PRENATAL SCREENING AND DIAGNOSIS

By

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- **Definition:**

'Prenatal diagnosis is defined as the detection of abnormalities in the fetus, before birth'

Screening is the process of surveying a population, usinga specific marker or markers and defined screening cut-off levels, to identify the individuals in the population at higher risk for a particular disorder.

Prenatal Diagnosis of fetal Abnormalities

- **Benefits:**

1. Malformation incompatible with life may be terminated.
2. Certain abnormalities may be correctible in-utero.
3. -Provides opportunity to arrange corrective measures before hand.

   - offer a chance to be delivered at a place where the required facilities are available.
4. Parents decision to continue pregnancy/ mentally prepare to have a handicapped child.

INDICATIONS OF PRENATAL DIAGNOSIS

1. Advanced maternal age.
2. Previous child with a chromosomal abnormality.
3. Family history of a chromosomal abnormality.
4. Family history of a single gene disorder.
5. Family history Neural Tube Defect.
6. Family history of other congenital structural abnormality.
7. Abnormalities identified in pregnancy.
8. Other risk factors(consanguinity,poor obs. History,maternal history)

Classification of Congenital Abnormalities

1 Chromosomal Abnormalities:
- Trisomy 21 (D.S)
- Trisomy 18 (E.S)
- Trisomy 13 (P.S)

2 Structural Abnormalities:
- CNS
- CVS
- GIT
- Bone
- Renal system

3 Genetic Disorders:
- Inborn error of metabolism
- Haemoglobinopathies

Concept of Screening

Population (pregnant women)

Screening test

Screen Positive

Diagnostic test

- Amniocentesis
- CVS
- Fetal blood sampling

Screen Negative

No further test

Screening Procedures .

1. **History**
2. **Features of current pregnancy**
3. **Ultrasound examination**
   - **nuchal translucency**
   - **soft markers**
4. **Maternal serum markers**
   - **serum alpha fetoprotien**
   - **serum BHCG**
   - **serum E3**
   - **serum inhibin**
   - **serum PAPPA**

Screening Procedures .

1. **History:**
   - Increasing maternal age
   - Congenital anomalies in previous children
   - F/Hx.
     . Still birth
     . Recurrent 1st trimester abortion
     . Cousin marriage

Screening Procedures ---Cont.

2. **Features of current pregnancy:**
   - Drug intake(antiepileptics e.g. warfarin, alcohol, smoking)
   - Radiation exposure
   - Maternal ch. diseases e.g.DM, cardiac, renal
   - Uterine fundas large/ small for date
   - Decrease fetal movements
   - Fetal malpresentation
   - Viral infection in early pregnancy

Screening Procedures .

3. **Ultrasonography:**

- Screening tool in all trimesters
- At 10-14 weeks if fetal nuchal translucency
- ≥ 2.5 mm- chromosomal anomalies association
- At 18-20 weeks 75% fetal abnormalities can be diagnose

1st Trimester Ultrasound

- Nuchal translucency Ultrasound

Nuchal Translucency

Increased NT associated with:

- Trisomies 21, 18, 13, triploidy and Turner syndrome
- Spontaneous fetal loss
- With normal chromosomes: cardiac defects, diaphragmatic hernia, pulmonary defects, skeletal dysplasias, congenital infection, metabolic/haem disorders, rare single gene disorders
- Normal pregnancy – chance of a normal birth varies with size of NT measurement

NT measurement	Chance of normal birth
≤ 3.4mm	95%
3.5 – 4.4mm	70-86%
4.5 – 5.4mm	50-77%
5.5 – 6.4mm	67%
≥ 6.5mm	31%

Nicolaides. Am J Obstet Gynecol 2004;191:45

Souka *et al. Ultrasound Onstet Gyncol* 2001;18:9

- SOFT MARKERS
- choroid pluxus cyst
- absent nasal bone
- digital abnormality
- mild ventriculomegaly

Screening Procedures .

4. **Maternal blood tests:**

- **Maternal Serum alpha fetoproteins:**

. Produced by

. Fetus &enter in maternal circulation.

. Yolk sac in first trimester

. Liver in second and third trimester

. Normally increase from 12-32 weeks

. Abnormally raise on fetal capillaries exposure to amniotic fluid e.g. in NTD.

