

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 condition



- 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

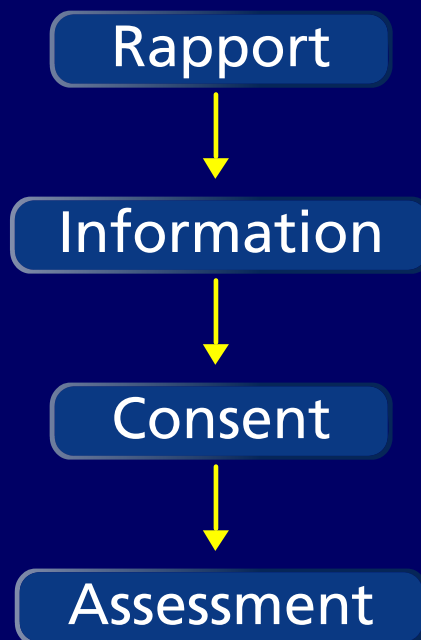
Optimum time from 15 - 20 weeks because:

- < 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

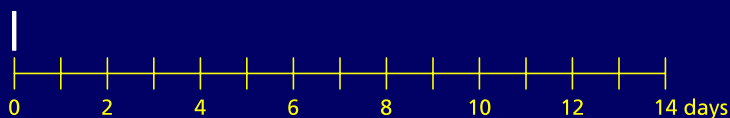
- Aims of prenatal testing
- Indications for testing
- Nature of the procedures
- Accuracy of results
- Complications - laboratory, maternal and fetal
- Limitations of the test
- Length of time to results and method of reporting
- Methods of termination for abnormal results

