

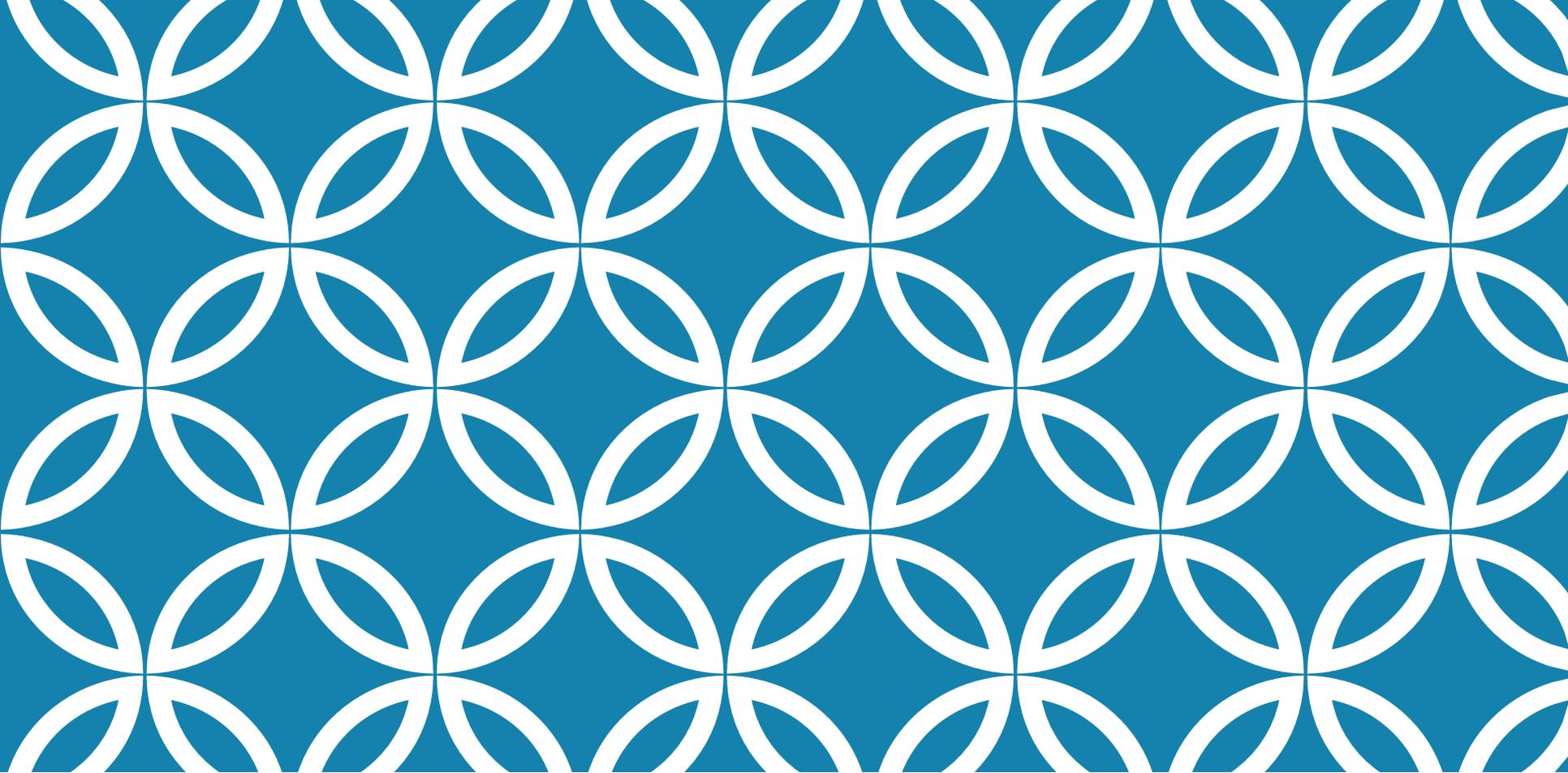


REPRODUCTIVE OPTIONS AND PGD IN LI FRAUMENI SYNDROME

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General genetics and PGD

OVERVIEW OF PRESENTATION

- Introduction to Prenatal Diagnosis (PND)
 - NIPD
 - CVS
 - Amniocentesis
- Preimplantation Genetic Diagnosis (PGD)
- Fertility Preservation
- Other options



