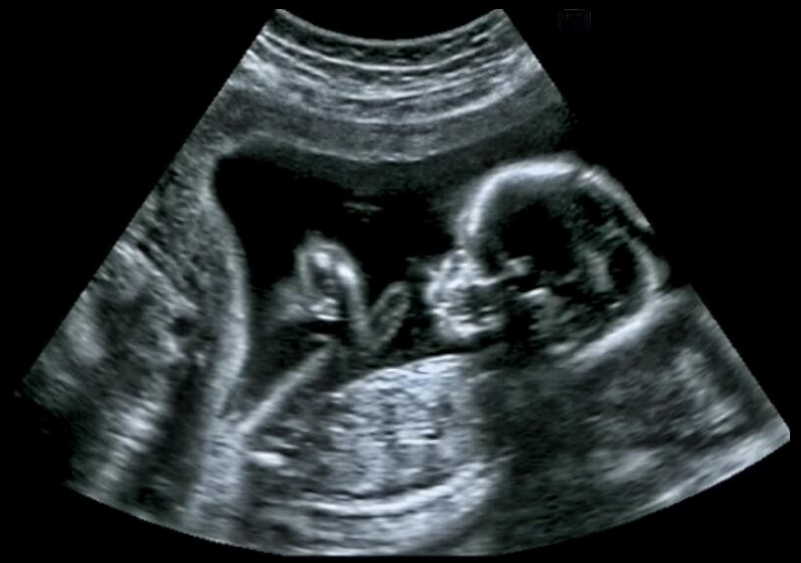
Genetic testing in pregancy



Amniocentesis

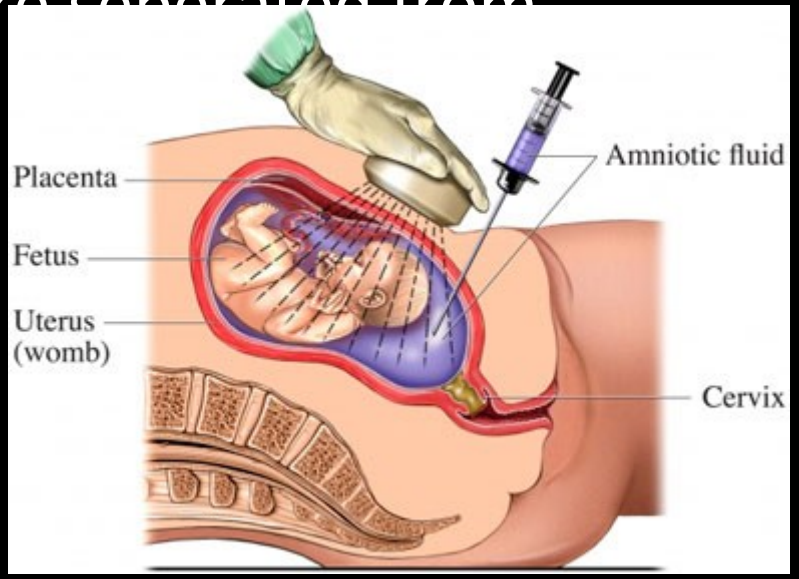
- Diagnostic test for withdrawing amniotic fluid from uterine cavity
- Using a needle via transabdominal approach
- Under continous ultrasound guidance
- To obtain a sample of fetal exfoliated cells, transudates, urine or secretion
- Used since 1960s
- Performed at 15-20 weeks

What it does

- Various chromosomal, biochemical, molecular and microbial studies are performed on amniotic fluid sample
- Most common reasons:
  - chromosomal disorders (Down‘s syndrome)
  - Sex chromosome abnormalities (Turner syndrome, Klinefelter syndrome)
  - Genetic disorders (cystic fibrosis, sickle cell disease)
  - Neural tube defects (spina bifida)
  - fetal infection and intra-amniotic inflammation
  - assess fetal lung maturity