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

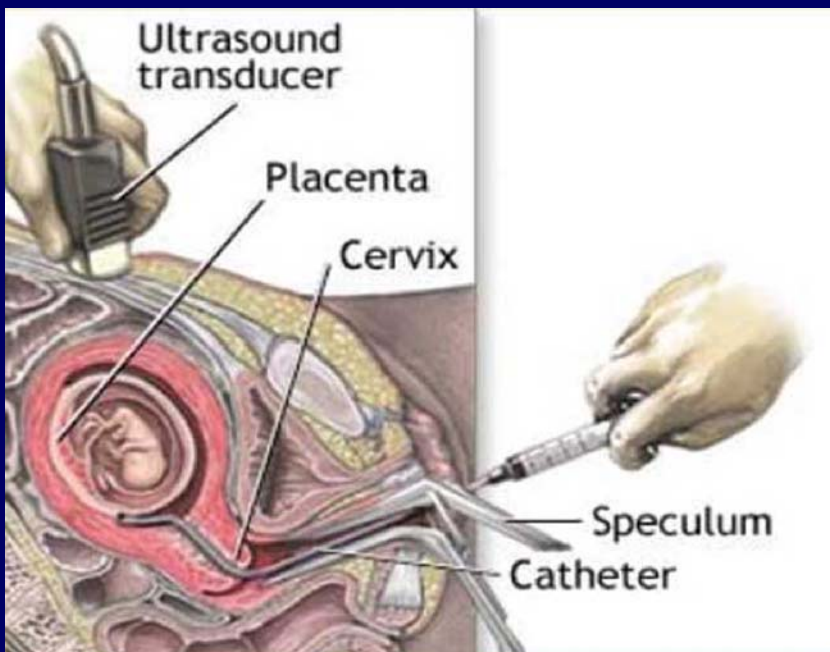
Discuss with Patient

- 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

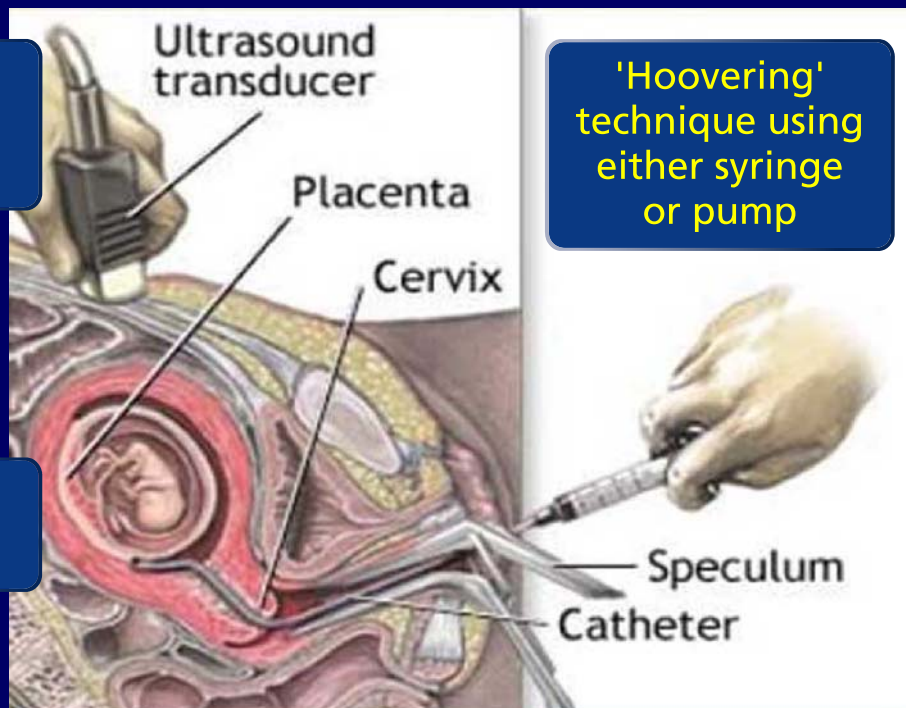
- Optimum time is about **10 - 12 weeks**
- Miscarriage risk is around 1% - 2%
- Avoid CVS in very early gestation (<10 weeks) as known to be associated with **Oromandibular Limb Hypoplasia**

Firth et al, 1991, 1994

Transcervical

Direct
ultrasound
guidance

Lithotomy
position



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

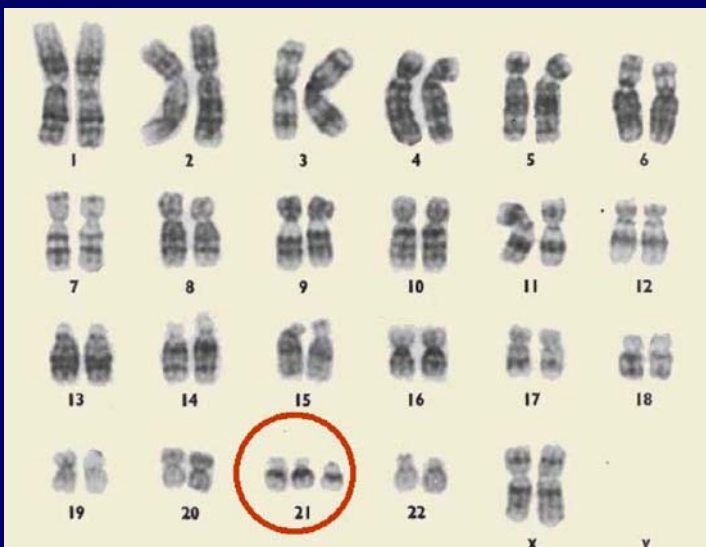
Both procedures require additional specialist training