PRENATAL DIAGNOSIS



NON INVASIVE (NIPD)

Cell free fetal DNA (cffDNA)

From 8 weeks

Maternal blood sample

**Used currently for foetal sexing/
Down syndrome**

Introduced for AD/AR conditions

**Not currently NHS approved in all of
England**

Potentially avoids prenatal diagnosis

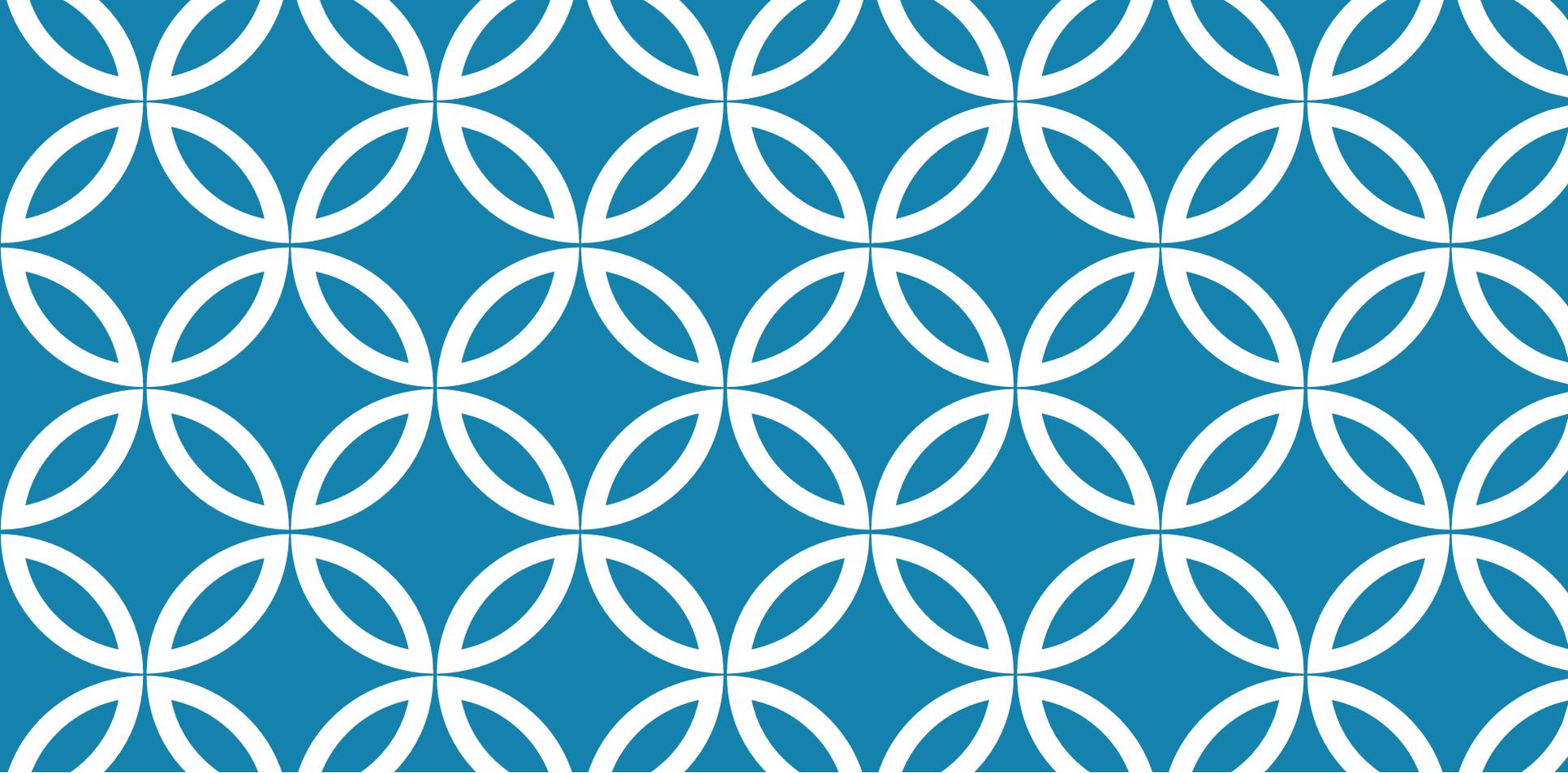
Ultrasound scanning

From 14 weeks

**Only Valuable if abnormality can be
detected on scan**

**Often serial scans needed into 2nd
trimester**

