Imperial College London

# Reproductive and Prenatal Genetic Counselling

*Angela Colangelo (Genetic Counsellor)*

*North West Thames Regional Genetics Service (NWTRGS)*

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# Overview

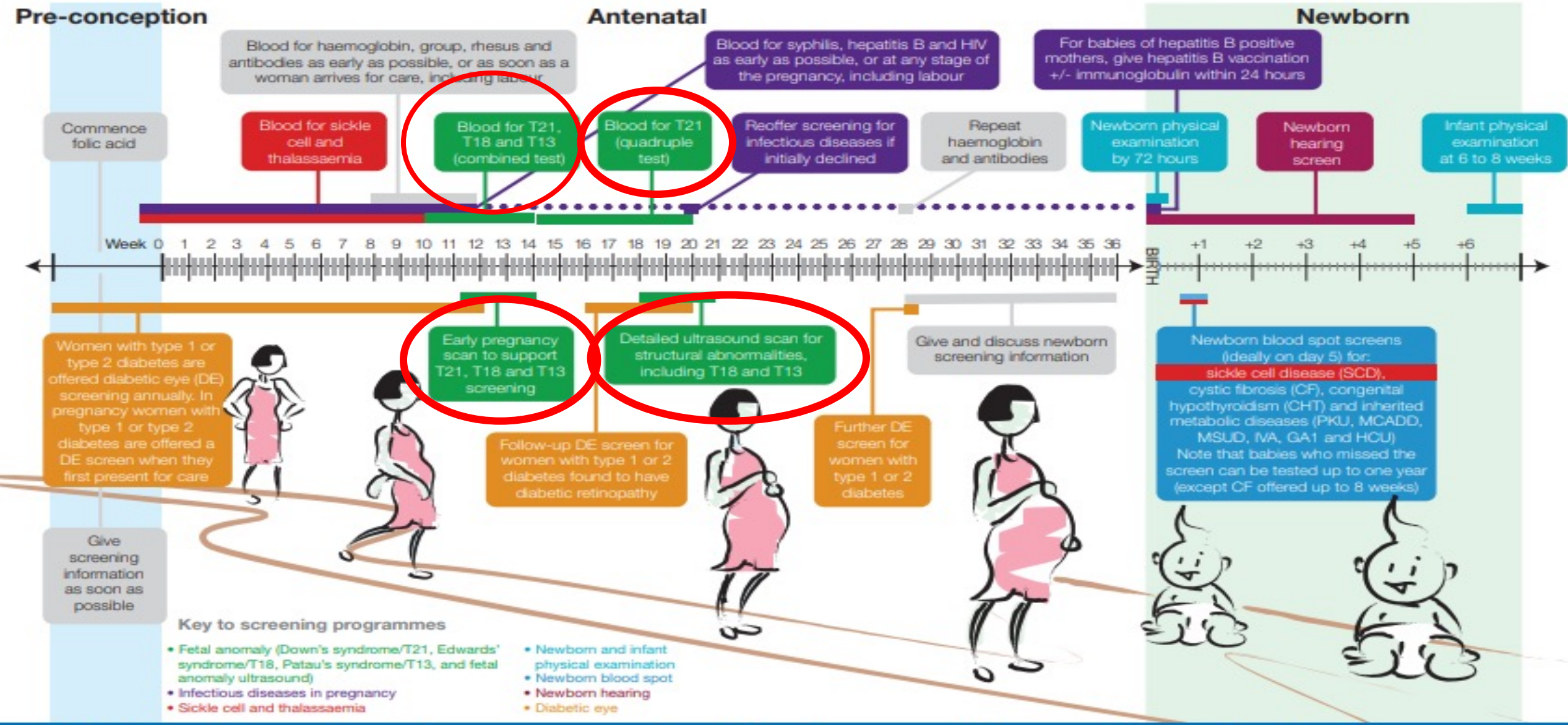
- Brief overview of screening in pregnancy
- Reproductive options
- Termination of Pregnancy
- Preimplantation Genetic Testing
- Genetic Counselling

# What happens in a "Normal" pregnancy?

- Positive pregnancy test – no longer confirmed at GP
- Book into antenatal care – see midwife
- Nuchal scan – 10-14 weeks' gestation
- Mid-trimester anomaly scan - 20-22 weeks' gestation

Public Health England

NHS




# Antenatal and newborn screening timeline – optimum times for testing

Screening should be a personal informed choice. Women and their families should be supported to understand the tests and choose what's right for them.