How it works

- Under guidance of ultrasound, a sterile needle is inserted through abdominal wall into amniotic sac
- A small amouhnt of amniotic fluid is withdrawn through needle
- The amniotic fluid contains fetal cells, which are seperated from amniotic fluid and cultured
- Test are performed on cultured cells



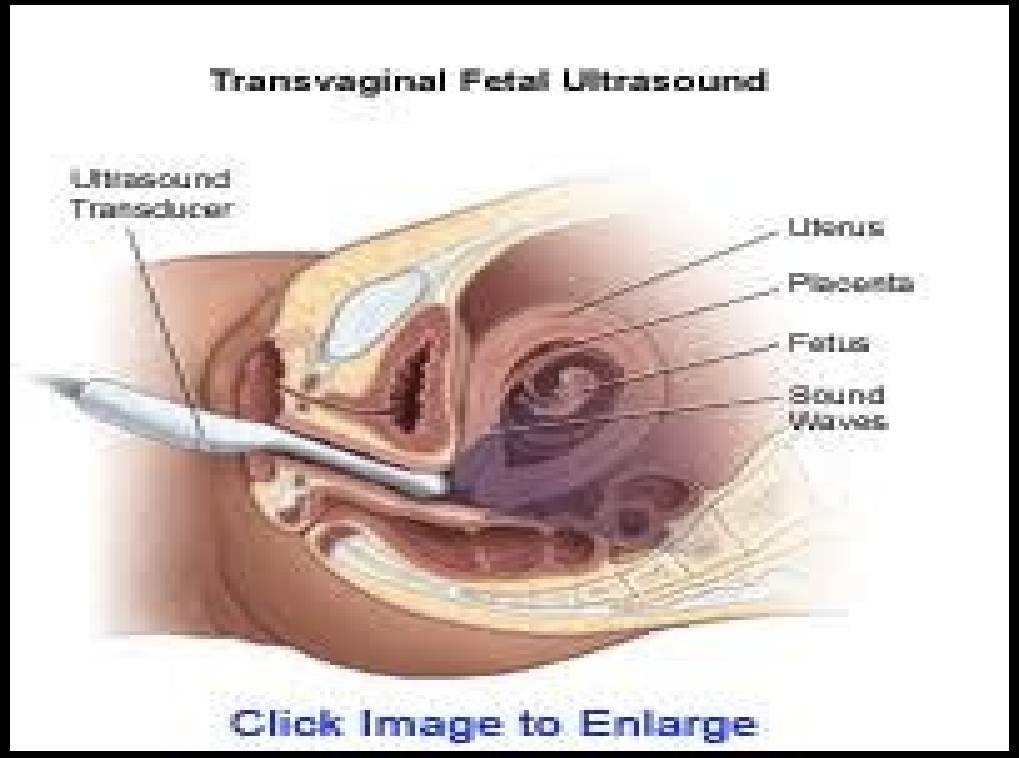
Candidate for amniocentesis

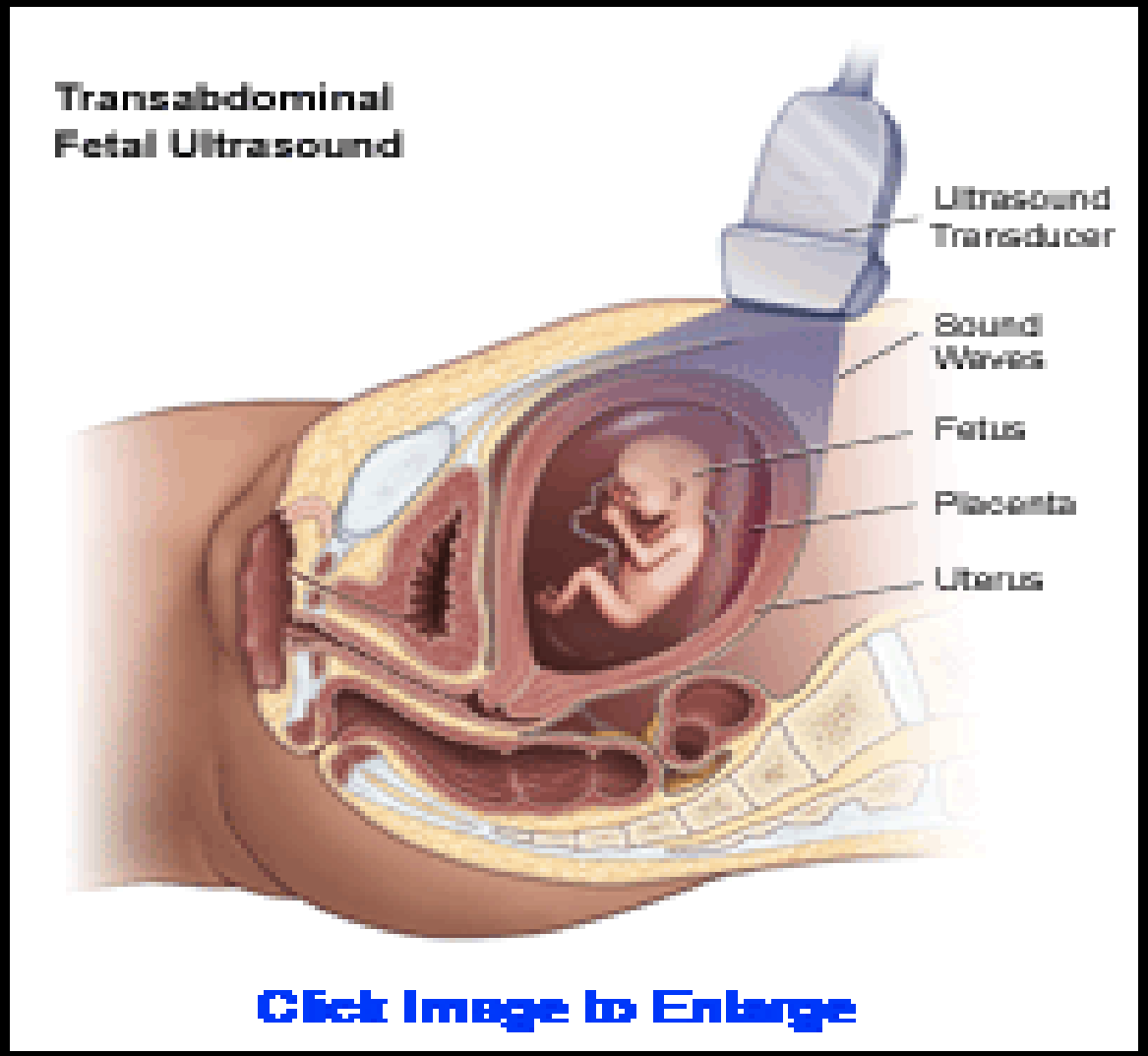
- Pregnant woman > 40 years
- Woman with high risk blood tests and fetal ultrasound
- Woman whose ultrasound shows potential fetal chromosomal anomaly
- Woman with family history or whose partner has family history of one or more incidents of chromosomal anomalies or genetic disorders
- Possible for woman < 40 years with nor history of genetic disorders to have amniocentesis; it is a matter of personal choice!