Avoids risk of procedure related miscarriage

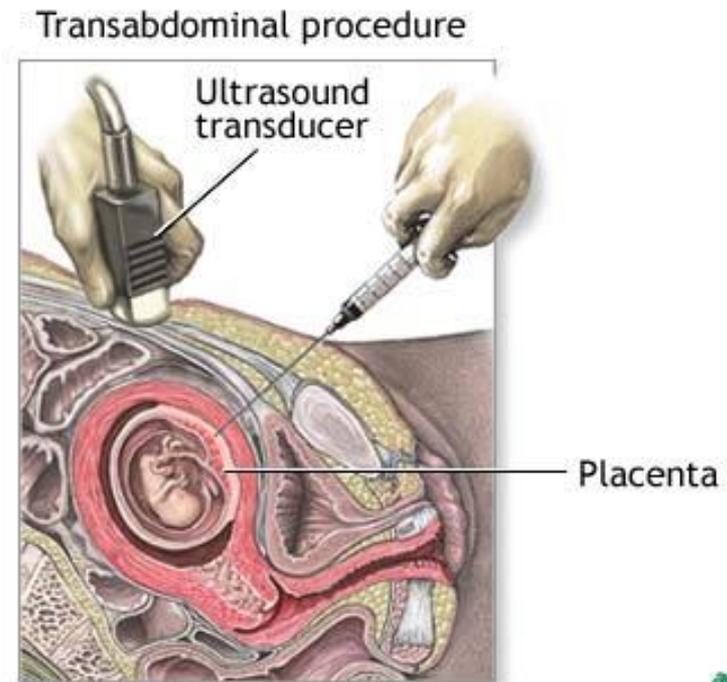


INVASIVE TESTING



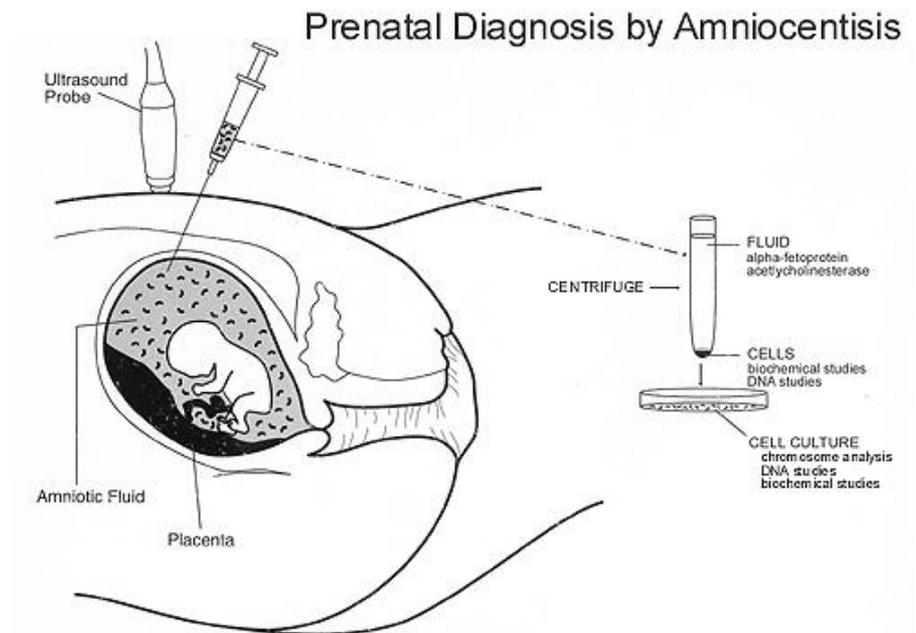
CHORIONIC VILLUS SAMPLING (CVS)

- **Test at 11+ weeks of pregnancy**
- **1% or less associated miscarriage risk**
- **Couples consider TOP**



AMNIOCENTESIS

- **Test at 16 weeks of pregnancy**
- **Couples consider TOP**
- **1% or less associated miscarriage risk**



