Session 11

Prenatal Testing and Reproductive Genetics

Intro

- Until recently, couples had to choose between taking the risk or considering other options.

- Over the past three decades, prenatal diagnosis—the ability to detect abnormalities in an unborn child—has been widely used.

- The ethical issues surrounding prenatal diagnosis and selective termination of pregnancy are both complex.

Techniques Used in Prenatal Diagnosis

- **Invasive**
  - Amniocentesis
  - Chorionic Villus Sampling
  - Fetoscopy
  - Cordocentesis

- **Non-Invasive**
  - Maternal Serum Screening
  - Ultrasound
Amniocentesis

- Aspiration of 10 to 20 ml of amniotic fluid, through the abdominal wall under ultrasonographic guidance.
- Usually performed around the 16th week of gestation.
- The sample is spun down to yield a pellet of cells and supernatant fluid.
- The fluid can be used for assay of α-fetoprotein.
- Cells for chromosome and DNA analysis.

- 0.5% to 1% risk of miscarriage.
- Possibility of having to consider a midtrimester termination of pregnancy.
- Trials of amniocentesis earlier in pregnancy, at 12 to 14 weeks’ gestation, yielded comparable rates of success.
Chorionic Villus Sampling

- This procedure is usually carried out at **11 to 12 weeks** gestation.
- Either trans cervical or, trans abdominal aspiration of chorionic villus (CV) tissue.
- Called placental biopsy, when the procedure is carried out at later stages of pregnancy.

Direct chromosomal analysis of CV tissue usually allows a provisional result to be given within 24 hours.

- The major advantage of CV sampling is that it offers **first-trimester** prenatal diagnosis.
- The procedure conveys a **1% to 2%** risk of causing miscarriage.
- Cause limb abnormalities in the embryo if carried out before **9 to 10 weeks’** gestation.

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Fasa University of Medical Sciences, December 2017
Fetoscopy

Ultrasonography

A prenatal diagnosis of structural abnormalities not associated with known chromosomal, biochemical or molecular defects

A offer routinely to all pregnant women at around 18 weeks gestation as screening for structural abnormalities
Nuchal thickening—an accumulation of fluid at the back of the neck.

Ultrasound at 18 weeks showing a rocker-bottom foot in a fetus subsequently found to have trisomy 18.

Maternal Serum Screening

- Maternal serum screening is offered for NTDs and Down syndrome.
- A blood sample obtained from the mother at 16 weeks' gestation.
- In this way up to 75% of all cases of open NTDs and 60% to 70% of all cases of Down syndrome can be detected.
Neural Tube Defects (NTD)

- Open NTDs could be detected at 16 weeks’ gestation by assay of Alpha-fetoprotein in maternal serum
- AFP is the fetal equivalent of albumin and is the major protein in fetal blood
- If the fetus has an open NTD, the level of AFP is raised in both the amniotic fluid and maternal serum
- Unfortunately maternal serum AFP screening for NTDs is neither 100% sensitive nor 100% specific

Maternal serum alpha-fetoprotein (AFP) levels at 16 weeks' gestation
Causes of Raised Maternal Serum AFP level

1. Anencephaly
2. Open spina bifida
3. Incorrect gestational age
4. Intrauterine fetal bleed
5. Threatened miscarriage
6. Multiple pregnancy
7. Abdominal wall defect

Screening for Down Syndrome (The Triple Test)

At 16 weeks’ gestation maternal serum:

- AFP
- Unconjugated estriol
- Human chorionic gonadotropin (hCG)
- Inhibin-A

Table 21.3 Detection Rates Using Different Down Syndrome Screening Strategies

<table>
<thead>
<tr>
<th>Screening Modality</th>
<th>Percent of All Pregancies Tested</th>
<th>Percent of Down Syndrome Cases Detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age alone</td>
<td>1.5</td>
<td>15</td>
</tr>
<tr>
<td>40 years and older</td>
<td>7</td>
<td>35</td>
</tr>
<tr>
<td>35 years and older</td>
<td>5</td>
<td>34</td>
</tr>
<tr>
<td>Age + AFP</td>
<td>5</td>
<td>61</td>
</tr>
<tr>
<td>Age + AFP, ßE3 + hCG</td>
<td>5</td>
<td>75</td>
</tr>
<tr>
<td>Age + AFP, ßE3, hCG + inhibin-A</td>
<td>5</td>
<td>61</td>
</tr>
<tr>
<td>NT alone</td>
<td>5</td>
<td>69</td>
</tr>
<tr>
<td>NT + age</td>
<td>5</td>
<td>73</td>
</tr>
<tr>
<td>hCG, AFP + age</td>
<td>5</td>
<td>86</td>
</tr>
<tr>
<td>NT + AFP, hCG + age</td>
<td>5</td>
<td>86</td>
</tr>
</tbody>
</table>
Indications for Prenatal Diagnosis

- Advanced Maternal Age
- Previous Child with a Chromosome Abnormality
- Family History of a Chromosome Abnormality
- Family History of a Single-Gene Disorder
- Family History of a Neural Tube Defect
- Abnormalities Identified In Pregnancy
- Other High-Risk Factors

Special Problems in Prenatal Diagnosis

- Failure to Obtain a Sample or Culture Failure
- An Ambiguous Chromosome Result
- An Unexpected Chromosome Result
  - A Different Numerical Chromosomal Abnormality
  - A Structural Chromosomal Rearrangement
  - The Presence of a Marker Chromosome