Prenatal diagnosis

- **It's the ability to detect abnormalities in an unborn child.**
- Prenatal diagnosis **is an option** which **is chosen by many couples at high risk** of having a child with a serious hereditary disorder.
- The goal of prenatal diagnosis is to help parents learn what *they* need to know about the health of their unborn child to help them make informed decisions for themselves and their family within the context of their own value system.
- All couples have ~3% risk of having a child with congenital problems requiring intervention
- No 100% guarantees - even if prenatal tests are 'normal'
- All couples bring unique ethnocultural, moral, and/or religious perspectives to the process
- Use of non-judgmental, non-directive genetic counseling is important in helping families make the best choice for them
- The decision to terminate or continue a pregnancy based on prenatal diagnostic findings is *never* an easy decision

The purpose of prenatal diagnosis not simply detect abnormalities in fetal life and termination, it rather has the following goals:

Goals of Prenatal Diagnosis and Counseling

- Assess pregnancy
- Determine specific risks to fetus
- Evaluate prenatal diagnostic options
- Educate family about diagnosis, likely outcomes, potential and management options
- Discuss risks, benefits, and uncertainties
- Explore family concerns
- Provide risk assessment for other family members
- Provide psychosocial support and follow-up

Benefits from prenatal diagnosis

- Older women (> 35) at increased risk of chromosome disorders
- Individuals in populations at increased risk of a genetic disease:
- Tay-Sachs: Ashkenazi Jews, French Canadians
- Sickle cell anemia: Africans, Mediterraneans, Arabs, Turks, Indo-Pakistanis
- Thalassemias: Mediterraneans, Arabs, Turks, Indo-Pakistanis, Southeast Asians
- Cystic Fibrosis: Caucasians
- Fragile X syndrome: All women (?)
- Family history of a genetic disease/chromosome disorder
- Maternal disease associated with increased risk of birth defects (diabetes, phenylketonuria)
- Known teratogen exposure during pregnancy
- Abnormal screening tests or ultrasounds
- Women who are concerned/worried

Prenatal diagnosis

Classification of Congenital Abnormalities:

1 Chromosomal Abnormalities:
- Trisomy 21 (Down Syndrome)
- Trisomy 18 (Edward Syndrome)
- Trisomy 13 (Patau's Syndrome)

2 Structural Abnormalities:
- Central nervous system defect
- Neural tube defect
- Limb defect
- Bone defect
- Renal system

3 Genetic Disorders:
- Inborn error of metabolism
- Haemoglobinopathies

Screening Procedures:

- History of genetic disease
- Increasing maternal age
- Congenital anomalies in previous children
- Still birth/fetal death
- Recurrent 1st trimester abortion
- Cousin marriage/Relative marriages

Features of current pregnancy:

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

Techniques used in prenatal diagnosis

Non-invasive

- Maternal **serum screening (**Triplet Test)
- Ultrasound

Invasive

- Amniocentesis
- Chorionic villus sampling (CVS)
- Fetoscopy

Prenatal diagnosis

NON INVASIVE TECHNIQES

1. Maternal serum alpha-fetoprotein (MSAFP)

- Alpha feto protein level increases with gestational age in amniotic fluid and cross placenta into maternal bloodstream
- With neural tube (anencephaly, spina bifida) and body wall defects (gastroschisis, omphalocele) AFP is HIGH
- Using MSAFP along with detailed ultrasound study is sensitive to detect open body wall and neural tube defects
- MSAFP is LOWER in trisomies but using MSAFP alone to pick up trisomies is not sensitive or specific
- MSAFP most sensitive between 16-18 weeks
- To interpret must know gestational age, twin status, maternal health status(diabetes), and race - falsely high and falsely low values are often due to poor gestational dating

Triple Test (AFP, hCG, uE3) **by circulating fetal in Maternal blood**

- Used for Down Syndrome (DS) Screening.
- AFP- Alpha feto prtotien, hCG- Human chorionic gonodotrophin and uE3-unconjugated oestriol
- Best carried at 15-18 weeks. In Down Syndrome AFP & uE3 are low while hCG is raised
- Triple test+ maternal age diagnosis- 60% DS
- In trisomy 18 all above components are low

2. Ultrasound scanning

- Non-invasive - no known risks to mother or fetus
- 2-D, 3-D high resolution and fetal echocardiograms
- Assess fetal proportions, sex, position, growth; placenta, amniotic fluid
- Accurately estimate fetal age
- At 6 weeks can see developing embryo
- Between 16-20 weeks' gestation is optimal time to screen for congenital anomalies.
- Screening tool in all trimesters Neural tube defects

Conditions detected by ultrasound:

- Body wall defects
- Major organ abnormalities
- Oligo- or polyhydramnios
- Major limb abnormalities
- Growth disturbances

Prenatal diagnosis

INVASIVE TECNIQUES

1. Amniocentesis

Invasive technique to obtain fetal cells. Study chromosomes, DNA, or biochemical profile of fetus. Approach via mother's abdomen under ultrasound guidance. It involves the **aspiration of 10-20ml of amniotic fluid through the abdominal wall under ultrasound guidance**. It usually performed around **the 16th week of gestation**. The sample is spun down to yield a **pellet of cells and supernatant fluid.** Enough fluid after 14 weeks of gestation to perform safely. Most often preformed between 15 and 20 weeks' gestation