PROS AND CONS OF PND

Pros

Fully NHS funded across UK

Ready access to procedures nationally

Provided mutation identified, no lengthy preparation time

Normal conception

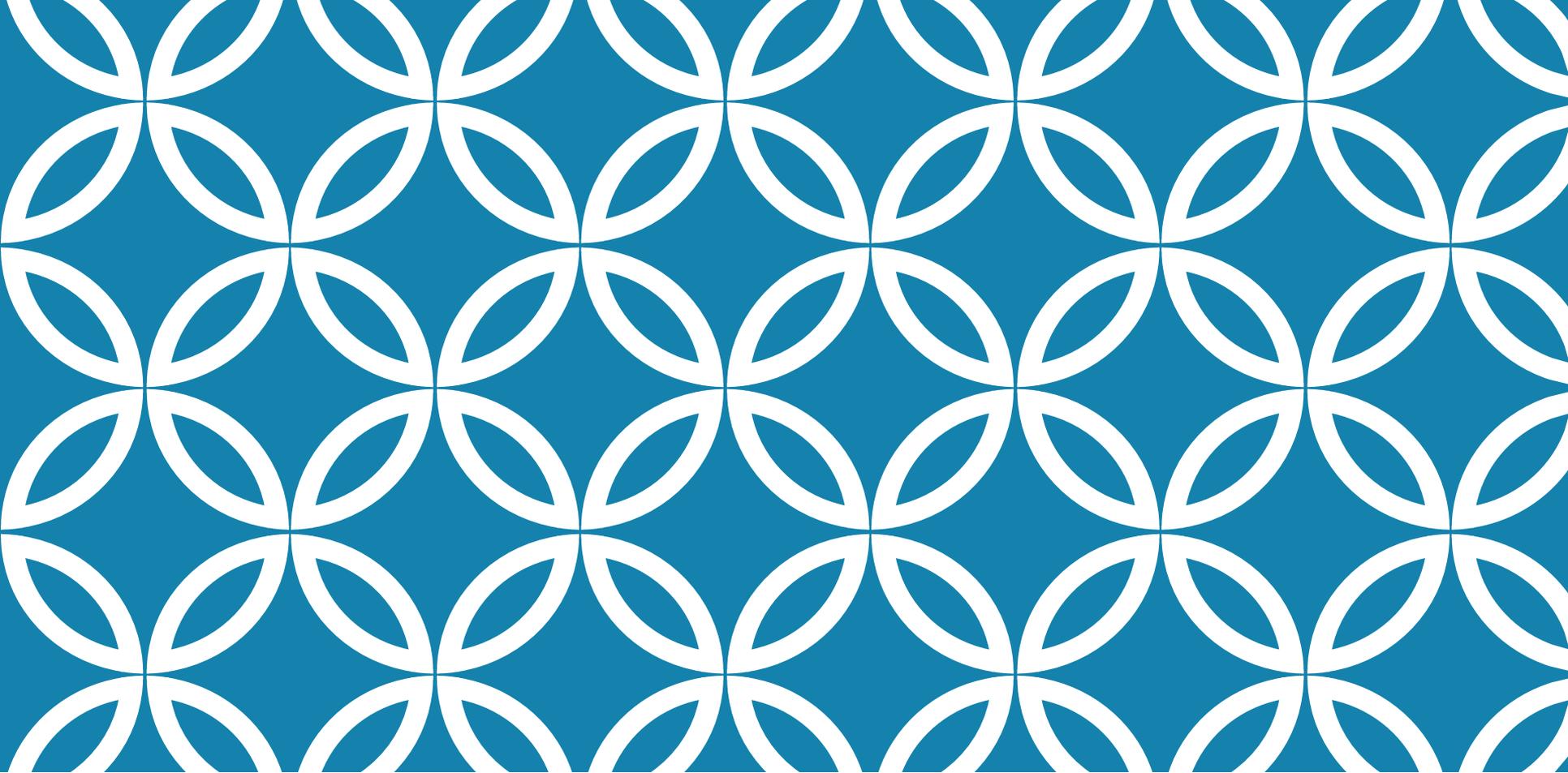
Cons

6-7 week wait after +ve HCG for test

Risk of miscarriage (small)

Potential termination of pregnancy & impact

Repeated pregnancy loss



PREIMPLANTATION GENETIC DIAGNOSIS



WHO IS NEEDED FOR THE PGD SERVICE?

**Genetic Counsellors &
Clinical Geneticists**

**Reproductive
medicine doctors &
nurses**

**Molecular &
cytogenetic
scientists**



**Administration
team**

Embryologists

WHY PGD?

