or "open back" mean?

The term neural tube defect comprehends different malformations which consist in an incomplete closure of the spinal cord or the brain during the embryonic development. These defects can be exposed (open defects) or covered with skin (closed defects). These abnormalities are often so severe that they lead to serious malformations and are incompatible with life (most severe form: anencephaly – non-development of the brain).

The risk for a neural tube defect is measured together with the risk for trisomy 21 in the triple test. If you want to have a risk evaluation for a neural tube defect, you can request the sole measurement of AFP (Alpha-fetoprotein). The risk for cleft lip and palate (hare lip, cleft palate) is not determined.



What is a MoM value?

In both screening tests, different lab markers are measured. As these are individual measured values that can change during pregnancy, their concentrations are issued as so-called MoM values. The abbreviation „MoM“ is derived from the term „multiple of the median“. It is the median of a comparison group of healthy pregnancies. The median divides a group exactly in the middle (50 % of women show lower and 50 % of the women show higher values).

Significance of the first trimester screening and the triple test

As previously mentioned, both tests indicate a risk calculation from the available data. The result is paraphrased as “no increased risk” or “increased risk”.

What does “no increased risk” mean?

There is a low probability to get a sick child (there is no increased risk in 95-97 % of pregnant women). However, this does not rule out completely that a child with a chromosomal defect is born.

What does “increased risk“ mean?

The probability is increased to have a sick child (in approx. 3-5 % of all pregnant women there is an increased risk). But this does not mean that a sick child is born in every case. The expectant mother merely belongs to a certain risk group. If the risk is e. g. 1:360, only 1 child of 360 pregnant women with this increased risk is born with a malformation (e. g. trisomy 21).

If an increased risk is calculated, further diagnostics may follow in consultation with the expectant mother, e. g. a chorionic villus sample or amniocentesis.

Why is an amniocentesis not done immediately?

Different chromosomal defects are accurately diagnosed with this procedure using genetic screening methods.

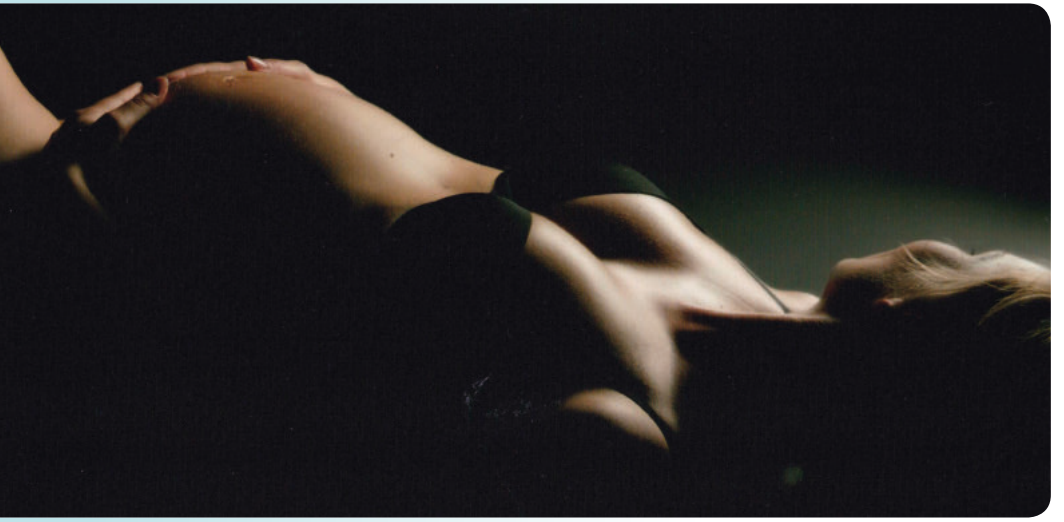
An amniocentesis is no routine procedure. It may cause, if only very rarely today (0.5-0.7 %), premature labour, bleedings, injuries of the unborn child or miscarriages. A physician will only perform an amniocentesis if there is a reason for it. This could be an increased calculated risk for malformations or genetic diseases in the family.

What is a non-invasive prenatal blood test (NIPT)?

A molecular-genetic blood test, as non-invasive method, was developed for the detection of genetic disorder of an unborn child recently.

It is based on the presence of foetal DNA in the mother's blood. Blood sampling for NIPT is possible at earliest at week 11 of pregnancy, since proportion of foetal DNA is >5 %. Genetic counselling is mandatory before NIPT is performed.

