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Praenatal-Medizin
und Genetik

Information on prenatal diagnostics

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Dear Patient,

Your gynaecologist has explained to you various prenatal examination methods. Perhaps you have not yet decided whether and which of these investigations are suitable for you.

Since we cooperate with your doctor, in this brochure we would like to give you a summary of the possibilities of prenatal diagnostics and the currently valid legal regulations.

For further information please contact:

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Prenatal Diagnostics

Prenatal diagnostics include medical examinations which check the health condition of the unborn child in the mother's body.

The use of the method depends on:

- the week of pregnancy
- the specific questions involved e.g. age, family history, prior diseases, suspicious ultrasound findings

➔ However, none of these studies can guarantee a perfectly healthy child.

When is genetic counselling necessary?

Your gynaecologist knows whether there are any special features in your own medical history or that of your family that could jeopardize your unborn child.
If this is the case, you are referred to genetic counselling, where on the basis of medical history and your family tree we discuss whether special investigations will be useful.
Your doctor will also advise you on genetic counselling before the planned examination between the 11th and 14th week of pregnancy. If you and your family do not have any anomalies, the genetic counselling will rarely bring additional insights. Prior to a planned examination of the amniotic fluid or placenta, genetic counselling is useful in order to jointly determine the scope of the investigation.

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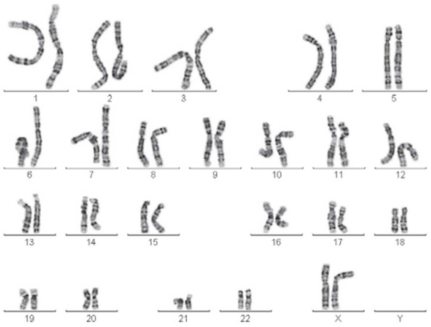
Cause of Disorders of the Unborn

Chromosome Disorders

A healthy person has 46 chromosomes in each cell of his body, 23 of which were inherited from the mother and 23 from the father. Each chromosome is therefore a pair. However, the number or the structure of the chromosomes can be changed. Due to division errors, a chromosome can be threefold instead of twofold. In this case, we speak of trisomy. The most common is the trisomy of chromosome 21, known as Down syndrome.

The number of sex chromosomes (X / Y chromosomes) can also be altered. Deviations in the structure of the chromosomes can also have an influence on the development of the unborn. Each pregnancy carries a small risk of such random chromosomal disorders.



Normal human chromosome set

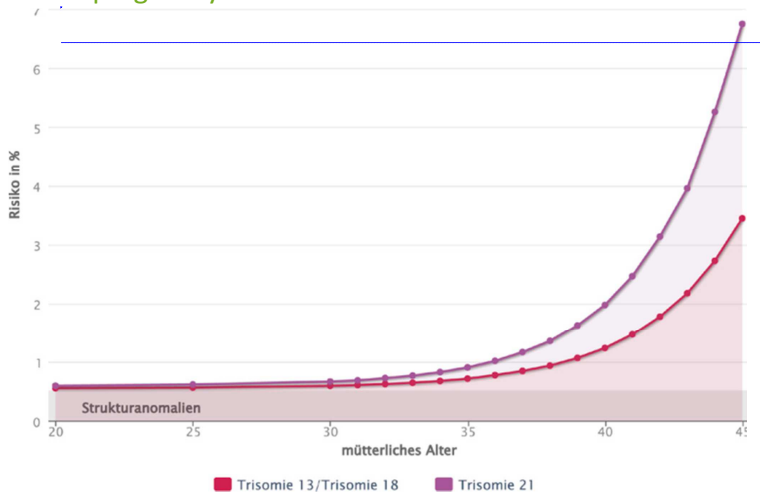
Age-dependent risk for trisomy 21
(in the 12th week of pregnancy)

20 years	1 : 1068	36 years	1 : 196
25 years	1 : 946	38 years	1 : 117
30 years	1 : 626	40 years	1 : 68
32 years	1 : 461	42 years	1 : 38
34 years	1 : 312	44 years	1 : 21

detailed information is available at praenatal.de

The medical history of your family and your own lifestyle have no influence on this. For some chromosomal disorders, however, the risk increases with age (see graph).