Maternal S. alpha fetoproteins .

- Raised level in neural tube defect(NTD).
  - Screen for NTD at 15-20 weeks if +ve confirm with detailed USG.
  - Also raised in following conditions:
    . Miscalculated dates . Multiple pregnancies
    . Threatened abortion . IUD
    . Teratoma . Congenital nephrosis
    . Ant. Abdominal wall defects

Maternal serum screening: uE3

Unconjugated estriol (uE3): concentration in maternal serum increase throughout pregnancy.

Pregnancies with fetal Down syndrome have significantly lower uE3 levels in the second trimester.

Maternal serum screening: HCG

Human chorionic gonadotropin (hcg): originates from the placenta, and levels decreased sharply between 10 and 20 weeks of pregnancy.

Down syndrome pregnancies have higher hcg levels, and hcg levels may be the best single marker for Down syndrome.

	AFP	HCG	E3
Down Syndrome	↓	↑	↓
Overestimate GA	↓	↑	↓
Underestimate GA	↑	↓	↑
Trisomy 18	↓	↓	↓
Spina Bifida	↑	N	N
Anencephaly	↑	N	↓
Triploidy pat	?	↑	↓
Turner hydrops	↓	↑	↓
Turner no hydrops	↓	↓	↓

☞ MATERNAL SERUM SCREENING

✓ **Downs syndrome :**

1st Trimester Screening Tests

- *Maternal Serum Markers*
  - -Preg. asso. Placental Protein A (PAPP-A)
  - -Free ß hCG

  } 65%

- Fetal Marker- Nuchal thickness

  } 60-75%

} 85%

2nd Trimester Screening Tests

- *Maternal Serum Markers*
  - -AFP
  - -E3
  - -hCG

  } ***Triple test 70%***

  - -Inhibin A

  } ***76% Quadruple test***

} 94%

DIAGNOSTIC TESTS

- For high risk women on basis of screening tests
- An ideal test should be :
  - Least invasive
  - diagnose c. abnormality in early pregnancy.
  - Minimally interfering developing pregnancy
- Diagnostic tests are also not risk free.

Counselling

- Organize an appointment
- Couple should be present
- Explain:

  - Risk of occurance of c. abnormality

  - All tests available, their procedure, cost, diagnostic ability and benefits, possible risks

  - Possible management plain

- If termination of pregnancy is unacceptable diagnostic tests would be fruitless.

- Diagnostic tests

non- invasive

- ultrasound
- detecting fetal cells in maternal blood

Invasive

- amniocentesis
- Chorionic villous sampling
- Cordocentesis (fetal blood sampling)
- fetoscopy
- PGD (preimplantation genetic diagnosis)

NON INVASIVE TESTS

- **Ultrasonography:**
- Diagnostic USG is different from screening USG,
  - It takes longer time
  - Dx. Wide range of c. anomalies
  - Non invasive and diagnosis at spot possible
  - But possible only at large gestational age
- Colour doppler further enhance the capability especially for cardiac malformations and renal agenesis.