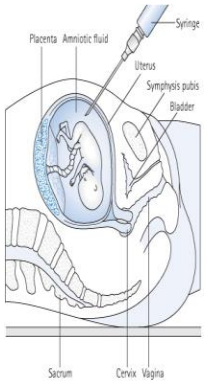
Risks: - Pregnancy loss 1% (Miscarriages)

Bleeding, Infection

Rupture of membrane

Preterm labour & IUD

Leaking of Amniotic fluid



2. Chorionic Villus Sampling:

- Invasive technique to obtain fetal cells
- Study chromosomes, DNA, or biochemical profile of fetus
- Most often approached through the vagina but may be approached through the abdomen of mother
- Most often performed between 10-13 weeks' gestation, but as early as 9 weeks and any time after 13 weeks
- More genetic material from cells to study right away
- Collection of fragments of placental tissue (chorionic villi)- cells are examined for Diagnosis of Chromosomal anamolies.
- Cytotrophoblastic (rapidly dividing) cells are used for direct karyotyping- result available within 24-48 h.
- Chorionic villi are best source of DNA

Prenatal diagnosis

Indications:

DNA analysis for thallesemias, Cystic fibrosis, hemophillias, Chromosomal abnormalities and Inborn error of metabolism

Procedure:

Trans-abdominal approach preferred –under USG guidance in supine position

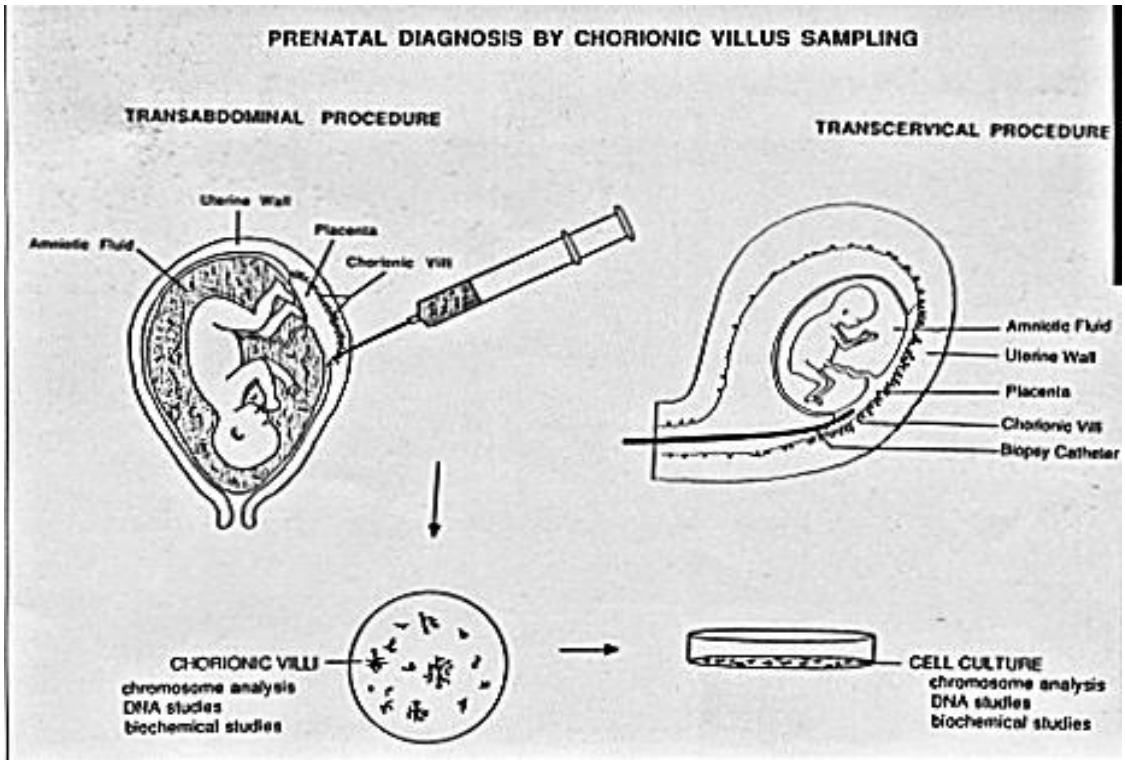
Trans-cervical approach is easy.

In lithotomy position, sterilize area & Aspiration catheter and biopsy forceps.

Introduce through Cervix under USG into placental tissue avoiding membrane rupture

Risks: Pregnancy loss 2-6%

Before 10 weeks- associated with limb deformities, micrognathia, microglassia.



3. FETAL BLOOD SAMPLING (FBS)

- Fetal blood- lymphocyte are rapidly cultured, results within 48-72 hours.
- DNA available for Cytogenetic Studies In failed amniocentesis, and mosaicism in chorion or amniotic fluid.

Prenatal diagnosis

- Fetal assessment: for red cell alloimmunization, (Hb;Hc,TrF) Hydrops fetalis, viral infection, platelets.
- Unfortunately Associated with highest rate of fetal loss.
- Currently used for blood transfusion in-utero in fetal A.

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 cells obtained by CVS and Amniocentesis can be used for prenatal Diagnosis.

For congenital anomalies by following new techniques

1- Southern blotting:

Cleavage of chromosomal DNA at specific sites and used for tests.

2- PCR

3- FISH

EMBRYOSCOPY & FETOSCOPY

- Direct visualization of embryo and fetus.
- Limited field of vision.
- Provide information only about external fetal structures.