Frequency of chromosomal abnormalities in the 12th week of pregnancy



Kommentar [RB1]: Risiko in %: Risk in %
Strukturanomalien: Anomalies in structure
mutterliches Alter: Age of the mother
Trisomie 13/ Trisomie 18: Trisomy 13/ trisomy 18
Trisomie 21: Trisomy 21

Congenital diseases

Congenital diseases derive from gene changes. They arise as new, or exist mostly unrecognised in just one or, more frequently, in both parents. Both the metabolic functionality as well as the body structure can be affected.

The possibility of prenatal recognition of a congenital disease and its potential consequences need to be clarified beforehand at an appointment with a genetic counsellor. Many diseases can be diagnosed prenatally with the help of molecular genetics.

Abnormalities of the child's organ development

Most of these abnormalities occur during the second and third month of gestation. Kidneys, urinary tract, heart and brain are most commonly affected. The main cause often cannot be determined; in rare cases external factors such as drugs, radiation or maternal infections can be responsible. Organ development abnormalities can be seen during an ultrasound examination.

Methods of examination

Examination	Optimal time
Early organ examination (possibly with risk calculation for trisomy)	**12th+0 – 13th+2 week**
DNA Test (from maternal blood)	**from 11tn +0 week**
Chorionic villus	**from 11th + 0 week**
Amniotic fluid test	**from 15th + 0 week**
Alpha-fetoprotein (AFP)	**from 15tn + 0 week**
Umbilical Cord	**from 18th + 0 week**
Obstetricultrasound/ echocardiography	**20tn +0 – 21st +6 week** (or sooner if recommended by your doctor)
Doppler ultrasound	**from 26tn + 0 week**

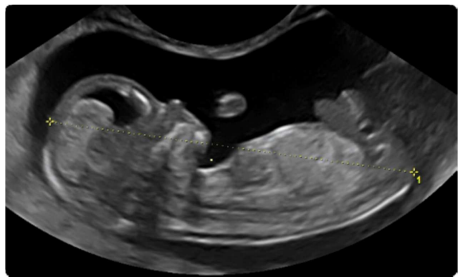
Explanation: 13th + 2 week means 13 completed pregnancy weeks plus 2 days, so it is equal to the second day of the 14th week.

Early Organ Diagnostics
(11th – 14th week)

This examination has been of increasing importance in recent years. The early examination of organs is not a part of the routine examinations in pregnancy. The costs are therefore covered by the statutory health insurance funds only in case of medically necessary examinations. Your gynaecologist will discuss with you whether he or she carries out this examination themselves or transfers you to us. The key point of early diagnosis is a comprehensive ultrasound examination.

➜ If the examination conditions are good, we receive a great deal of information about the development and the organs of the child.

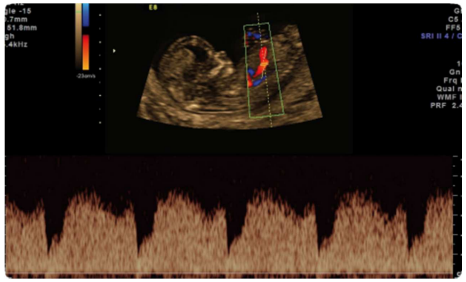
We recommend the examination between 12th + 0 and 13th + 2 week.



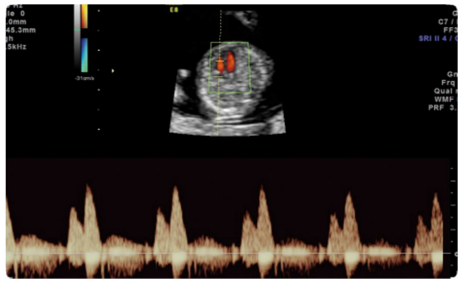
Foetus in the 13th week. Measurement of the crown-heel length

Risk Screening

A trisomy 21 (the cause of Down syndrome) of the unborn can occur at any age of the mother, just like the rarer trisomy 18 or 13, but the probability increases with the maternal age. If you wish to determine your personal risk of a trisomy 21, we record additional markers (nasal bone, tricuspid valve, ductus venosus) during the examination and perform a probability calculation using the Fetal Medicine Foundation (FMF) London method (www .fetalmedicine.org).