Version 8.4, January 2019, Gateway ref: 2014696, www.gov.uk/phe/screening

# Why Offer Screening?

"You will be offered some screening tests during pregnancy to try to find any health conditions that could affect you or your baby."

"The tests can help you make choices about further tests and care or treatment during your pregnancy or after your baby is born. All screening tests offered by the NHS are free."

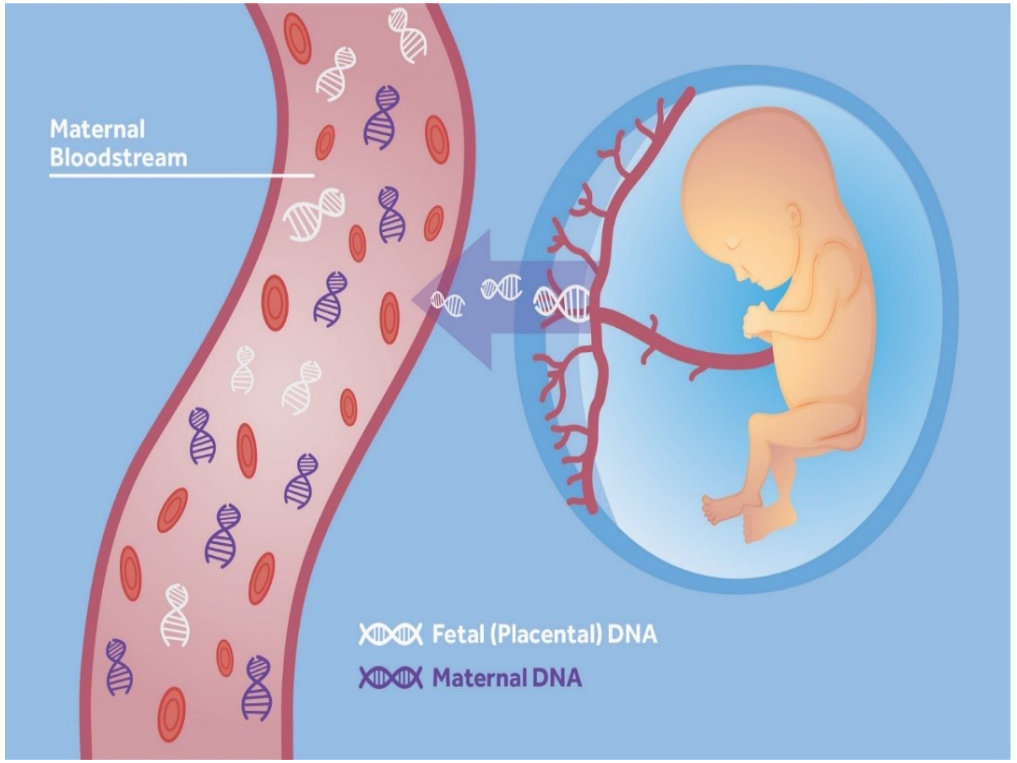
https://www.nhs.uk/pregnancy/your-pregnancy-care/screening-tests/

# First Trimester Combined Screening Test

- Screens for trisomy 13, 18 and 21.
- Offered at 11-14/40 weeks.
- Test Includes:
  - Maternal age
  - **Ultrasound scan measurements**
    nuchal translucency (NT)
    crown rump length (CRL)
  - Biochemical markers:
    - free beta human chorionic gonadotropin (bhCG)
    - Pregnancy associated plasma protein-A (PAPP-A).

# NIPT (Non-Invasive Prenatal Testing)

- Fetal (placental) DNA leaks into the maternal blood circulation.
- The DNA is shed as fragments, not as whole chromosomes
- Cell free DNA (cfDNA) in maternal plasma is a mixture of maternal and fetal cfDNA.
- The proportion of cfDNA from the fetus is known as 'fetal fraction'.
- Average fetal fraction is 10% (between 2% to 20%)



# NIPT (Non-Invasive Prenatal Testing)

This screens chromosomes, it provides a risk but not a diagnosis and needs confirmation by CVS or amniocentesis.

As of June 2021, NIPT is now available on the NHS for T13, T18, T21, for women who receive a higher chance (>1 in 150) result from a combined or quadruple test.

