Prenatal Investigations and Laboratory Analysis

Element F

Aims and Objectives

- To develop an understanding of Amniocentesis and Chorionic Villus Sampling (CVS)
- To understand the reasons for these tests being performed
- To understand the advantages, disadvantages, risks and benefits of both tests and how this can affect the woman's physical and psychological wellbeing
- Gain an awareness of the variety of tests used to detect chromosomal and genetic abnormalities prenatally

Indications for Prenatal Diagnosis

- Abnormal maternal serum biochemistry
- Risk of Down's syndrome
  Higher Risk
  1 in 85 at term
- Genetic condi
- Abnormal ultrasound findings

Amniocentesis

Amniocentesis is the commonest invasive prenatal diagnostic procedure in the UK.

It is the transabdominal surgical removal of amniotic fluid (liquor) under direct ultrasound guidance during pregnancy for the purpose of analysis.

Green Top Guidelines

- Early amniocentesis should be avoided
- Direct ultrasound control
- Transplacental approach if necessary
- If difficulties, further opinion should be sought
- Ultrasound training (level of MRCOG/PGDipUS)
- 30 amniocentesis performed under supervision
  Amniocentesis and audit performed on a regular basis

RCOG, Clinical Guidelines, No. 8, Feb 2000

Timing

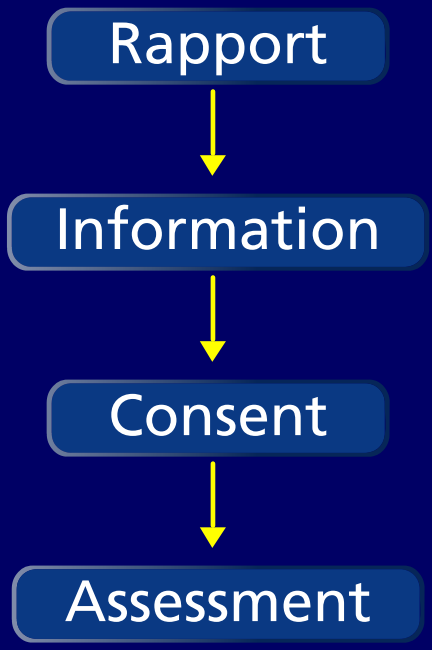
Optimum time from 15 - 20 weeks because:

- < 14 weeks should be avoided
- Should be avoided where AFP levels are raised

Range of Tests

- Karyotyping
- DNA studies
- Virology studies
- Infection screen
- Fetal sexing
- Spectrophotometry

Pre-Test Procedure



Prior to testing the following issues must be discussed with the patient

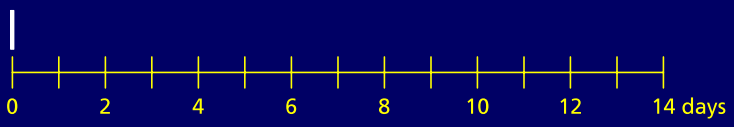
- Aims of prenatal testing
- Indications for testing
- Nature of the procedures
- Accuracy of results
- Complications - laboratory, maternal and fetal
- Limitations of the test
- Length of time to results and method of reporting
- Methods of termination for abnormal results

Amniocentesis - Advantages

- Outpatient appointment
- Fairly simple and quick procedure
- Performed within mid-trimester of pregnancy
- Risk of miscarriage marginally less than CVS
- Approximately a 99.9% reliability