Normal flow through ductus venosus 13th week



Normal tricuspid valve 13th week

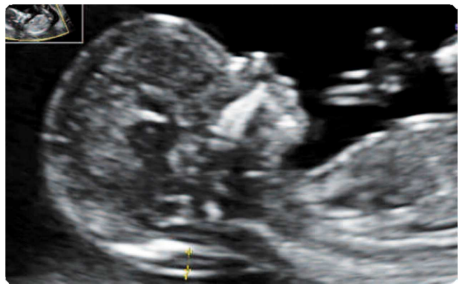
However, please note that

- **an ultrasound examination with no suspicious findings does not guarantee a healthy child. The result of the risk analysis does not give you any certainty as to whether or not your child has a chromosomal disorder.**

- The probability calculation only detects the risk of a trisomy of the chromosomes 21, 13 and 18.

It is very important that you become aware beforehand of the extent to which a simple probability statement is helpful to you and what consequences you could draw from a high or low level of risk. If you want to rule out the most frequent chromosome disorders, we recommend a chromosome analysis of the child's cells.

For this purpose, chorionic villus sampling (from 11th + 0 week), or an amniotic fluid test (from 15th + 0 week) is necessary. We would be glad to explain the possibilities and risks of these investigations during an appointment with a genetic counsellor.



Nuchal translucency measurement with the presentation of nasal bones in the 13th week

How is the risk of trisomy calculated?

The first trimester screening can only be carried out between 11th + 0 and 13th + 6 weeks. By means of ultrasound, the so-called nuchal translucency (NT) of the unborn is measured. If the NT is increased, the probability of your child having a disease increases. Also, two values in the maternal blood (the concentration of the protein PAPP-A and the free ß-HCG hormone) can be determined.
The risk is indicated as a ratio: a risk of Down syndrome from 1 to 500 means that out of 500 pregnant women with the same risk, one woman has a child with Down syndrome. When the markers like nasal bone, heart valve and ductus venosus are included, the certainty of the first trimester screening is about 90%.

According to the Genetic Diagnostics Act (GenDG), which has been in force since February 2010, an ultrasound examination with subsequent risk assessment is also a genetic examination. The performing physicians are obliged, just as e.g. before the amniotic fluid test, to explain to you the examination method, to offer you genetic counselling and to provide you with information material. You must declare your consent or refusal in writing. At any genetic examination you can always revoke your consent to its execution or to the storage of the results.

Other causes for increased nuchal translucency

Heart defects, diaphragm / umbilical hernia, skeletal defects or metabolic diseases can also be causes of increased NT. Sometimes there is no particular cause, and the pregnancy continues without complications. In addition to the first-trimester screening, additional complementary antibody screening tests from maternal blood are offered, but they have less significance. Low values of the protein PAPP-A can also indicate an increased risk of problems of placental function and maternal blood pressure during pregnancy.

➔ **Please note:**
The first trimester screening is not a part of the regular screening examinations. The costs of consultation, ultrasound and laboratory examination are not covered by the statutory health insurance funds.

Early detection of preeclampsia

Preeclampsia (PE) is a complication that occurs during pregnancy, affecting approximately one in 100 women. The main symptoms are hypertension, water retention in the tissues (oedema), and increased protein in the urine. The unborn child is in many cases endangered by a diminished function of the placenta. In one out of 200 women, birth before the 34th week is required in order to protect both the mother and the child.

If the patient is diagnosed early in the first half of the pregnancy, the doctor can take preventive means and initiate appropriate control examinations. We therefore carry out the examination for preeclampsia risk along with first trimester screening and recommend determining the level of PlGF from the mother's blood sample.

For the risk assessment, we need data related to previous pregnancies and a thorough health history, but also:

- Height and weight
- Blood pressure measurements on both arms
- Doppler flow measurements in the uterine arteries
- PAPP-A levels in the blood (also measured to determine trisomy risk during first trimester screening) and PlGF (Placenta Growth Factor)

One out of every 200 pregnant women develops early-beginning, severe pre-eclampsia. With an individual risk ratio of **1: 100 (1%)** or more we currently recommend the precautionary intake of acetylsalicylic acid (ASA). The investigation of blood coagulation can be also useful in individual cases.