Results

- Lower chance
- Higher chance – CVS/Amniocentesis

# 20 Weeks Screening Scan

- "Anomaly scan"
- Done between 18 to 21 weeks.
- 11 conditions are screened for:
  - Condition may benefit from treatment before birth.
  - Give parents options.
  - Facilitate planned delivery at appropriate centre.
  - Optimise treatment at birth.
  - May indicate that the baby may die shortly after birth.
- Has a detection rate >50%

# Why carry out diagnostic testing in pregnancy?

- Abnormalities identified on scan.
- High risk screening result.
- Family History of a genetic condition.

The purpose of prenatal diagnosis:

1. To inform and prepare parents for the birth of an affected infant.
2. To allow *in utero* treatment or delivery at a specialist centre for immediate postnatal treatment.
3. To allow termination of an affected fetus.

# Reproductive Options in Families with Genetic Diseases & Chromosome Rearrangements

- Natural Conception with no additional tests.
- Gamete (egg or sperm) donation.
- Fostering/Adoption.
- **Prenatal Diagnosis**
  - Non-invasive prenatal diagnosis (NIPD).
  - Invasive: chorionic villus sampling (CVS) or amniocentesis.
- Preimplantation Genetic Testing for Monogenic disorders (PGT-M)

# Invasive Prenatal Diagnosis

Optional tests, offered to women who:

- are found to be at higher chance of genetic problems, usually as a result of an earlier screening test for T13, T18 or T21.
- have had an ultrasound scan which suggests there may be a physical difference with the baby, suggestive of an inherited condition – diagnostic testing by panel, exome or WGS
- are at increased risk of having a baby with a genetic disease, and for whom a prenatal test is known to be available (known familial variant).

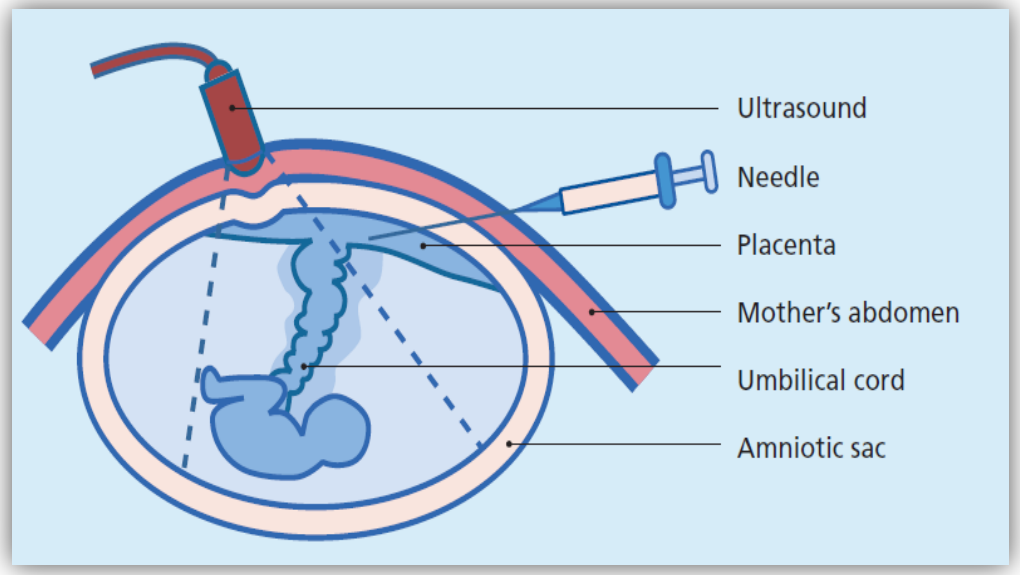
# Chorionic Villus Sampling (CVS)

From 12-13 weeks gestation.

Small sample of the placenta.

Miscarriage risk ~1% (higher rate of spontaneous loss during this trimester).

Complications – Posterior placenta, high maternal BMI.