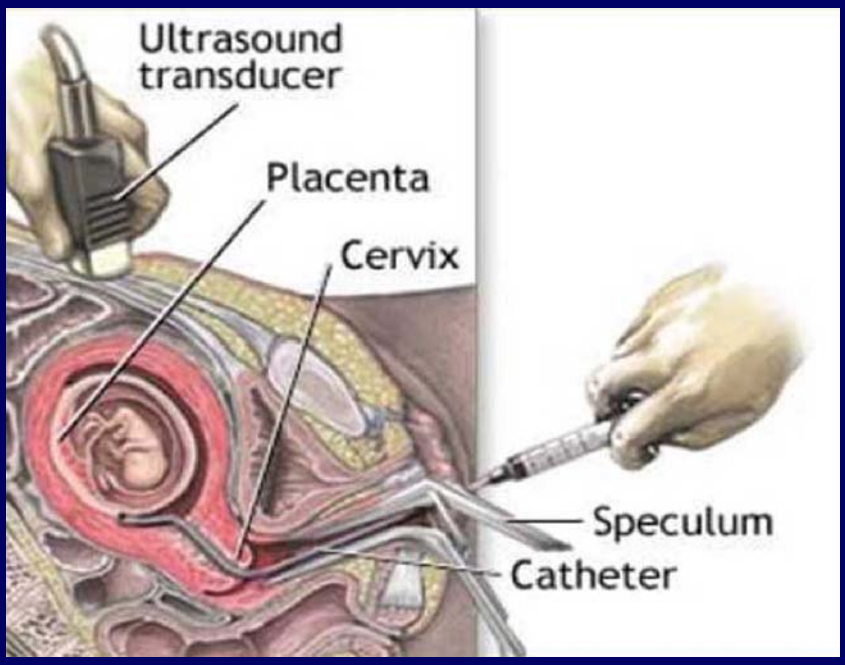
Discuss with Patient

- Results can take up to 14 days
  (But check times with local cytogenetics unit)



- Some women may experience fetal movements

Procedure



The needle is gently inserted into the womb under direct ultrasound guidance

Chorionic Villus Sampling (CVS)

The transabdominal or transcervical surgical removal of tissue from the developing chorion frondosum under direct ultrasound guidance within the first trimester for analysis.

CVS Timing

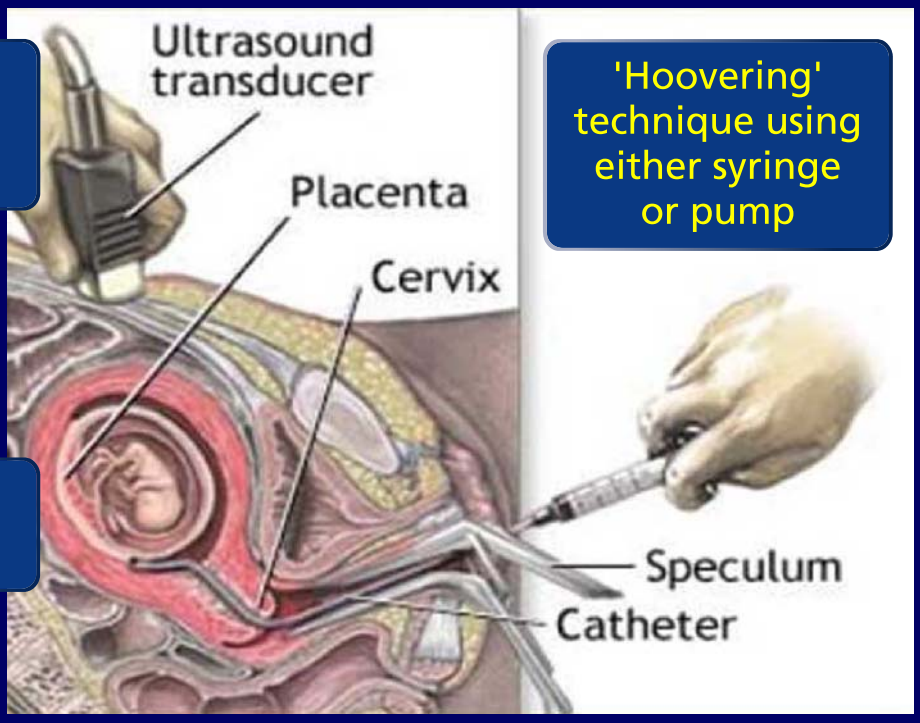
- Optimum time is about **10 - 12 weeks**
- Miscarriage risk is around 1% - 2%
- Avoid CVS in very early gestation (<10 weeks) as known to be associated with Oromandibular Limb Hypoplasia