Risks and Complications

- Risk of fetal loss of approximaltely 0,5%
- Amniotic fluid leakage
- Placental hemorrhage
- Intra-amniotic infection
- Abdominal wall hematoma
- Fetal lesion

- Prenatal Ultrasound





Prenatal Ultrasound

- Technique for identifying physical signs of gene abnormalities
- Non-invasive use of US equipment
- Safe and painless for mother and fetus
- Practical use in decision making regarding keeping/not keeping fetus
- Used as “double testing” together with serological test of the mother
- Used since 1960s
- Performed at 11-14th week, also repeated in second and third trimesters

What it does

- Image of the fetus within the womb
- Allows the doctor to access physical abnormalities of the fetus
- Especially the fetus' neck is accessed for extra fluid or thickening – indication for trisomy 13, 18, 21
- Use for determining length of pregnancy, number of fetuses, condition of uterus and cervix

How it works

- Gell will be applied on the belly, the transducer is applied and emits high-frequency sound waves
- These waves are interpreted into images by a computer
- The woman is often asked to maintain a full bladder, to increase the image resolution
- Transvaginal US is possible, f.ex early in pregnancy when better seen from this angle
- Duration proximate 30 min

Candidate for fetal ultrasound diagnosis

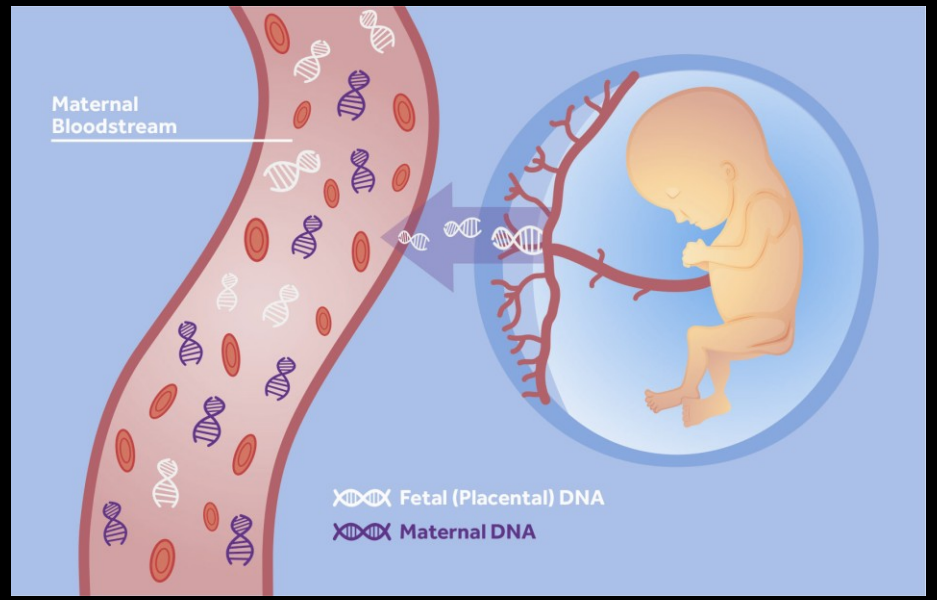
- Mothers of higher age, 38+
- Family history of genetic disorders – hereditary diseases
- Genetic parents previously having had a child with genetic abnormality
- Mother in risk group, e.g., she is a drug user, use certain medications etc.
- A previous US examination showed indications for abnormality → new “double examination” with US and serology
- Ultrasound examination as part of prenatal care (Norway)

Risks and Complications

- No risk related to the ultrasound
- If probable finding of genetic defect the doctor will recommend amniotic fluid sampling to confirm the diagnosis

Maternal blood test

- Noninvasive screening test that helps to assess the risk of chromosomal abnormalities and neural tube defects
- It is usually used in a combined form with other tests



How it works

- Blood from the mother is taken in the first and second trimester of the pregnancy.
- First trimester blood (week 9-13) is tested for the levels of hCG and pregnancy associated plasma protein
- Second trimester blood (week 15-17)is tested for multiple markers like AFP, hCG, Estriol and Inhibin.
- The fetus or placenta produces those markers. Over the placenta those markers enter the maternal blood.
- The amount of those markers changes during pregnancy and also in case of chromosomal abnormalities and neural tube defects.

Maternal blood testing

- First trimester screening for:
  - pregnancy-associated plasma protein (PAPP-A)– placental protein
  - Human chorionic gonadotropin– placental hormone of early pregnancy
  - Abnormal levels of PAPP-A or hCG indicate a higher risk for chromosomal defects such as Trisomy 18 or trisomy 21.