Trisomy Screening of DNA from maternal blood (NIPT)

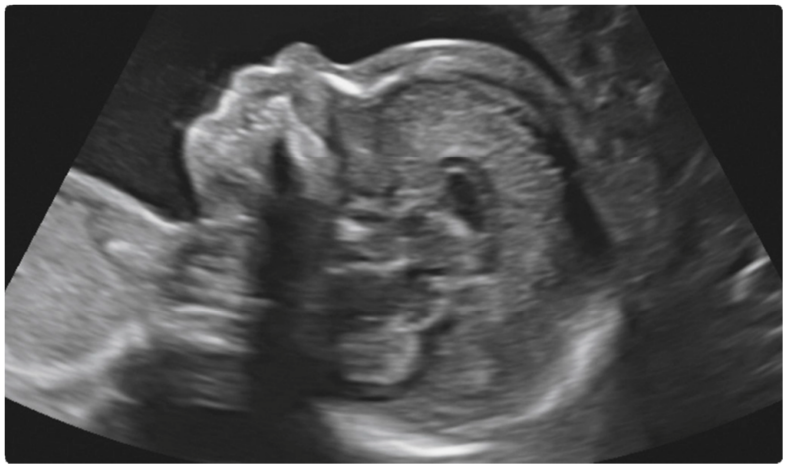
Tiny fragments of genetic material (DNA) circulate in the blood plasma of every human. In pregnant women, part of this DNA comes from the placenta of the unborn child. In recent years, laboratory investigations have been developed to obtain evidence of genetic disorders from this material derived from the maternal blood.

In Germany, several placental DNA tests are offered. We will be happy to advise you on the differences between them and also the current costs.

These tests **only** examine whether a high risk of a trisomy or an anomaly of the sex chromosomes is present in the foetus. Tests on other genetic disorders are currently not offered as a routine. The detection rate of trisomy 21 is above 99%. If you have questions about these tests, we can discuss them during an individual appointment.

Like all other prenatal genetic examinations, the blood tests are conducted by us only, **only in connection** with individual **genetic counselling and detailed ultrasound diagnostics** of the foetus.

Obstetric Ultrasound Diagnostics



Beween 20th and 22nd week of pregnancy, we can perform a detailed organ ultrasound. This is much more comprehensive than the ultrasound provided in the maternity guidelines for this period. Apart from special equipment, a great deal of experience on the part of the examiner is also required. The gynaecologist decides whether there is a need for such an ultrasound examination. Otherwise, this examination can also be done as a self-payment service.

We examine all the presentable organs and characteristics of the unborn:
- Age-related growth of the child
- The amount of amniotic fluid
- The appearance and function of all visible organs
- The location and appearance of the placenta

In the case of an in-depth ultrasound examination, some unborn children may also present characteristics which increase the statistical risk for the presence of a trisomy. These abnormalities are neither malformations nor do they affect the considered organs.

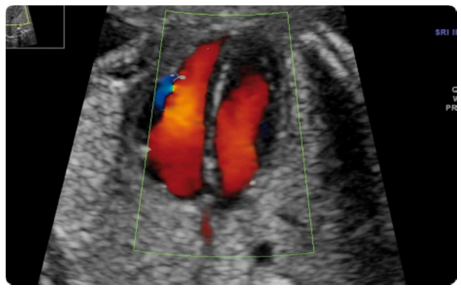
If we detect one or more of these "markers" during the examination, we can carry out a risk assessment with regard to trisomy 21, 18 and 13, taking into account your age.

Another component of this study is the assessment of the child's heart and large blood vessels: echocardiography.

Here we check:
- Position, size and symmetry of the heart
- Anatomy of the heart structures
- Function of the heart valves and chambers
- Heart rate
- Position of the large arterial and venous vessels

The blood flow in the umbilical cord, in the child's blood vessels and in the uterine vessels is also shown in colour and acoustically with the use of the Doppler ultrasound.

The Doppler ultrasound of the child's and the maternal vessels is particularly useful in late pregnancy (26th - 38th week) if there is suspicion of acute or chronic deficiency in the supply of the unborn child.

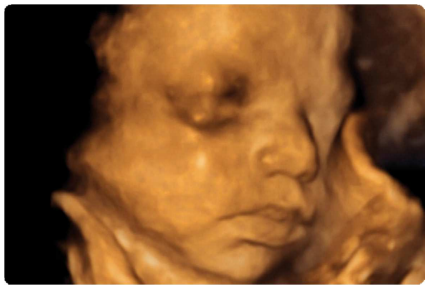


Colour coded echocardiography 22nd week: Four-chamber view

More and more pregnant women are interested in the possibilities which 3D / 4D ultrasound brings. The fascinating image is certainly the focus. This modern method provides supplementary answers to specific questions.
For this reason, we only use the 3D / 4D representation if we can expect additional diagnostic information. We do not perform 3D / 4D imaging without simultaneous organ ultrasound.