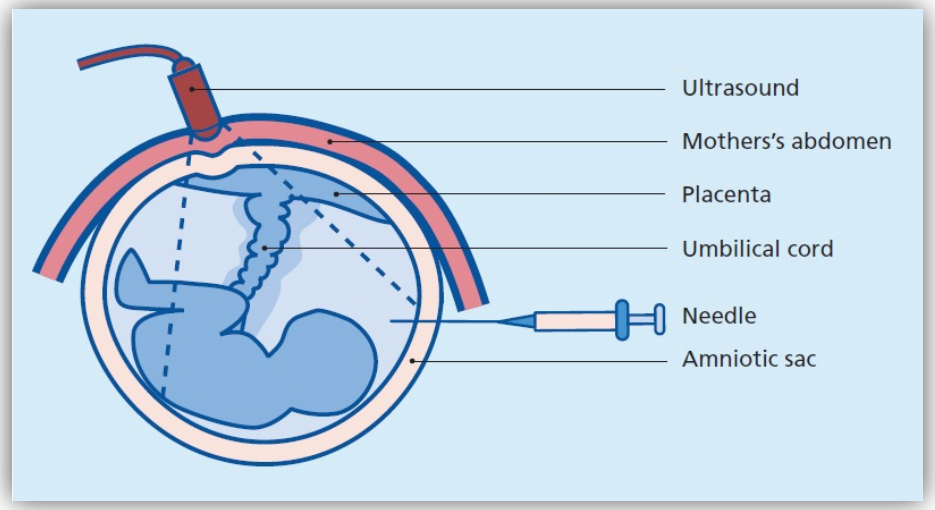


# Amniocentesis

From 15 weeks.

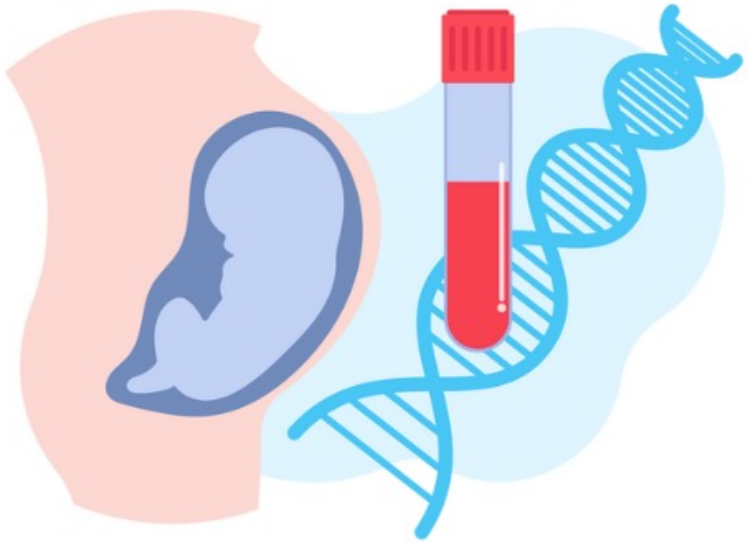
Small sample of amniotic fluid.

Miscarriage risk ~1%



# Non-Invasive Prenatal Diagnosis (NIPD)

- Offered when there is an increased chance of having a baby with a genetic condition due to a known familial variant(s).
- This is a single gene test that is accurate enough to be diagnostic.
- Accuracy 99.8-99.9%



# NIPD cont.

- Maternal blood test from around 9 weeks of pregnancy
- Autosomal dominant single gene disorders inherited from the father e.g. HD
- Recessive conditions where the mother and father carry different mutations in the same gene
  - If the paternal mutation has been inherited by the fetus invasive prenatal testing can be offered
- Bespoke NIPD for specific conditions where both parents are carriers
  - Not an option for consanguineous couples as markers too similar
- X-linked in males e.g. DMD, BMD
- Certain conditions if a couple have a previously affected child e.g. Skeletal dysplasias
- If couple have had a previous baby with 'de novo' dominant mutation they can self-fund to have NIPD

| |
|---|
| Fetal Sexing – for presence of the SRY sequence (Y chromosome) |
| Cystic fibrosis |
| Duchenne & Becker muscular dystrophy (DMD & BMD) |
| Spinal Muscular Atrophy (SMA) |
| Apert syndrome (FGFR2) |
| FGFR2-related craniosynostosis syndromes |
| Crouzon syndrome with acanthosis nigricans (FGFR3) |
| FGFR3-related skeletal dysplasias |
| Congenital Adrenal Hyperplasia (CAH) |
| Bespoke NIPD – requires set up PRIOR to pregnancy<br>• Paternal exclusion<br>  • Paternally inherited autosomal dominant condition.<br>  • Autosomal recessive condition where couple have different variants.<br>• De novo variants (not NHS funded) |