INVASIVE TESTS

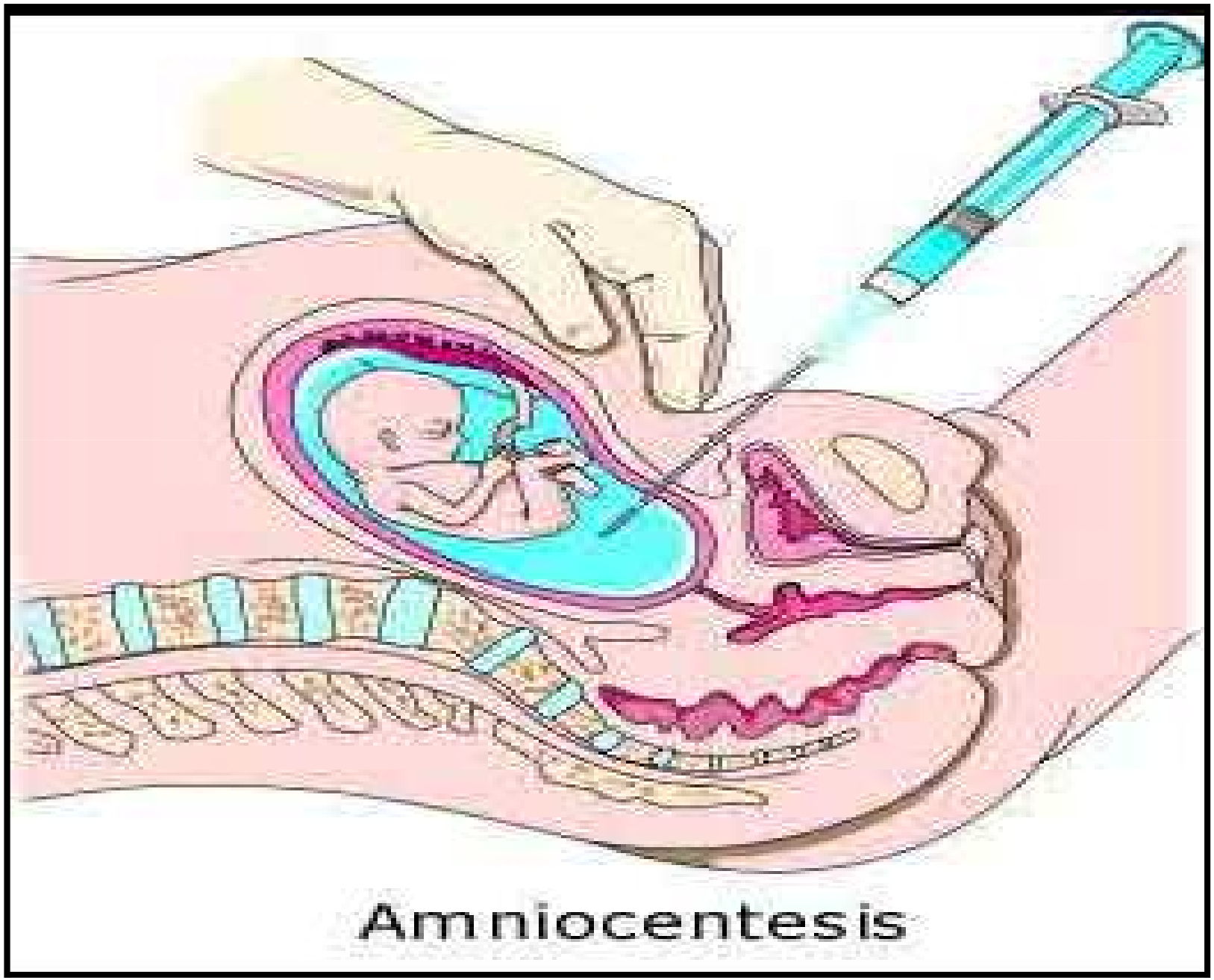
AMNIOCENTESIS:

- Aspiration of amniotic fluid which contain fetal cells
- Fluid can be used for estimation of
  - bilirubin level (for fetal haemolytic disease).
  - AFP
  -Acetyl cholinesterase
- Cells used for karyotyping (Chromosomal dis.)
- Fetal cells-cultured for 3 weeks- karyotyping.
- New technique-PCR, FISH-give result in 48 h.
- Preferred time of test 16weeks of pregnancy.

AMNIOCENTESIS---Cont.

- **Procedure:**
- Preliminary USG to confirm-duration of gestation, -placental site,- adequacy of liqour (150-200 ml)
- Sterilize the abdomen
- 22 G spinal needle is used.
- About 20 cc amniotic fluid is withdrawn.
- Give Anti- D to all Rh-ve mothers.
- Ask rest for 30 min.& restrict movements for 48h

Amniocentesis



AMNIOCENTESIS---Cont.