Concern about having a child who inherits a hereditary condition

Other options to prevent passing on the gene not acceptable or not first choice

Other options include:

Take a chance

Test a pregnancy (prenatal diagnosis)

Sperm or egg donation

Adoption

Have no children



WHO IS ELIGIBLE – INCLUSION CRITERIA

- Couple must have confirmed molecular genetic diagnosis
- Have been seen by a clinical genetics service.
- Female age under 40**
- Female BMI 19-29
- Non smokers
- Lived together as couple for 1 year

WHAT MAY COMPLICATE DECISION MAKING

Variability of phenotype- mild to severe

Does the severity justify prenatal diagnosis/PGD?

Impact of timeframe for testing

Does couple understand implications of testing?

Is pregnancy safe?

Health of affected parent

UK LAW & LICENSING



All centres must have a licence to offer PGD

A licence is necessary for each new PGD condition



CANCER LICENCES AVAILABLE

- Li- Fraumeni Syndrome (TP53)
- Cowden Syndrome (PTEN)
- Ataxia Telangiectasia (ATM)
- Peutz-Jeghers Syndrome (PJS)
- PALB2
- BRCA1 and BRCA2
- Lynch Syndrome

And various others that you can check on the HFEA website....

COST & FUNDING

NHS England funding policy (since 2013)

- Up to 3 cycles
- Scotland, Wales & Northern Ireland have different policies

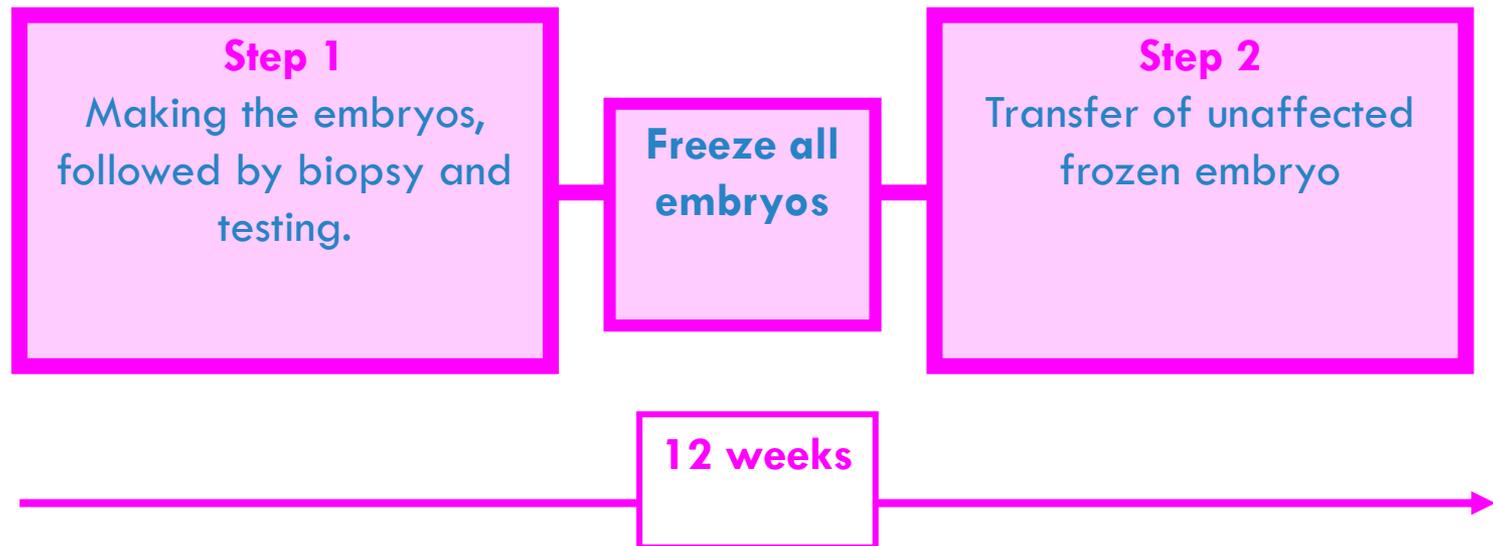
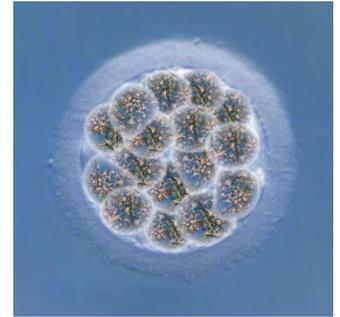
To have funding agreed certain criteria must be met