# Limitations of NIPD and NIPT

- Multiple pregnancies
- Women with a high BMI
- Women not always appropriately counselled about implications
- An invasive test may still be required to confirm an abnormal result

# Benefits of NIPD and NIPT

- The number of invasive tests carried out is likely to reduce as a result
- There is no increased risk of miscarriage
- Less expertise is required to perform a blood test than an invasive test
- In many cases we can offer NIPD /NIPT earlier than traditional invasive testing, thereby getting a result earlier

# Termination of Pregnancy (TOP)


https://www.bpas.org/abortion-care/abortion-treatments/

# Termination of Pregnancy (TOP)

**Surgical (sTOP)**

Vacuum aspiration

- suction device placed into uterus and fetal tissue & placenta removed
- Up to 14 weeks, this can be done with local anaesthetic.
- Up to 15 weeks this can be done with sedation or under general anaesthetic.

Dilatation and Evacuation

- between 15 and 24 weeks of pregnancy.
- Up to 18 weeks, it can be done under light sedation or general anaesthetic.
- From 18 weeks only under general anaesthetic.
- the pregnancy is removed using narrow forceps through the cervix.

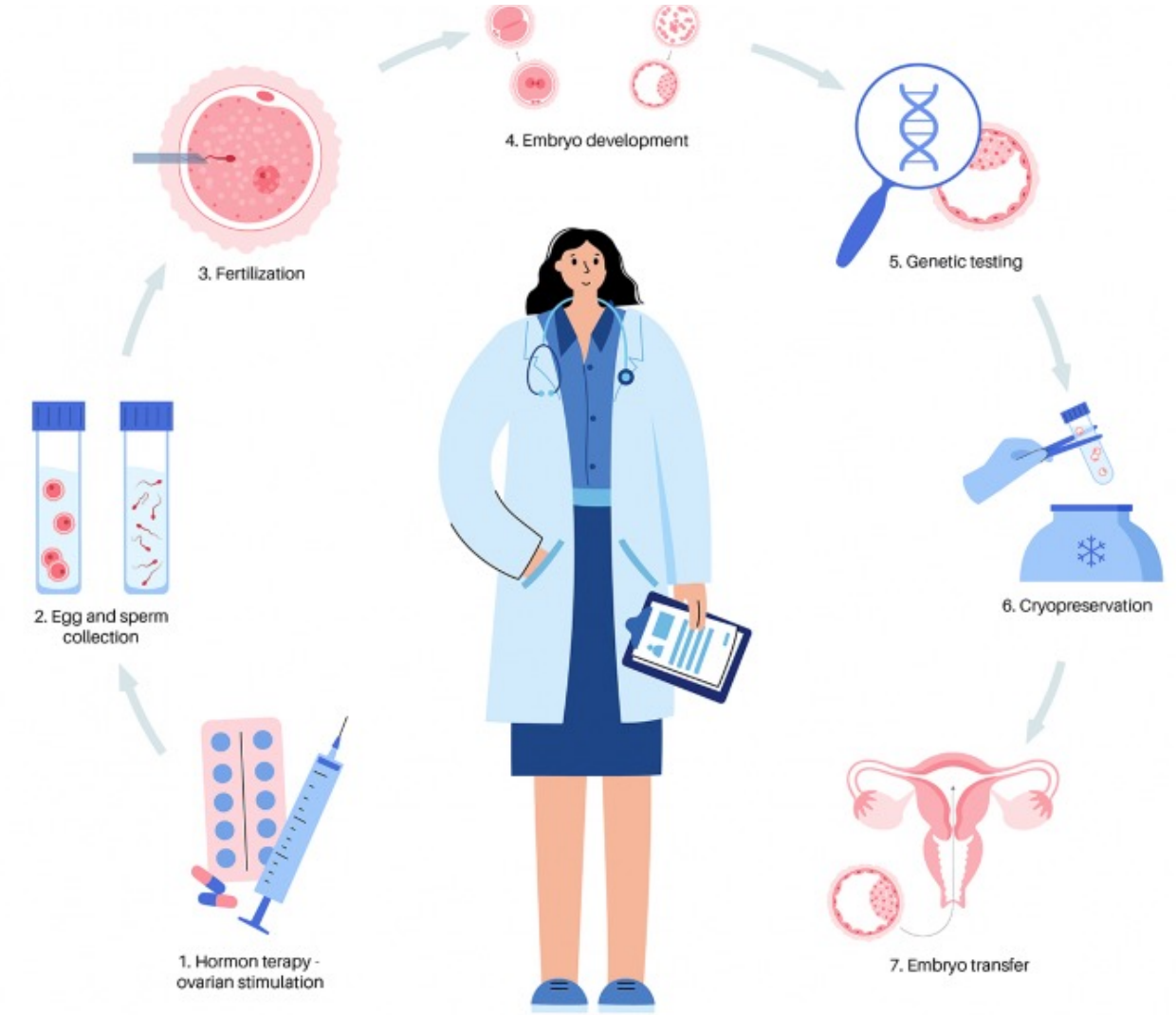
Counselling offered.