- **Limitations** (difficulties)of procedure: if
  - Anteriorly placed placenta
  - Multiple pregnancy.
  - Maternal obesity
  - Oligohydramnios
- **Risks**:
  - Pregnancy loss 1 %
  - Bleeding , Infection,
  - Rupture of membrane
  - Preterm labour&IUD
  - Leaking of Amniotic fluid
  - Increase risk of RDS in newborn

CHORIONIC VILLUS SAMPLING

- Collection of fragments of placental tissue (chorionic villi)- cells are examined for Dx. of C.Anomalies.
- Cytotrophoblastic (rapidly dividing) cells are used for direct karyotyping- result available within 24-48 h.
- Chorionic villi are best source of DNA
- CVS can be performed at 10 weeks gestation.
- **Indications:**

1-DNA analysis for SCD,thallasemias, CF. hemophillias

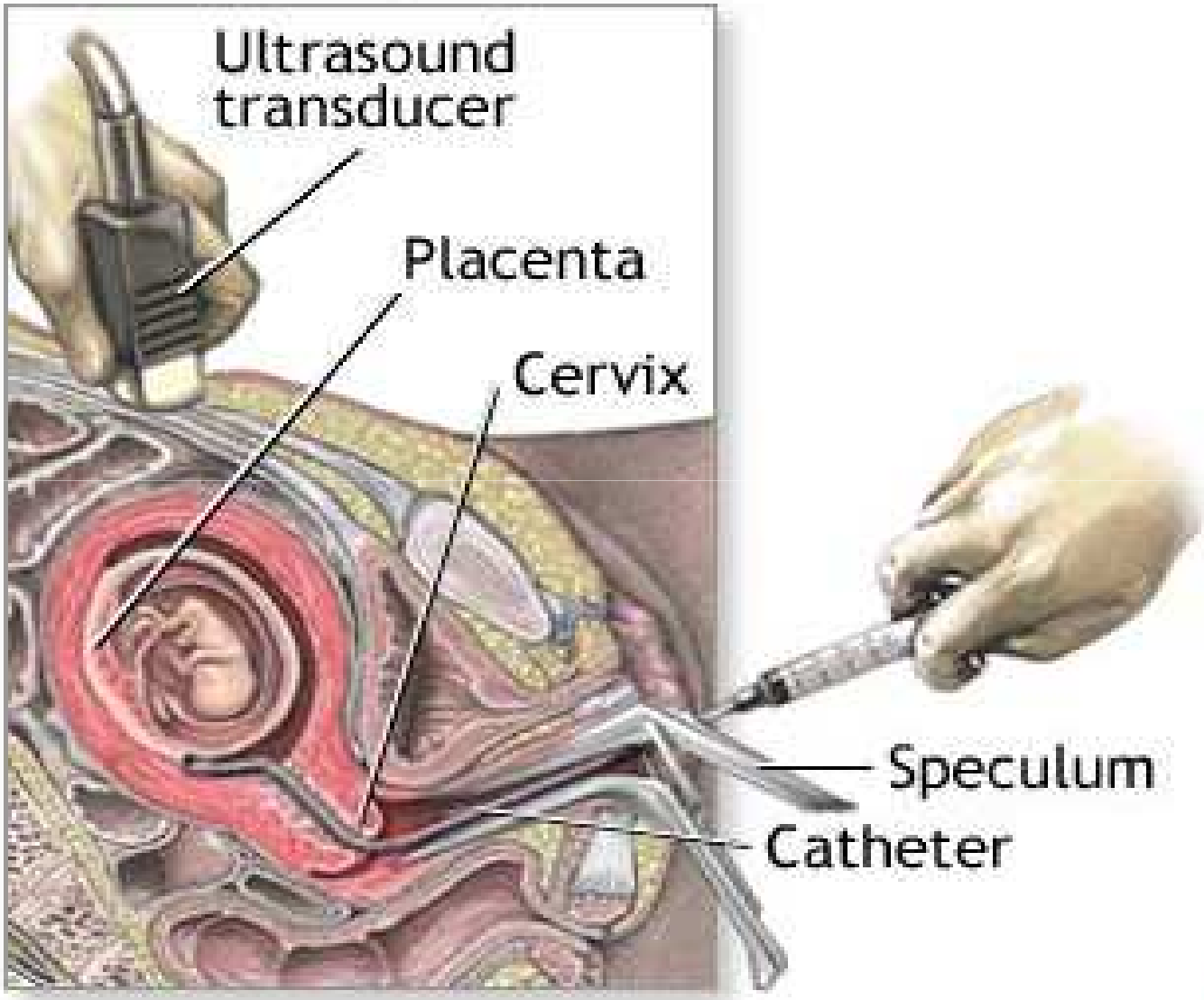
2-Chromosomal abnormalities