Please note
Even with good equipment quality and care, all malformations and illnesses can never be fully excluded with complete certainty. In case of poor examination conditions or very small defects, e. g. a small hole in the cardiac septum or minor defects in the spinal column, ultrasound technology reaches its limits.

An ultrasound examination can never rule out a chromosomal disorder since such diseases do not necessarily have to be associated with organ defects.



Child's face in the 30th week, 3D image

Amniotic Fluid Test (from 15th + 0 week)

Amniotic fluid provides us with the child's cells which contain genetic material (chromosomes) that can be analysed. Numerous chromosomal disorders can thus be excluded with very high certainty. We perform the amniotic fluid test (amniocentesis) when at least 15th week of gestation is completed.

How is amniocentesis carried out?

Under continuous ultrasound control, a very thin needle (0.7 mm in diameter) is inserted into the amniotic sac through the mother's abdominal wall so that injuries to the unborn are excluded. Approximately 10 mL of amniotic fluid is taken. This is less than one tenth of the total amount.

The puncture itself takes one to two minutes and causes only a slight dragging feeling in the belly. Immediately after the puncture, the tiny puncture channel closes again, since the tissue is very elastic. Cell cultures are prepared from the child's cells derived from the amniotic fluid. It takes some time for the cells to grow.

Which diseases can be detected with the help of amniotic fluid cells?

Microscopically visible chromosomal disorders can be detected by the analysis of the amniotic fluid cells. In the case of special questions, molecular genetics methods can also help detect non-visible chromosome changes and many congenital diseases. A protein (alpha-fetoprotein, AFP) and an enzyme (acetylcholinesterase, AChE) in the amniotic fluid have to be compulsorily determined to exclude the formation of splits of the backbone (spina bifida) with high certainty.

Array-CGH analysis (chip analysis)

The array- CGH examination method is a useful addition to classic chromosome analysis. With the new computer-assisted analysis method, smallest chromosome changes can be detected, which could not be detected with previous examination methods. Array CGH analysis can thus provide new insights even in the case of inconspicuous genetic findings.
In prenatal diagnostics, array- CGH has developed into a very important examination method, which allows much more precise information on micro-changes of the genome to be obtained within just a few days.

The cost of array- CGH in prenatal diagnostics is unfortunately only rarely covered by the insurer, even in cases of abnormalities of the foetus.

What are the risks of amniotic fluid puncture?

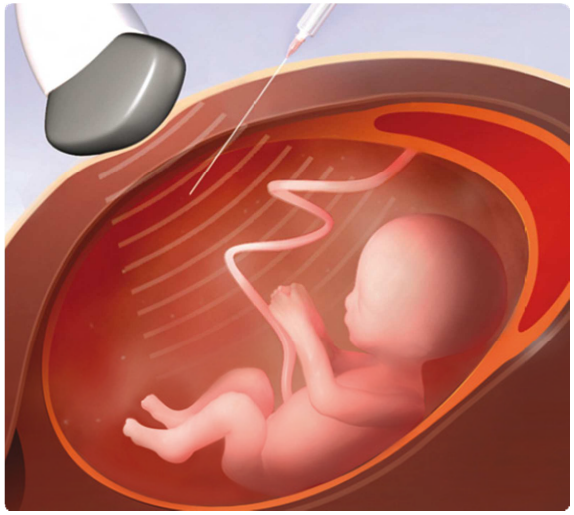
The risks of amniotic fluid puncture are often overestimated. In every pregnancy there is a natural risk of miscarriage, even without an intervention.
In the case of a puncture performed after the 15th week, the risk of miscarriage in an uncomplicated pregnancy is increased to about **1 out of 1,000**. We can give an individual assessment after discussing previous medical history and an ultrasound examination.

Quick test after amniotic fluid puncture

In order to make the waiting time for the final result easier for you, we offer you a quick test (PCR). This usually enables the definite exclusion of most frequent chromosomal disorders (trisomy 13, 18, 21) as well as information about the sex within half a working day after the puncture.

The final result of chromosome examination is available 10-14 days after the puncture.