# Medical TOP

- Given a tablet of Mifepristone to block the progesterone hormone.
- Admitted to Hospital ~36hrs later to be given Misoprostol (to induce labour).
- Given another dose every 3hrs for 12hrs until delivery.
- Pain medication & antibiotics prescribed.
- Patients up to 18-19 weeks are placed onto the gynae ward.
- Over 19 weeks patients are on a labour ward in a separate bereavement room.
- At 22 weeks we offer intracardiac KCL prior to TOP.
- Bereavement team support.

# Pre-implantation Genetic Testing for Monogenic disorders (PGT-M)

- Available to couples that are at risk of having a child with a specific genetic or chromosome disorder.
- Prevents the birth of an affected child by testing an embryo before it is transferred to the uterus.
- The eggs are fertilised in the laboratory, a few cells are removed from each embryo, and genetic testing carried out to identify unaffected embryos.
- Only an unaffected embryo is transferred into the uterus for implantation.



# When is PGT-M funded?

The risk of conceiving a pregnancy affected by a serious genetic condition should be 10% or more.

Treatment must start before the woman is 40.

Female partner must have a BMI of >19 and <30.

Both partners must be non-smokers & not vaping.

Couple should be in a stable relationship of >1 year and living at the same address.

Couples who already have an unaffected child together are not eligible for funding.

Couples who fulfil the criteria are eligible for up to 3 cycles of PGT-M treatment.

**Referrals must come from a Clinical Geneticist or Registered Genetic Counsellor**

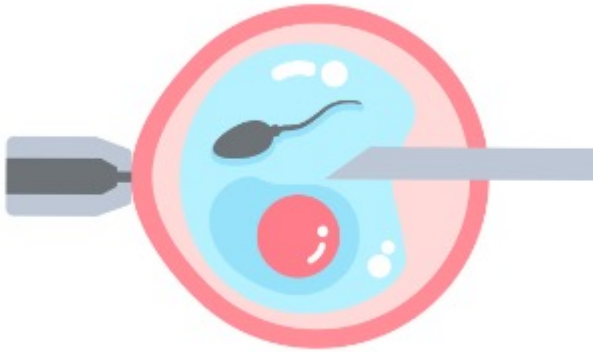
PGT-M can be used to test for almost any genetic condition where the specific familial variant is known.

Over **600** conditions have been approved by the HFEA for testing.

About **1** in **3** cycles will result in a baby.
If a couple completes the process and has embryo(s) suitable for transfer, there is about a 1 in 2 (**50%**) chance of a pregnancy.

PGD is a long process with many ups and downs. Involves:

- Hormonal stimulation
- Decreasing numbers of available embryos
- Waiting
- Travel



# Where is PGT Available?

The Centre for Reproductive & Genetic Health
Formerly known as The Assisted Conception Unit

Carefertility

TFP

Guy's and St Thomas' NHS
NHS Foundation Trust

Centre for Preimplantation Genetic Diagnosis

# The role of a Genetic Counsellor in prenatal testing

- Arrange & explain CVS, amniocentesis, NIPD, PGT
- Facilitate decision-making
- Give results
- See patients in clinic following a diagnosis
- Arrange termination if requested
- Discuss recurrence risks and plans for future pregnancies

# Facilitating decision-making

- Needs to consider:
  - Values
  - Situation
  - Hopes and fears

- Non-directiveness.
- Difficult to achieve.
- Need to be able to manage your own thoughts and feelings.
- Present information and options in a non-bias manner.

- The role of the counsellor is to help people to see all the possible consequences of having or not having the tests in question and to determine which set of consequences is most acceptable to them.

- ****TIME PRESSURE****

# Thank You!

# Any Questions?

angela.colangelo2@nhs.net