In which situations are prenatal genetic testing recommended?

■ Increased risks for fetal aneuploidies due to maternal age or according to risk calculation algorithms (i.e. first trimester screening)

The risk for fetal aneuploidies (i.e. chromosome errors), such as the Trisomy 21 (also called Down Syndrome), increases with maternal age. Hence, an AC or CVS is usually recommended for pregnant woman beyond the age of 34. Based on a combination of ultrasound measurements and maternal blood levels for certain pregnancy hormones, a personalized risk for fetal chromosome aberrations may be calculated, which may aid the decision on further testing (AC or CVS).

■ Suspicious ultrasound observations

Fetal ultrasound findings such as actual malformations or findings, which are not as such pathogenic but are statistically associated with diseases (so called soft markers), may hint to fetal aneuploidies.

■ Familial genetic risks

Sometimes the family history or previous pregnancies indicate that special genetic risks are present. If the underlying genetic factors (i.e. known mutations), a targeted genetic testing from fetal cells is possible.

■ Other

Sometimes an amniocentesis is used to test for infections of the fetus. Finally, purely personal reasons such as fear of genetic conditions in the fetus may justify an amniocentesis.

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Surname:

Name:

PC-Number:

Date:

■ Information on Prenatal Chromosome Analysis

■ **Pränatalmedizin, Gynäkologie und Genetik (MVZ)**

Nürnberg ■ Bayreuth ■ Ansbach

■ Bankgasse 3, 90402 Nürnberg

■ Telefon 0911 - 2061010
■ Fax 0911 - 2061012
■ eMail kontakt@praenatal.com
■ web praenatal.com

praenatal.com

praenatal.com

Pränatalmedizin, Gynäkologie und Genetik (MVZ)
Nürnberg ■ Bayreuth ■ Ansbach

Frauenheilkunde und Humangenetik

praenatal.com

■ Dear Patient,

A prenatal chromosome analysis was recommended by your obstetrician or requested by yourself.

For this kind of test fetal cells are required. These can be obtained either by a chorion villi sampling (CVS, possible from gestational week 12 onwards) or by an amniocentesis (AC, possible from gestational week 16 onwards).

Which method is most appropriate for you will be decided jointly after the sessions of genetic counselling and ultrasound and depending on the medical results and your personal preference.

The chromosome test can diagnose (or exclude) several genetic diseases, which cannot be diagnosed by ultrasound alone.

According to the german "Gendiagnostikgesetz (GenDG)" (law regulating genetic diagnostics) it is up to your personal discretion which genetic features of the fetus shall be investigate and who shall be informed of the results.

In case of pathological findings in the fetus you are entitled to receive psychological support. This may also be appropriate if i.e. the waiting time for laboratory results should pose emotional stress for you.

As a prerequisite for the invasive procedure and genetic testing of the fetus we require your written and signed consent. Please read this information leaflet carefully and ask the genetic counselor or ultrasound doctor if any questions arise.

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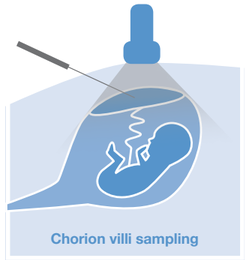
How is chorion villi sampling (CVS) done?

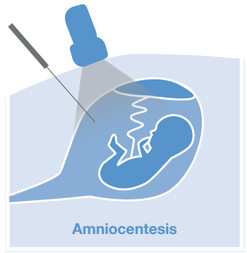
A CVS may be done **from the 12th gestational week** onwards. The abdominal skin area, in which the CVS is planned, will be disinfected and a needle will be stuck through the skin under permanent ultrasound observation and guidance in order to reach the placenta.
Since the amniotic cavity will not be entered, there is no danger of fetal injuries. The biopsy is done after a light local anesthesia. However, a little pain, comparable to menstrual pains, may occur.
The first, preliminary result (from direct preparation) may be expected 1-2 days after the biopsy from a low quality chromosome analysis, which only judges the number of chromosomes. The final and definitive result will be derived from cultivated cells and reported **10-15 days** after the biopsy.


Chorion villi sampling

How is an amniocentesis (AC) done?

Similar to the CVS an AC works under sterile conditions and under permanent ultrasound control of the biopsy needle. Injuries of the baby are extremely rare. However, an AC should only be done **after 15th gestational week.** A local anesthesia will not be necessary. Most women describe the AC related pain as comparable to that when drawing blood from the arm veins.
We usually draw 15-20 ml of amniotic fluid. This will naturally be replenished within few hours.