3-Inborn error of metabolism

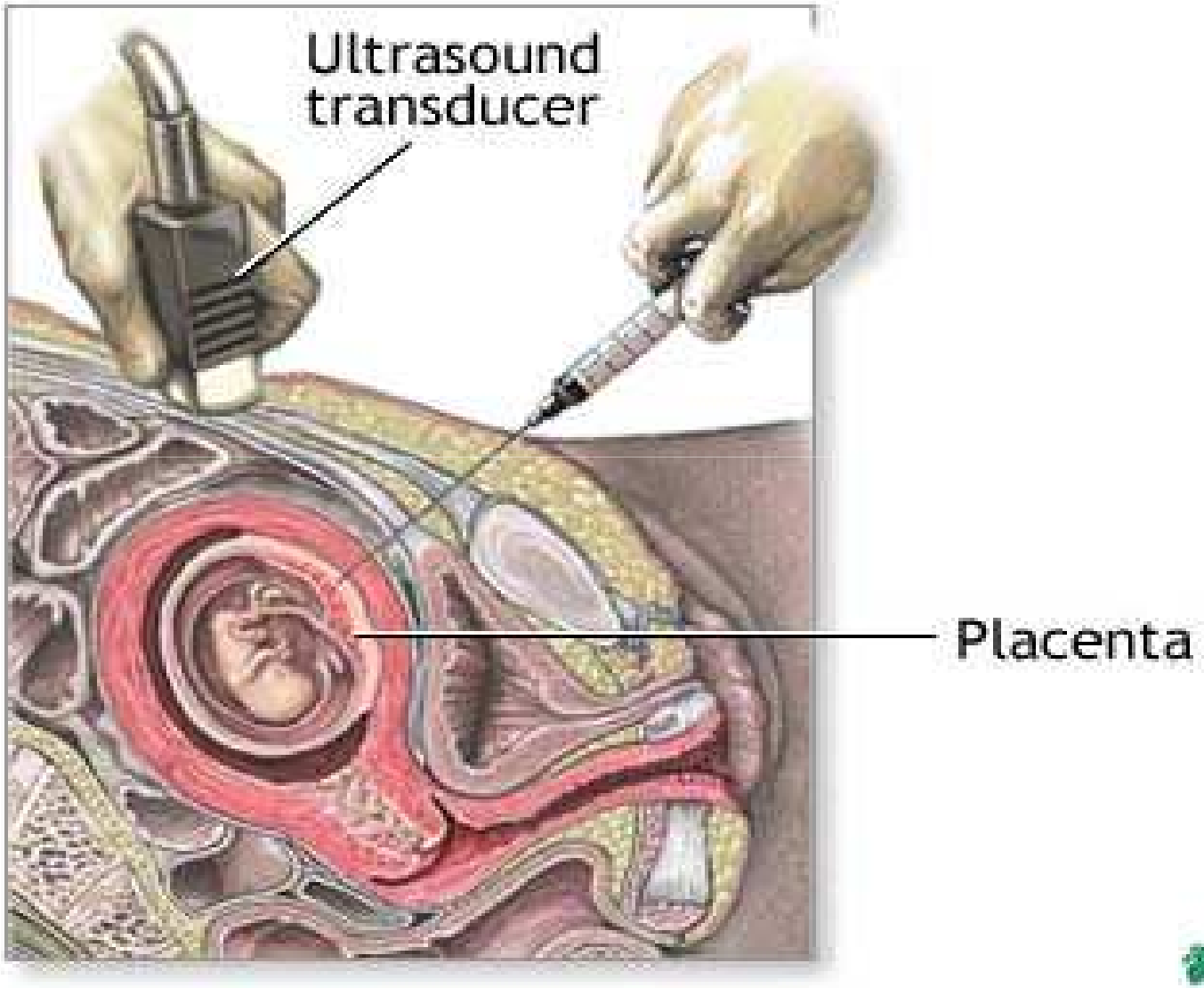
CHORIONIC VILLUS SAMPLING

- **Procedure**:
- Trans-abdominal approach preferred –under USG guidance in supine position
- Trans-cervical approach is easy.
- In lithotomy position, sterilize area & Aspiration catheter and biopsy forceps.
- Introduce through Cx. under USG into placental tissue avoiding membrane rupture
- ***Risks***: Pregnancy loss 2-6%
- Before 10 weeks- associated with limb deformities, micrognathia, microglassia

Transcervical procedure



Transabdominal procedure



FETAL BLOOD SAMPLING (FBS)

- Fetal blood- lymphocyte are rapidly cultured, results within 48-72 hours.
- **Indications:**
- 1- Prenatal Dx. DNA available for Cytogenetic studies In failed amniocentesis, and mosaicism in chorion or amniotic fluid.