NIPT analyses copy-numbers of few selected chromosomes (21, 18, 13, X and Y) in the blood to extrapolate corresponding numbers for the foetus. Methodology of NIPT is based on "Next Generation Sequencing" and provides excellent diagnostic accuracy; both sensitivity and specificity are >99.8 %. A noticeable finding by NIPT should be followed up by further diagnostics (e. g. ultrasound and or amniocentesis).



These tests are offered by various manufacturers/laboratories (e. g. PraenaTest®, Harmony Test®, Panorama Test®) and the costs will be covered by health insurance from 01.07.2022 for certain indications. The NIPT tests are based on the Next Generation Sequencing methodology, which guarantees a very high quality of the test results.

In the event of abnormalities, further diagnostics (e. g. ultrasound and/or amniocentesis) usually follow.

6. Additional information on prenatal care: Folic acid and iodine prophylaxis

In addition to vaccine protection, vitamins and trace elements also play an especially important role.

Among vitamins folic acid is particularly important, because there is a significantly increased need due to the increased blood and cell formation. The consequences of a folic acid deficiency can be developmental disorders of the foetal brain as well as an "open back" or cleft lip and palate. By means of an early, systematic administration of folic acid, the risk for malformations can be reduced by up to 50 %.

To some extent, this is achieved by conscious nutrition using food with an increased level of folic acid (e. g. kale, Brussels sprouts, spinach, wholegrain products, fruits and egg yolk). As even a conscious nutrition often does not completely cover the daily requirements, different medical societies and the German Association for Nutrition (Deutsche Gesellschaft für Ernährung) strongly recommend taking special folic acid preparations.

Equally as important as folic acid is the trace element iodine which is needed in the thyroid to produce thyroid hormones.

It plays a crucial role in the regulation of metabolic processes, growth of internal organs, the muscles, the nervous system and the mental development of the unborn child. As there is a generally increased need, the mother's iodine deficiency and thus the development of hypothyroidism (goitre) are to be avoided by a systematic, daily iodine intake.

7. Overview of the necessary prenatal care screenings and optional services during pregnancy

	care screenings	optional services
planning a pregnancy	• check vaccination card and, if needed, get boosters for missed vaccinations • check medications • antibody screening of the mother‘s blood for: - rubella - chickenpox	• antibody screening of the mother‘s blood for: - cytomegaly - fifth disease - toxoplasmosis
first trimester (6th-12th week)	• general gynaecological examination (every 4 weeks) • first mandatory ultrasound • blood pressure • weight check • urine screening (protein, sugar, inflammation markers, blood) • blood screening (haemoglobin) • blood typing incl. Rhesus factor • first antiglobulin test • antibody screening of the mother‘s blood for: - rubella - HIV (only with consent) - lues • urine screening for Chlamydia trachomatis • in analogy to the current guidelines for hepatitis B, we recommend screening in the first trimester of pregnancy	• 10th-14th week of pregnancy first trimester screening • if necessary antibody screening of the mother‘s blood for: - cytomegaly - fifth disease - toxoplasmosis - chickenpox • from 11th week of pregnancy non-invasive prenatal blood test
second trimester (13th-27th week)	• general gynaecological examination (every 4 weeks) • second mandatory ultrasound • blood pressure • weight check • fetal RhD trait from maternal blood (for RhD-negative women, optimal from the 19th SSW) • urine screening (protein, sugar, inflammation markers, blood) • blood screening (haemoglobin)	• 14th-22th week TRIPLE test • from 20th week obstetric ultrasonography (covered by health insurance if indicated) • if necessary antibody screening of the mother‘s blood for: - cytomegaly - fifth disease - toxoplasmosis

	care screenings	optional services
second trimester (13th-27th week)	• from 24th week second antiglobulin test • from 24th week glucose tolerance test (oGTT)	
third trimester (28th-40th week)	• general gynaecological examination (from week 32 every 2 weeks) • CTG screenings • 3rd mandatory ultrasound • blood pressure • weight check • urine screening (protein, sugar, inflammation markers, blood) • blood screening for hepatitis B	• vaginal and rectal smear test for group B streptococci • if necessary antibody screening of the mother's blood for: - cytomegaly - fifth disease - toxoplasmosis

8. References

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9. Acknowledgement

This booklet was translated from german into english by Sylvia Dyczek (graduate translator).

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