**Prenatal diagnosis**

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**Definition :** is the identification of structural or functional abnormalities—birth defects—in the fetus prior to birth.

**Indications of prenatal diagnosis:**

1.Family history- genetic disease with a known recurrence risk.

2.Past obstetrical history –Rh alloimmunization.

3. Abnormal serum screening test result-trisomy 21.

4.ultrasound screening-20 weeks anomaly scan.

5.Advanced maternal age .

6. Multiple pregnancy losses (>3).

7.Medical diseases like diabetes .

8.chronic drug use.

9.Fever by itself of what ever the cause.

**Prenatal diagnosis usually follows a prenatal screening test.-**

**-Attributes of prenatal screening tests:**

**1.**The relavance the condition screened for must be **relavant and imprtant**

 **2. alternative management** options must be available.

 **3.Sensitivity-** test with high detection rate for the condition.

**4.Specifity-**test exclude the vast majority who don't have the condition.

**5.Predictive value-**the test must predict accurately who dose or doesn't have the condition.

**6.Affordability-**cheap enough to be cost effective **.**

**7.Equity-**The test should be available to all.

**Prenatal screening testing:** They are applied to all women to select a high risk group by using maternal history , serum biochemistry ,ultrasound , maternal virology, as a prerequisites to diagnostic tests.

**Prenatal diagnostic testing:** They are tests applied to women at high risk to diagnose abnormalities.

**Classification of diagnostic techniques :**

**1.Non invasive procedures 2.Invasive procedures.**

***Non invasive procedures:***

**A. *Ultrasound*-** Sonographic Screening for Aneuploidy.

**1.Major Structural Defects**- Cystic hygroma, Nonimmune hydrops, Ventriculomegaly.

**2.-First-Trimester Nuchal Translucency**:-

-The increased sonolucent area at the back of the fetal neck is termed the nuchal translucency, or NT.

-the scan is carried out at 11–13+6 weeks pregnancy and assesses the quantity of fluid collecting within the nape of the fetal neck. Increased nuchal translucency is thought to be related to dilated lymphatic channels

- Increased NT itself is not a fetal abnormality ,the NT measurement can be combined with serum analytes to calculate an accurate composite risk.

**Conditions associated with increased nuchal translucency:**

- Down syndrome

-Cardiac defect.

-Diaphramatic hernia.

-Exomphalos.

-Achondroplasia.

**3. Second-Trimester Sonographic Markers—"Soft Signs":**

sonographic detection of aneuploidy, particularly Down syndrome, may be increased by the addition of minor sonographic markers**.** Nuchal fold thickening, Nasal bone absence or hypoplasia**,** Nasal bone absence or hypoplasia**,** Shortened frontal lobe or brachycephaly, Short ear length**,** Echogenic intracardiac focus**,** Echogenic bowel.

***2.maternal blood markers-*** Includes:

* 1.**Free β-HCG** normally decreases in pregnancy, but is increased in fetuses affected with trisomy 21.
* 2.**PAPP**-A( pregnancy associated plasma protein –A ) normally increases in pregnancy, but is decreased in fetuses affected with trisomy 21.

3. maternal serum alpha-fetoprotein**(MSAFP).**

**4. un-conjugated estradiol ,inhibin-alpha**

HCG discrimination is greatest at 13 weeks, whereas PAPP-A’s is greatest at 10 weeks, making **11 weeks the optimal time for first trimester analyte screening.**

**-Second Trimester screening(Maternal analyte screening) :-**Triple screening-

1.Alpha feto protein.

2.HCG

3. un-conjugated estradiol

**-Objective is to increase the prenatal detection of ;-**

Down syndrome, neural tube defects, Trisomy 18.

**Timing ONLY between 14-21 weeks.**

- **Inhibin was added to analyte screening (quadruple screen)**, but, since levels correlate somewhat with HCG, it is not an independent predictor like the other markers, and the increase in detection is more limited.

* **Alpha-Fetoprotein (AFP):**

-This glycoprotein is synthesized early in gestation by the fetal yolk sac and later by the fetal gastrointestinal tract and liver. It is the major serum protein in the embryo-fetus and is analogous to albumin.

 -its concentration increases steadily in both fetal serum and amnionic fluid until 13 weeks, after which, levels rapidly decrease. Conversely, AFP is found in steadily increasing quantities in maternal serum after 12 weeks.

**Abnormal maternal alpha fetoprotein level :-**

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| **High level** | **Low level** |
| Underestimated gestational age | Obesity |
| Multifetal gestation | Diabetes |
| Fetal death | Chromosomal trisomies |
| Neural-tube defects | Gestational trophoblastic disease |
| Gastroschisis | Fetal death |
| Omphalocele |  |
|  |  |

***Invasive diagnostic procedures:***

**1.1st trimester Chorionic Villus Sampling (CVS):-**

-It is a procedure amis to take a sample of fetal trophoplast cells which is a rapidly dividing cells from the developing placenta.