2-Fetal assessment: for red cell alloimmunization, (Hb;Hc,TrF) Hydrops fetalis, viral infection, platelets alloimmunization

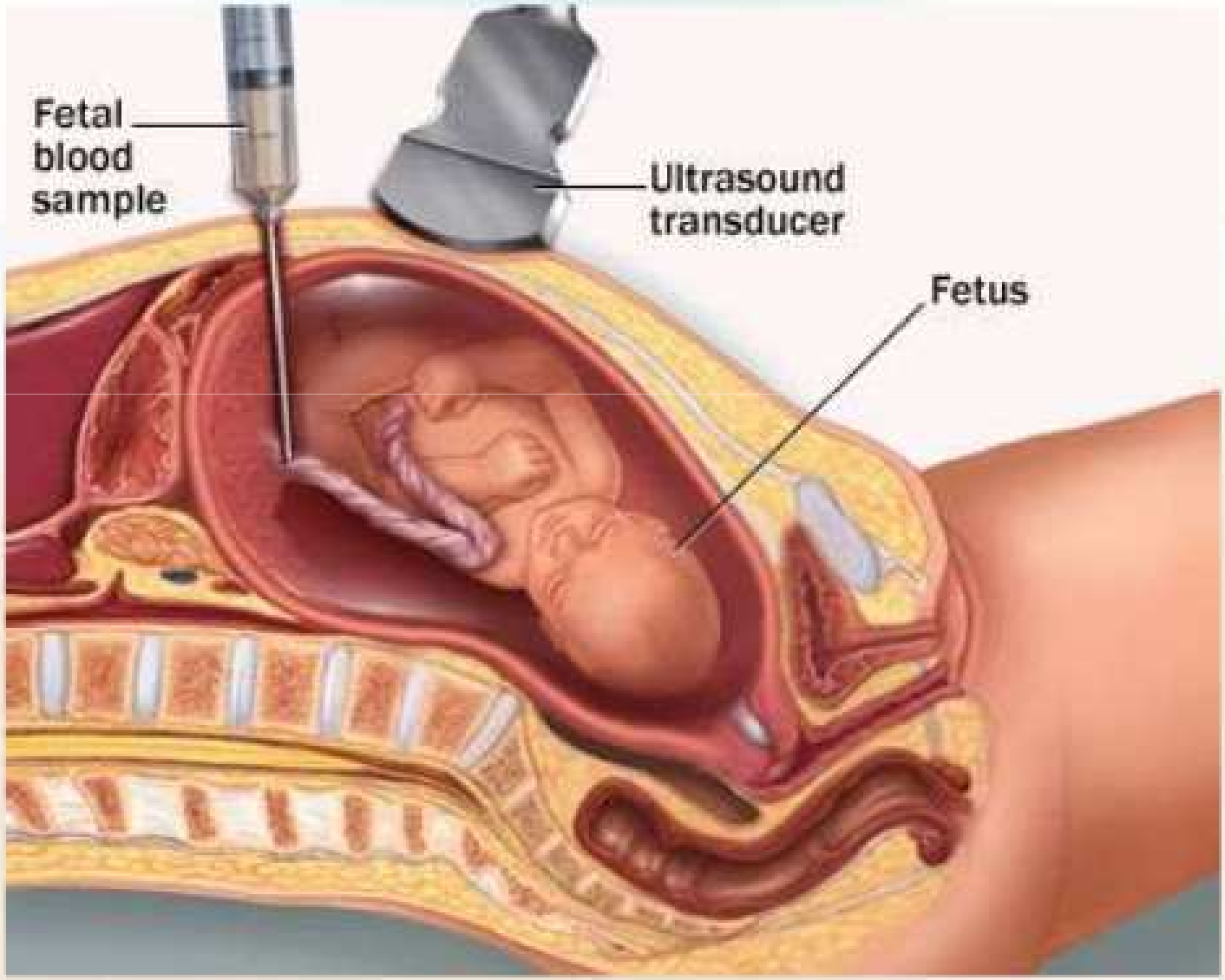
- Unfortunately Associated with highest rate of fetal loss.
- Currently used for blood transfusion in-utero in fetal A.