Usually performed by two operators

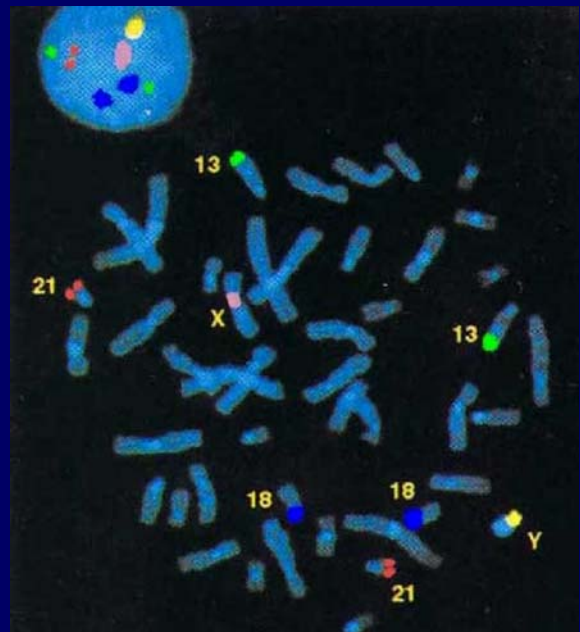
Partial/full bladder required

Cytogenetic Laboratory

Karyotyping



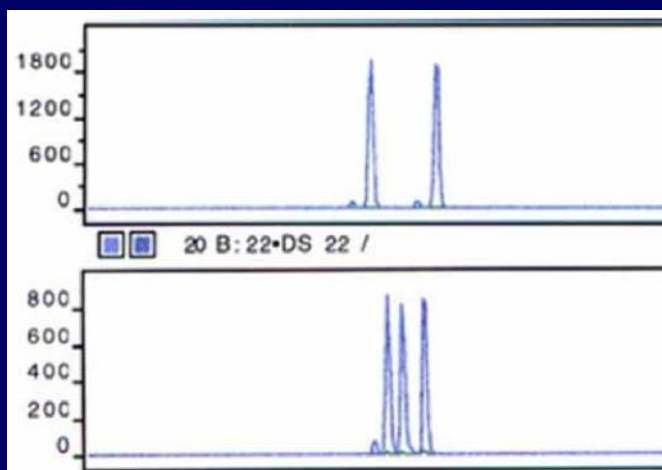
Karyotype = 47, XX+21



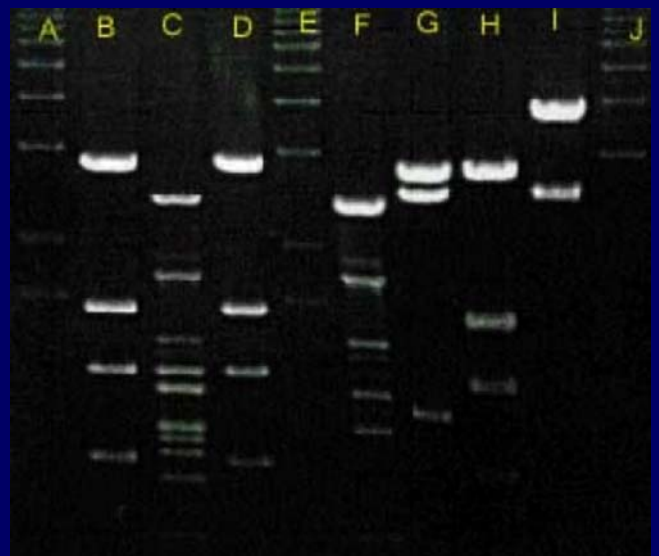
FISH (Fluorescent In-Situ Hybridisation)