- Second trimester screening:
  - Alpha-fetoprotein screening– made by the fetal liver and is found in amniotic fluid. Abnormal levels indicate:
    - open neural tube defects e.g. spina bifida
    - Chromosomal problems e.g. down syndrome
    - Twins
    - Incorrect due date– levels vary throughout pregnancy
  - hCG
  - Estriol
  - Inhibin

What it does:

- it is a screening test to identify pregnancies with a higher risk for chromosomal abnormalities like down syndrome (trisomy 21) or Edwards syndrome (trisomy 18).
- It can also be used to search for neural tube defects.
- Twins or multiples produce more of some markers and can therefore be detected.
- It is not very accurate and therefore a positive result is not a diagnosis, it is only an indication for further testing. The test will detect between 69-81% of babies with down syndrome and about 80% of neural tube defects. Exact detection rates depends on the number of proteins tested and the laboratories. To increase the accuracy of the tests it is often used in combined forms with other tests.

Risks, complications and indication

- The risks are the same as for any other blood draw during pregnancy. If correctly performed it is a very safe test.
- It is indicated in all pregnancies.

Chorionic villus sampling

- Technique to obtain placental tissue.
- Can be performed as a needle biopsy through the belly or by inserting a catheter through the cervix.
- The test increases the risk of miscarriage and is therefore only used if indicated by other tests
- Was performed for the first time in 1983 in Milan.
- Can be used as early as in week 8 of pregnancy.
- Can detect more than 200 different disease.

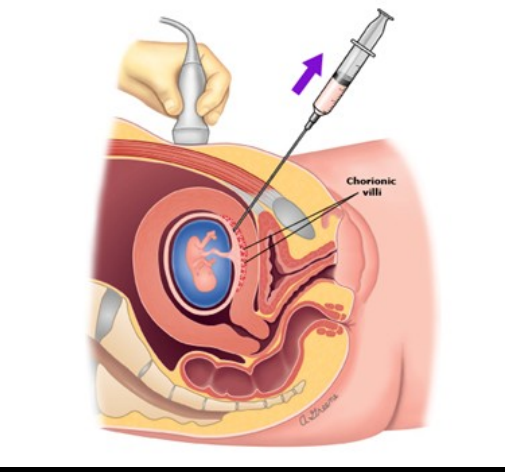
What it does

- Identifies:

- chromosomal disorders (Down‘s syndrome)
- Sex chromosome abnormalities (Turner syndrome, Klinefelter syndrome)
- Genetic disorders (cystic fibrosis, sickle cell disease)

- Can be used to obtain fetal stem cells.

How it works



- First the position of the placenta is identified by ultrasound.
- Transabdominal chorionic villus sampling– a long thin needle is inserted through the abdominal wall into the uterus to obtain the tissue sample
- Transcervical chorionic villus sampling– a hollow tube is inserted through the cervix and when the catheter reaches the placenta a small tissue sample is obtained by suction.
  - The procedure is not performed in case of an active cervical or vaginal infection, bleeding or an inaccessible placenta due to a tilted uterus.
- The procedure is quided by ultrasound
- The genetic material of the obtained sample will be evaluated

Candidates for chorionic villi sampling

- Women with abnormal first trimester screen results
- Family history of chromosomal abnormalities or other genetic disorders
- Age of the mother over 35 years
- Abnormal findings on ultrasound

Risks and complications

- The risk of miscarriage after CVS is 1-2%.
- Some research suggest that the increased risk may not be only due to the sampling but also due to the higher risk of miscarriage in
- Infection from the puncture site
- Amniotic fluid leakage that may result in oligohydramnios (low amniotic fluid levels)
- Untreated oligohydramnios may result in hypoplastic lungs
- Risk of Limb Reduction Defects
- Rh sensitization