Firth et al, 1991, 1994

Transcervical

Direct ultrasound guidance

Lithotomy position



'Hoovering' technique using either syringe or pump

Advantages of CVS

- Outpatient appointment
- Performed within 1st trimester
- **Option** of suction termination
- Two methods (TA and TC) available
- Chorion is an excellent source of DNA

Disadvantages of CVS

Transabdominal

- Marginal increase in miscarriage compared to amniocentesis

Transcervical

- Carries a higher risk of miscarriage compared to TA
- Similar to having a cervical smear

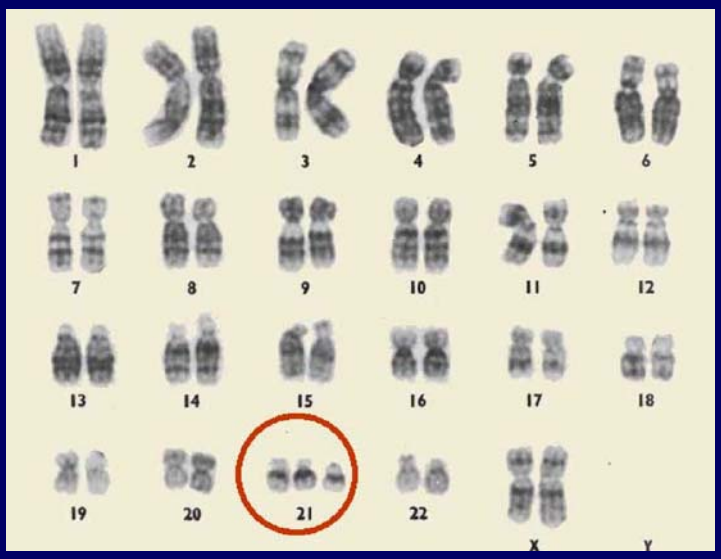
Both procedures require additional specialist training