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

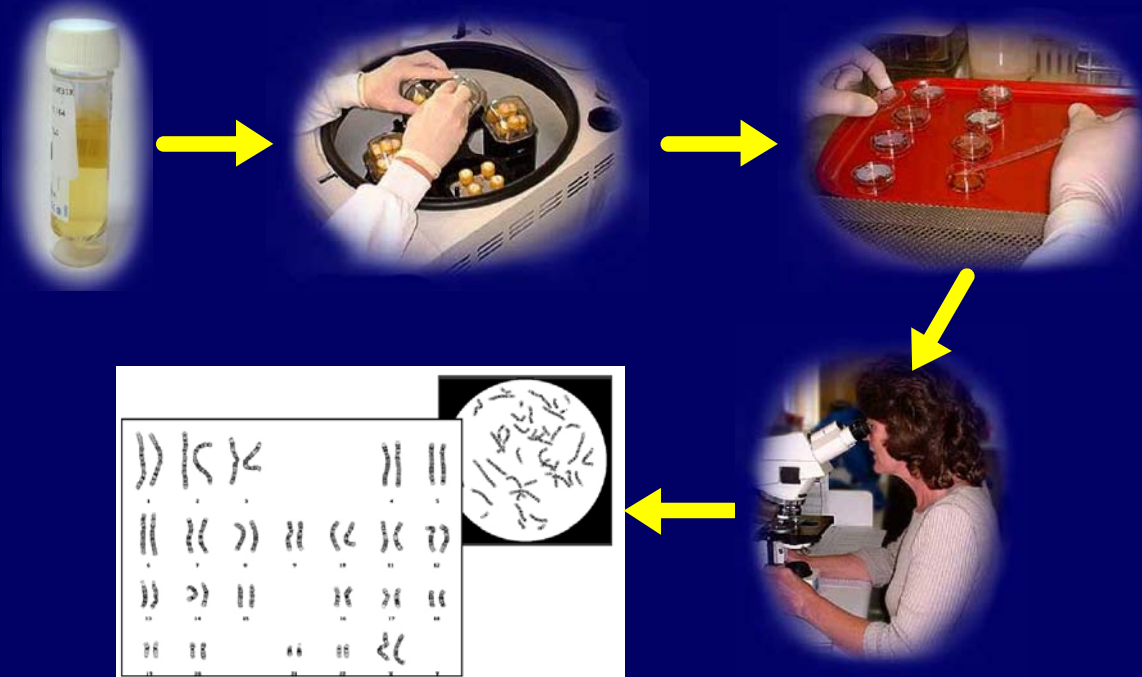
Amniocentesis

Excess Miscarriage risk is 0.5%-1%

Chorionic Villus Sampling

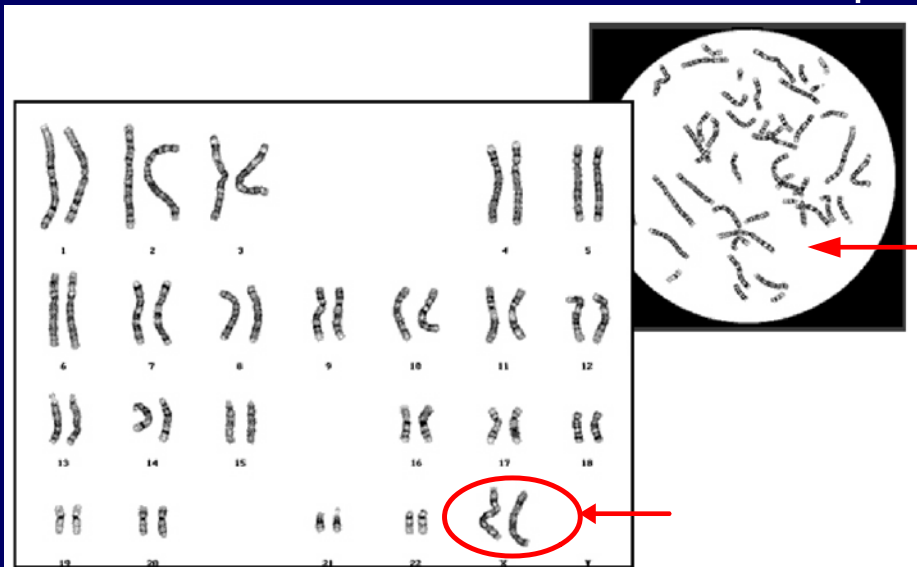
Excess Miscarriage risk is 1%-2%

Standard Karyotype



Under the Microscope

Chromosome spread



female karyotype
46, XX

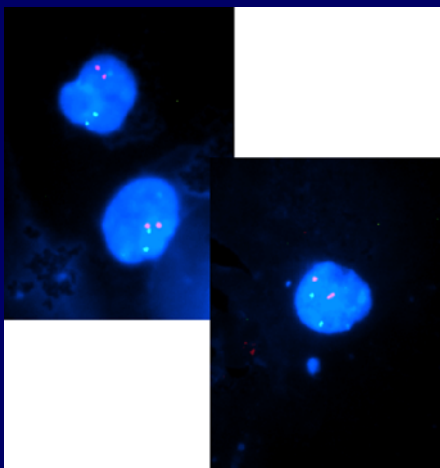
Reasons for Culture Failure

Standard Karyotype

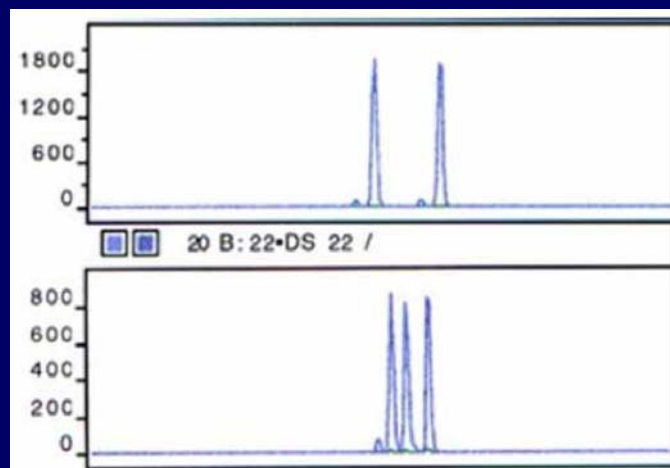
- Insufficient villi **or** amniocytes in sample
- Insufficient fetal cells in sample