Since for chromosome analysis cultivated cells are required, the results may be expected **10-15 days after** the AC.


Amniocentesis

What is a FISH assay?

FISH (fluorescent in situ hybridization) is a technique which allows very fast staining of special chromosome segments without the need for cell cultivation. This technique may be used to count chromosomes of interest. For example, frequent trisomies such as Trisomy 21 (Down Syndrome) and Trisomy 18 (Edwards Syndrome) may be excluded or diagnosed 1-2 days after the AC via an aneuploidy FISH.
In certain cases, chromosomes may be tested for losses (deletions) of small fragments by special FISH assays (microdeletion FISH).
FISH tests can only complement the regular chromosome analysis on cultivated cells, which is the basis for any reliable chromosome result.

Which diseases may be diagnosed by CVS or AC?

Chromosome analyses after both kinds of biopsies will detect **numerical** (i.e. trisomies) **and structural chromosome errors**.
Molecular genetic methods may also search for monogenic diseases, such as cystic fibrosis. However, these tests will usually only be done if a familial genetic burden is present and the underlying DNA mutations are known.

Measuring the level of AFP (alpha fetoprotein) in the amniotic fluid may aid the detection of neural tube defects (spina bifida) or clefts of the abdominal wall. Finally, the amniotic fluid may be tested for antibodies, viruses or other infectious agents if **infections** are being suspected.
It is important to realize that tests sometimes deliver so-called incidential findings, i.e. results which were discovered by chance and have not been looked for in the first instance.
All laboratory results will be discussed with you in depth. If appropriate we will contact specialists (i.e. pediatricians) to discuss consequences, therapies and the like. **Luckily, most results are benign, thereby confirming the good development of the fetus.**

How reliable is the chromosome analysis from CVS and AC, respectively? Which problems may occur in the laboratory?

Every biopsy consists of two independent cell cultures whose results mutually confirm each other. A normal result in the AC culture is absolutely reliable.
Very rarely false negative results can occur in the final results of CVS cell culture. The first results from the direct preparation after CVS will be preliminary; false negative/positive results occur at a frequency of 1-3%.
For formal reasons FISH-results are being considered preliminary as well, however, hardly ever false results have been observed.
In less than 0,5% of all biopsies a final evaluation is not possible due to poor growth of the cells in culture. In this case or in the case that the CVS gives contradictory or unclear results, **a second biopsy (usually AC)** will have to be discussed.

Which kind of diseases cannot be detected by CVS or AC?

All diseases with a non-genetic origin cannot be detected by genetic tests. Genetic diseases or malformations, which are being caused by DNA errors (i.e. mutations), usually will only be detected, if a (familial) mutation is known beforehand. Only for a limited number of syndromes and in case of typical ultrasound findings a DNA test without such prior information is possible. A general test for all genetic diseases is not feasible.
Anatomical malformations such as heart malformations and cleft palate can only be detected by ultrasound but not by chromosome or DNA tests. **Hence, an extended ultrasound investigation in week 20-23 is recommended to exclude such malformations.**

Which risks are being associated with an AC or CVS?

Complications are rare. AC may cause a **partial or total loss of the amniotic fluid** in far less than 1%. Half of these will end in **preterm labor and miscarriage**. The total risk of miscarriage is approx. 0,3% after AC and 0,8-1% after CVS. The natural rate of miscarriage after week 12 is 1-2%. **Infections** and **bleedings** occur rarely (<<1%). **Injuries** of the baby or the mother are even less likely, since we use a continuous control of the biopsy needle via ultrasound observation.

What should you consider after an AC or CVS?

Directly after the biopsy you stay under observation for 15-20 minutes. If your blood is rhesus–negative, you will receive an injection, which inhibits an anti-D reaction and avoids rhesus-complications in future pregnancies (anti-D prophylaxes).
We suggest refraining from extensive **physical activities** for three days. Normal daily activities such as walking around, light house work, desk work and so on are o.k.. You may take a bath or shower.
Please meet your local gynecologist for a **brief check** in the next week. In case of complications or any unusual observation **(bleeding, loss of amniotic fluid, strong pains, fever)** immediately contact your gynecologist, the nearest hospital or our practice.