FETAL BLOOD SAMPLING (FBS)

- **Procedure** : (cordocentesis):
- The sites for FBS are placental insertion of umbilical cord, abdominal insertion of cord, intrahepatic fetal vein and fetal heart.
- Suitable time is 20-28 weeks
- **Risks**:

  - Bleeding from site of puncture
  - Cord haematoma
  - Fetal bradycardia
  - Fetal death

Fetal blood sampling (cordocentesis)



☞ Fetal visualization

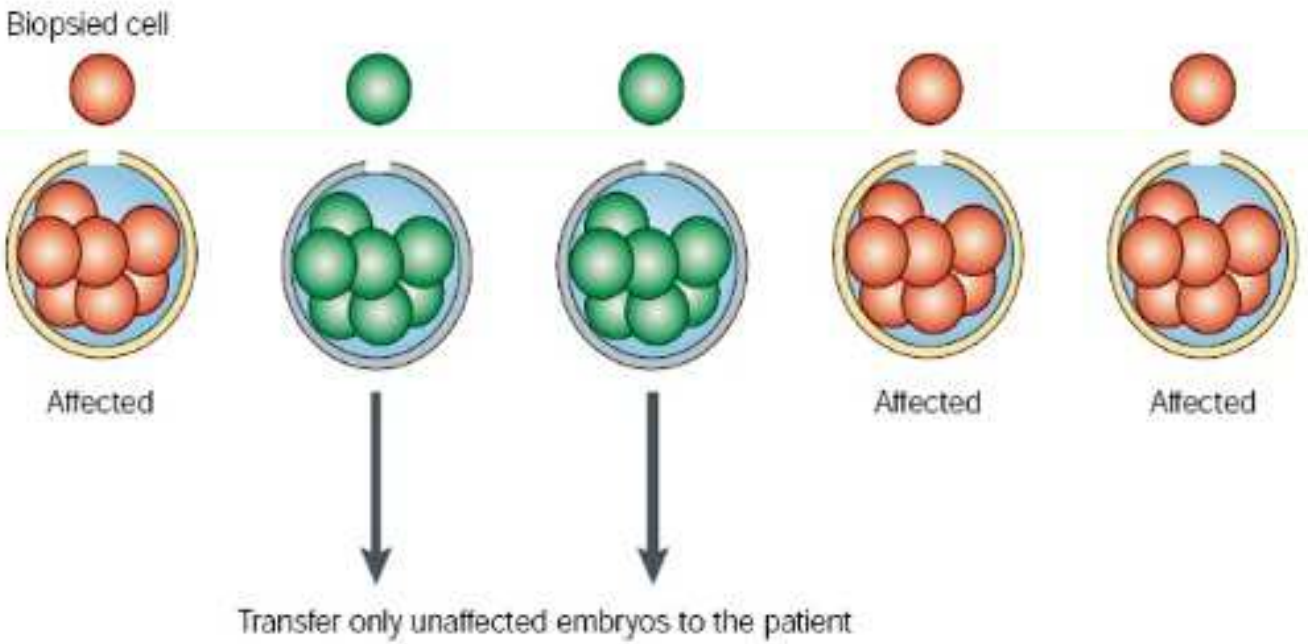
-Fetoscopy

- ✓ Fetoscopy is performed during the second trimester (after 16 weeks' gestation).
- ✓ In this technique, a fine-caliber endoscope is inserted into the amniotic cavity through a small maternal abdominal incision, under sterile conditions and ultrasound guidance, for the visualization of the embryo to detect the presence of subtle structural abnormalities.
- ✓ It also is used for fetal blood and tissue sampling.
- ✓ Fetoscopy is associated with a 3-5% risk of miscarriage;


Fetoscope
Placenta

Preimplantation Genetic Diagnosis

- **Definition:** "A process which allows parents to have the option of detecting potential defects in an embryo within days after conception."



THANKS