- Maternal cell contamination

Rapid Techniques

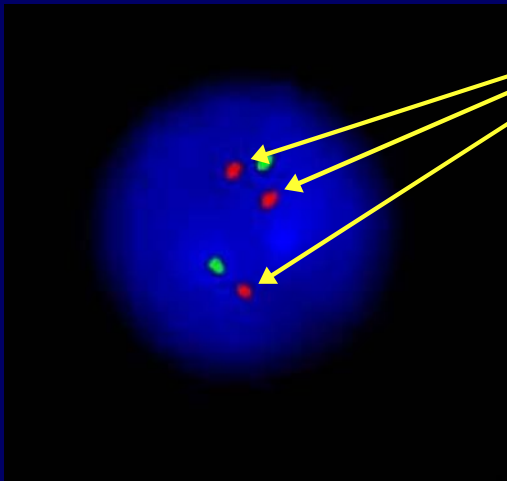
Fluorescence In-Situ Hybridisation (FISH)



Polymerase Chain Reaction (QF-PCR)



FISH



3 **Red** signals from
chromosome 21 probe
indicating Trisomy 21

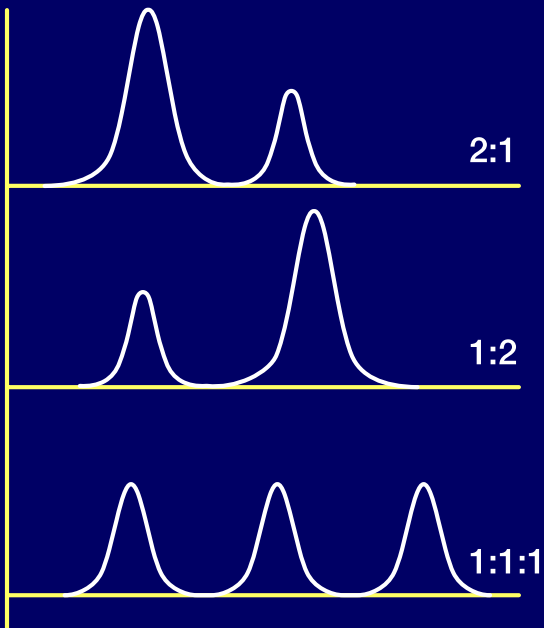


Limitations of Rapid Prenatal Diagnostic Techniques

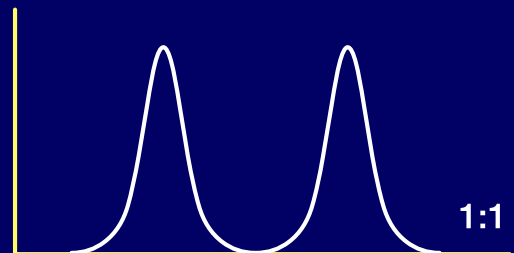
- Some abnormalities will not be identified
- Blood stained samples cannot be processed
- Occasionally a result cannot be generated

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