For the PCR quick test, the laboratory requires only minimal amounts of genetic material (DNA), so that no additional amniotic fluid must be taken. The costs for rapid diagnostics are not always covered by the statutory health insurers and private insurers.



Amniotic fluid puncture

Chorinic Villus Sampling (from 11th + 0 week)

Since the placenta (called a chorion in early pregnancy) derives from the fertilised egg, cells from this can be used to analyse the child's chromosomes.

Chorionic villus biopsy is useful when a chromosomal analysis is necessary in a very early stage of pregnancy:

- in case of abnormalities in the ultrasound image
- at high risk presented on the basis of the first- trimester screening
- in congenital diseases or metabolic disorders
- if you desire a particularly early diagnosis

We carry out a chorion biopsy at earliest from the 11th completed pregnancy week. This method does not give any information about splits of the backbone ("spina bifida").

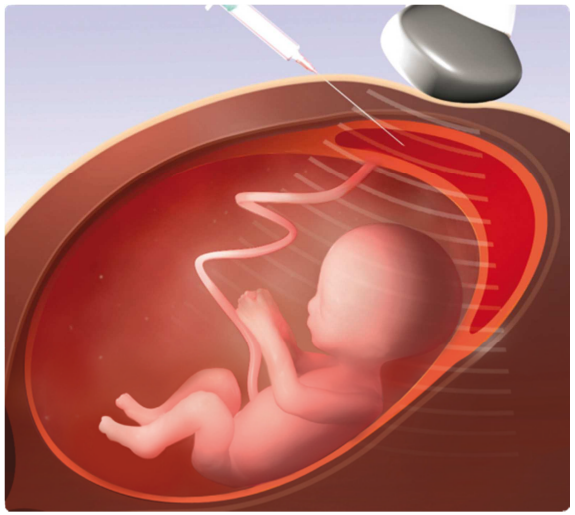
How is a chorion villus biopsy carried out?

After a careful ultrasound examination, a thin needle is inserted into the placenta through the patient's abdominal wall, and a few tiny tissue samples are taken. The puncture usually lasts only from one to two minutes. During the procedure, most women have a strong dragging feeling in their belly.

Cultures are created from the obtained cells, which need some time for growth and multiplication. The result is available about ten days later. If the amount of tissue is sufficient, a short-term test is also carried out, which can be used to exclude the most frequent chromosomal disorders. The results are available in two working days' time after the puncture.

What is the risk of chorion villus sampling?

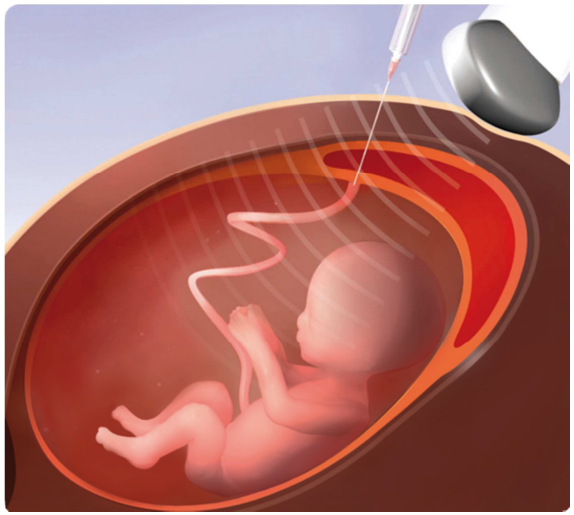
The risk of a chorionic villus biopsy is very similar to the one of amniotic fluid puncture. As in the amniocentesis, in uncomplicated pregnancies the probability of miscarriage is about **1 to 1,000**, which is higher than that for natural miscarriage.



Chorion villus biopsy

Umbilical Cord Puncture (from 18th + 0 week)

The umbilical cord puncture is used only in special cases, such as anaemia, infections or late-discovered abnormalities of the child. In some cases blood or medication can be given to the child.



Umbilical cord puncture

How certain is the examination of the child's cells?

The investigation of cells from amniotic fluid, placenta tissue or the blood of the unborn is still the only way to rule out numerous chromosomal disorders and genetic defects with a very high, but not complete degree of certainty.

All parents, however, bear a so-called basic risk of 4-7% for the birth of a child with more or less serious malformations or illnesses. The risk of a serious malformation or disease also depends on parental age, and is about 1%.