Usually performed by two operators

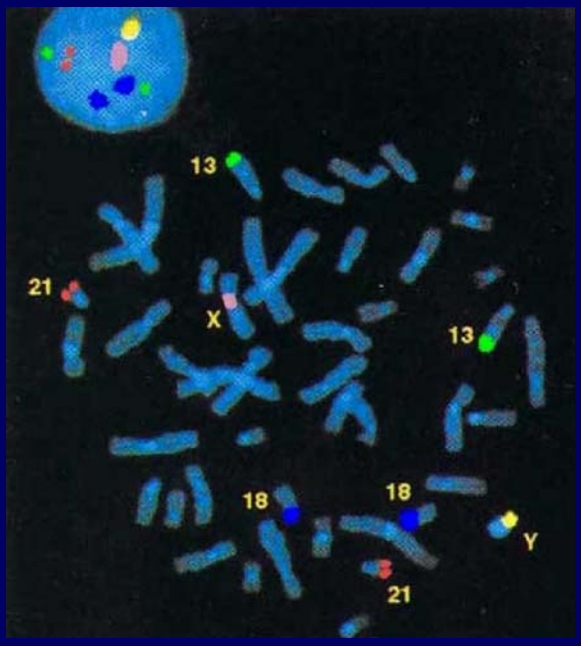
Partial/full bladder required

Cytogenetic Laboratory

Karyotyping



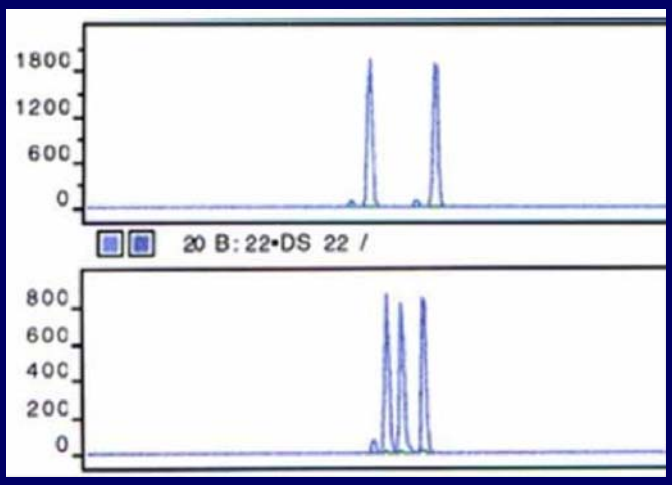
Karyotype = 47, XX+21



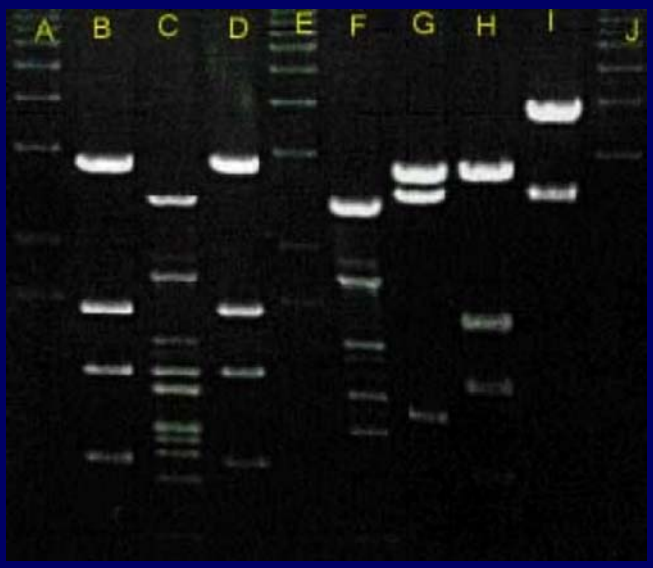
FISH (Florescent
In-Situ Hybridisation)

Molecular Genetics Laboratory

QF-PCR



DNA Analysis



Complications

Maternal

- Miscarriage
- Chorionamnioitis
- Haemorrhage
- Haematoma
- Embolism
- Sensitisation
- Uterine contractions

Fetal

- Miscarriage
- Fetal infection
- Placental trauma
- Fetal injury
- Ruptured membranes
- Amniotic bands
- Intrauterine death