- By passing a needle under ultrasound guidance through the abdominal wall or by fine catheter through the cervix into the placenta ,depending on which route allows easiest access to the placenta. Transabdominal is performed more commonly.

-**Ultrasound is done before the procedure inorder to** :

* Confirm it is a viable pregnancy.
* Confirm gestational age (not < 10 weeks) usually performed at 10-13 weeks.
* To ensure it is singleton pregnancy.
* Localize the placenta.

-**The result for common aneuploidies T 21, 13, 18 provided within 48 hours for CVS sample.**

**Indications:**

* **Advantage of it over the amniocentesis is that it can be done in early pregnancy at a stage when surgical termination is possible.**
* detects chromosome abnormalities (i.e. [Down syndrome](http://americanpregnancy.org/birth-defects/down-syndrome/)) and genetic disorders (i.e. cystic fibrosis.). This test is different from [amniocentesis](http://americanpregnancy.org/prenatal-testing/amniocentesis/) in that it does not allow for testing for neural tube defects.

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* provides access to DNA for [paternity testing](http://americanpregnancy.org/prenatal-testing/paternity-testing/) prior to delivery.

**-The disadvantage of it compared to amniocentesis is that it may be associated with a higher risk of miscarriage.**

-**Complications:**

* Risk of miscarriage is 2%.
* amnionic fluid leakage or infection is < 0.5 %.

 -**Relative contraindications** :

* vaginal bleeding or spotting.
* active genital tract infection.
* extreme uterine ante- or retroflexion.
* body habitus precluding easy uterine access or clear sonographic visualization of its contents.

**2. Second-Trimester Amniocentesis:**

* **It is a procedure amis** to take a sample of 15-20 ml of amniotic fluid which contain fibroblasts, amniocytes cells shed from fetal membrane , skin , fetal genitourinary tract.
* **is performed between 15 and 20 weeks.**
* **Under the sonographic guidance** is used to pass a 20- to 22-gauge spinal needle into the amnionic sac while avoiding the placenta, umbilical cord, and fetus.
* Because the initial 1 or 2 mL of fluid aspirate may be contaminated with maternal cells, it is either discarded or used for amnionic fluid AFP testing. Another approximately 20 mL of fluid is then collected for fetal karyotyping, and the needle is removed.

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* Sonographically the uterine puncture site is observed for bleeding, and fetal cardiac motion is documented at the end of the procedure.

- **The result for common aneuploidies T 21, 13, 18 provided within 48 hours for CVS sample, full culture results take 7-10 days and results for genetic disorders take a varying amount of time, which is similar to CVS.**

* **-Indications :**

1.Maternal age ≥ 35 years at the time of delivery with a singleton pregnancy .

2.Parent or previous child with chromosomal abnormality

3. Both parents carriers for a recessive disorder or an autosomal dominant disorder diagnosable by amniotic fluid analysis

4.Mother a carrier for an X-linked recessive disorder diagnosable by amniotic fluid analysis .

5. Parent or previous child with a neural tube defect

6.Elevated maternal serum alpha-fetoprotein

7. Multiple marker screening test indicating increased risk of Down syndrome or trisomy 18

* **Complications:**
* transient vaginal spotting .
* amnionic fluid leakage in 1-2%
* chorioamnionitis < 0.1 %.
* Needle injuries to the fetus are rare.
* Fetal cells obtained during amniocentesis rarely fail to grow in culture. However, this is more likely if the fetus is abnormal .
* Digital PCR of uncultured amniocytes and chorionic villous tissue provides rapid detection of aneuploidy and may prove promising for expanded clinical use .
* fetal loss ≈0.5 5%

**3. Fetal Blood Sampling(cordocentesis percutaneous umbilical blood sampling (PUBS):**



* it is performed when fetal blood is needed, or when a rapid full culture for karyotyping is needed.
* Check the fetal platelet count , when alloimmune thrombocytopenia is suspected.
* diagnosis of fetal infection.
* determination of fetal Rh(D) status
* some direct fetal therapy via the fetal umbilical vessels.
* A 22-gauge spinal needle is passed under ultrasound guidance into the umbilical cord to puncture the umbilical vein.
* at a point where it inserts into the placenta because the umbilical cord is fixed and does not move
* Performed from about **the 20 weeks gestation**.
* **Complications:**
* The risk of miscarriage is 2-5 %.
* cord vessel bleeding .
* cord hematoma.
* fetal-maternal hemorrhage 66 % with an anterior placenta and 17 % with a posterior placenta
* fetal bradycardia .
* **Down's syndrome:**
* **The most common reason for performing prenatal invasive testing** .
* Recommended that all women should be offered screening for down's as part of there routine antenatal care.
* **Combined tests** should be performed between 11-14 weeks gestation , involves the combination of an US to measure NT + blood tests to measure the levels of HCG and the PAPP-A in the maternal plasma.
* **The risk** increases with maternal age and calculated for each by taking the agew related risk and then adjusted based on the us and blood measurement.