Even if certain chromosomal disorders have been excluded after a puncture, a basic risk remains for other diseases and malformations. Generally speaking, physical malformations, mental disabilities or metabolic diseases cannot be ruled out completely by chromosome analysis.

- Changes of very small chromosome fragments or of individual genes are not detectable under the microscope.
- If, which is rarely the case, a smaller part of the body cells of the foetus carries a different chromosomal set (mosaic), this cannot always be detected with certainty.
- In a few cases cell cultures grow very slowly so that the result is available later than usual.
- In extremely rare cases, maternal cells are examined instead of the child's.
- Very rarely, the analysis is not possible. In this case, we should discuss the consequences with you and your doctor. If a quick test has been carried out, it may be possible to avoid the next puncture.

What should you do after a puncture?

You should lie down for at least a half an hour in our resting room immediately after each puncture (chorionic villus biopsy, amniocentesis, umbilical cord puncture). If complications occur after a puncture, they usually occur within the first 24 hours. We therefore advise you to stay at home on the day of a puncture and the day following and to rest.

Avoid heavy physical activities (such as sports, lifting heavy items, frequent climbing of stairs) on the day of a puncture and the following day. If you are professionally active, please let your gynaecologist write a sick note for these two days. One or two days after the puncture, you should consult with your gynaecologist for a check-up.

If you lose fluid or blood or suspect this, or have strong abdominal pain or other discomfort, please consult your doctor or clinic. If there are no complications after the puncture, sports and air travel, as well as a sexual intercourse will be possible without any problem one week later, unless your doctor has already given you a different recommendation.

What happens with

a suspicious finding?

Although the vast majority of children are born healthy, a small number of unborn children are diagnosed with a suspicious finding or a disease. If this were the case, you would not be left alone with this result. In such situation it is important that you to receive both medical and non-medical counselling and assistance.

We, a team of gynaecologists, geneticists and psychosocial counsellors, search together with you for the best solutions for you and your unborn child.

Consultants from Donum Vitae (a pregnancy counselling organisation) are available in our practice in Düsseldorf. If necessary, we draw on experts from other specialist areas, such as paediatricians, cardiologists or paediatric surgeons. Whenever you need to make a decision, we offer you all the support you need.

Your appointment in our practice

Before we begin a planned investigation, we address all your questions in a personal manner. Please therefore sign the declaration of consent for a planned examination immediately after the consultation.

- We take a lot of time for each examination. In addition, any prenatal screening may require discussions or measures that we cannot foresee when scheduling. We apologise for any inconvenience. Please make sure that you plan a time of at least two hours for your appointment.
- For this reason do not bring children of preschool age to your appointment.
- Together with your pregnancy record, please bring along previous medical records, laboratory tests, etc.
- After your visit to our practice you will find a feedback card in your pregnancy record. We would like to ask you to help us evaluate the quality of our work.

The whole team will be ready to assist you before, during and after your appointment.

We look forward to seeing you
Your team at praenatal.de

Your Notes

praenatal.de in Düsseldorf

Praenatal-Medizin und Genetik
Graf-Adolf-Str. 35
40210 Düsseldorf

praenatal.de in the University Clinic Düsseldorf

Klinik für Frauenheilkunde und Geburtshilfe
Moorenstraße 5
Gebäude 14.24 (Erdgeschoss)
40225 Düsseldorf

Tel 0211-38457-0
Fax 0211-38457-33

institut@praenatal.de
www.praenatal.de

praenatal.de was founded in 1991 as a specialist medical practice for prenatal diagnostics in Düsseldorf. Today, the services of praenatal.de are available to you in our two joint practices (Düsseldorf and the University Gynaecology Clinic Düsseldorf), as well as in two hospitals with which we cooperate.

- Protestant Hospital Düsseldorf
  Department for prenatal diagnostics
  and therapy

- Florence Nightingale Hospital Düsseldorf
  Kaiserswerther Diakonie
  Department of Prenatal Medicine

Please contact our practice in Düsseldorf to make an appointment. We will coordinate your appointment for the location in question.

Further information e.g. about parking and public transport is available at **praenatal.de**

16/08/22_V08

Prenatal Medicine and Genetics

Doctors Partnership
Kozlowski und Partner
Düsseldorf
AG Essen PR 1853

praenatal.de
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und Genetik