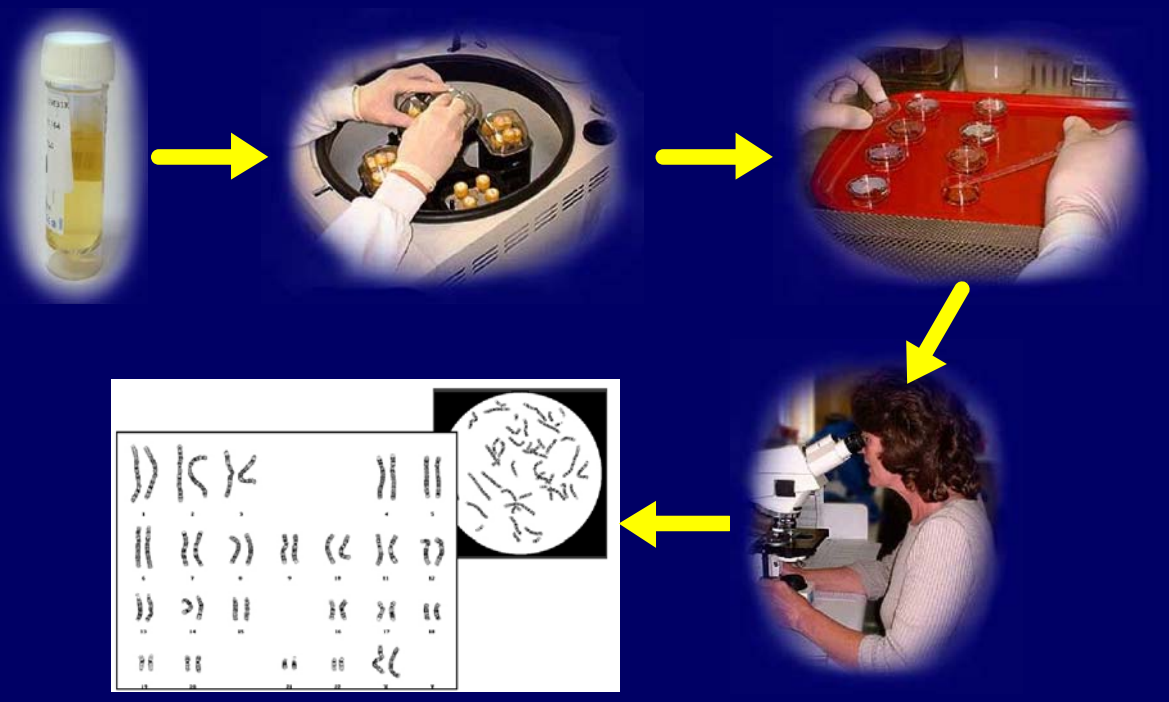
Amniocentesis

Excess Miscarriage risk is 0.5%-1%

Chorionic Villus Sampling

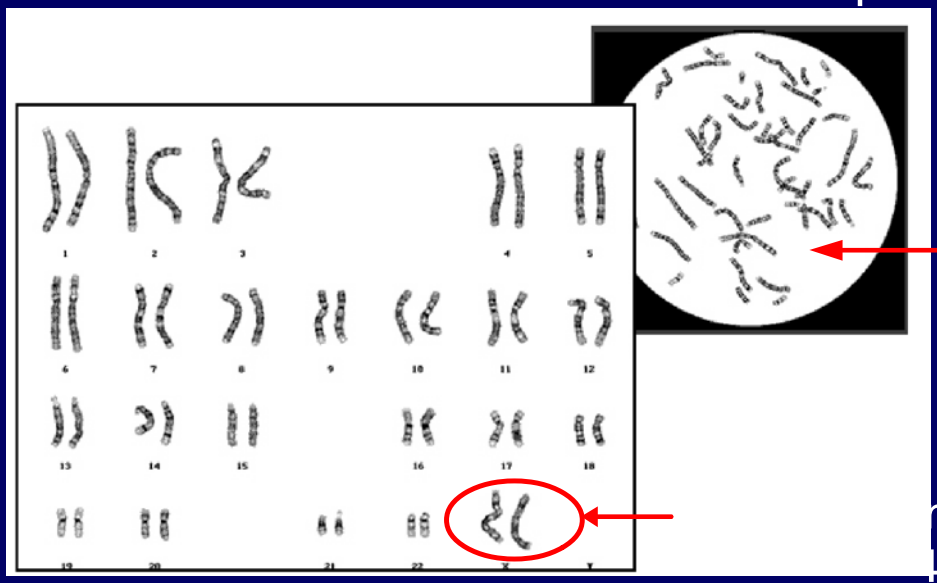
Excess Miscarriage risk is 1%-2%

Standard Karyotype



Under the Microscope

Chromosome spread



male karyotype
46, XX

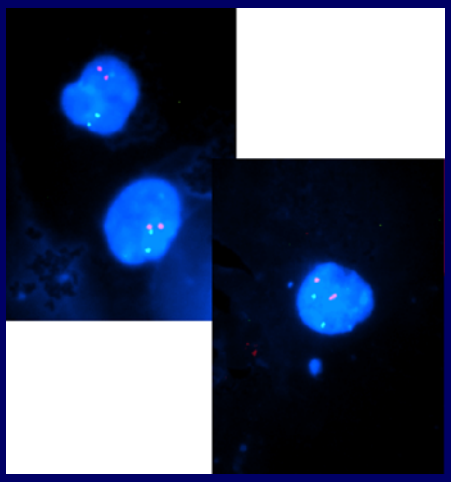
Reasons for Culture Failure

Standard Karyotype

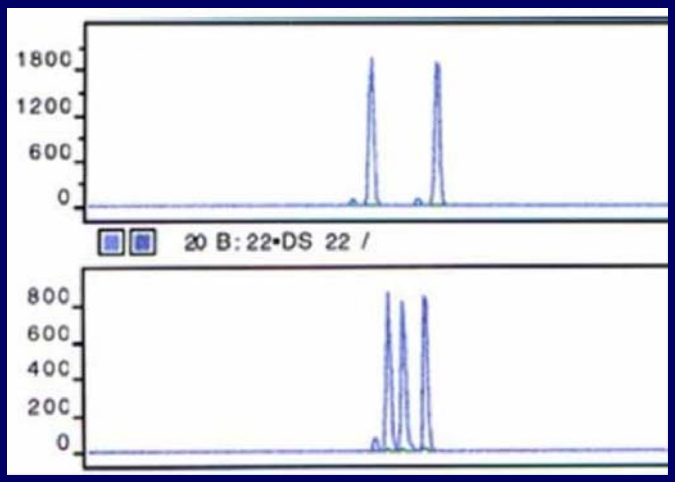
- Insufficient villi **or** amniocytes in sample
- Insufficient fetal cells in sample
- Maternal cell contamination

Rapid Techniques

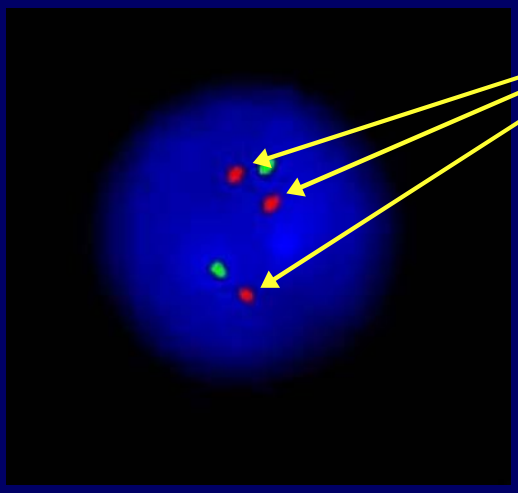
Fluorescence In-Situ Hybridisation (FISH)



Polymerase Chain Reaction (QF-PCR)



FISH



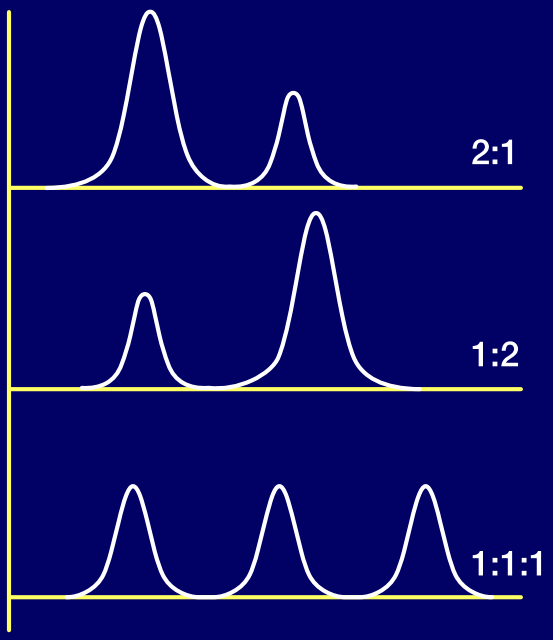
3 Red signals from chromosone 21 probe indicating Trisomy 21

Limitations of Rapid Prenatal Diagnostic Techniques

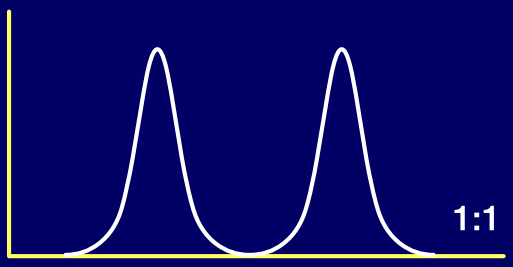
- Some abnormalities will not be identified
- Blood stained samples cannot be processed
- Occasionally a result cannot be generated

QF-PCR

Trisomy 21



Normal



Results are displayed graphically on a computer screen

Summary

Prenatal diagnosis should:

- Allow the widest possible range of informed choice to women/couples at risk of having children with an anomaly
- Prepare women/couples of a seriously affected child and provide alternative options
- Ensure optimal treatment of affected infants through early diagnosis