If couple have to self fund it is around £12,000 per cycle

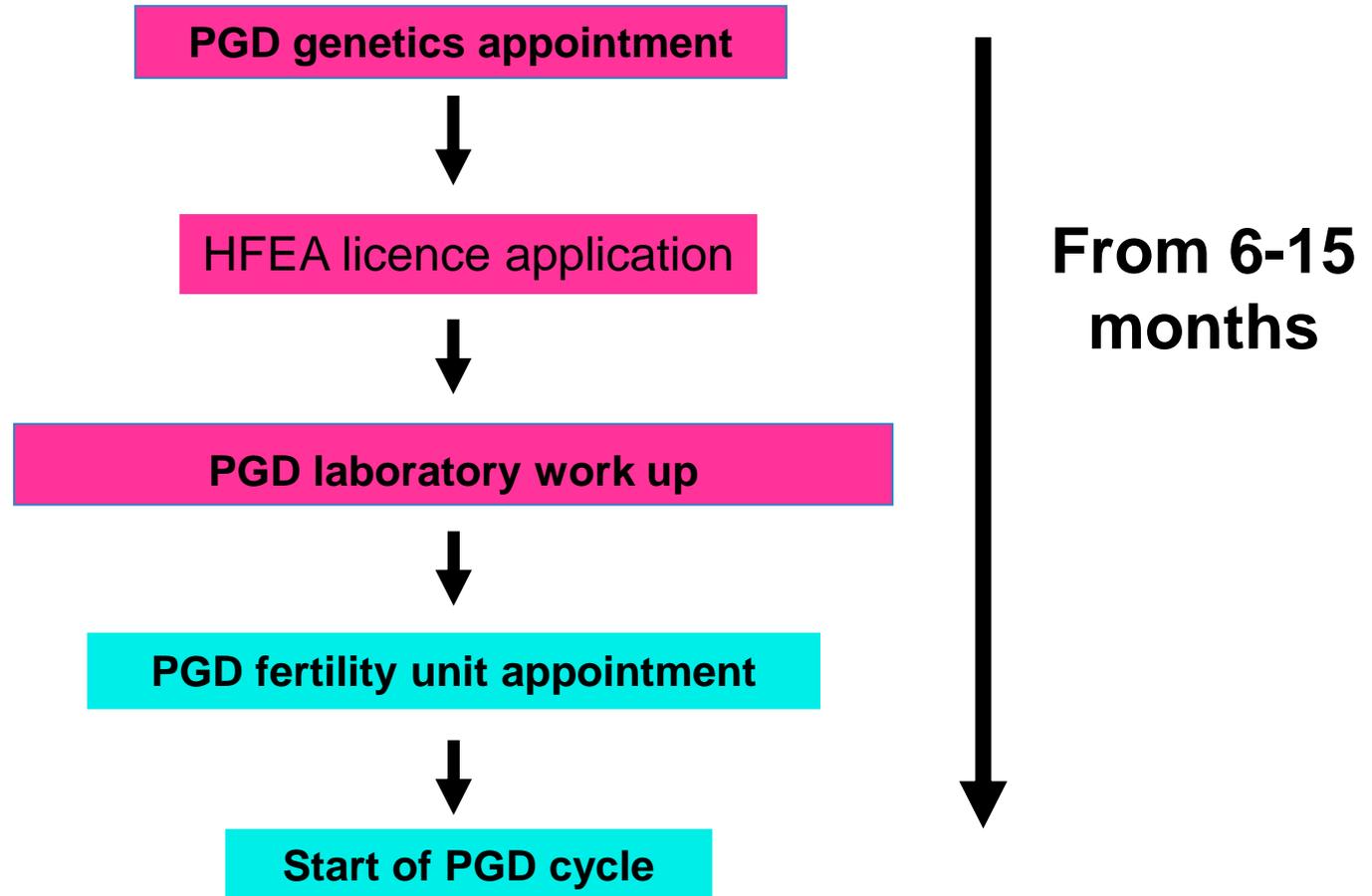


PGD CYCLE

Blastocyst biopsy with freezing



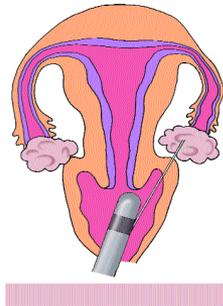
PGD PREPARATION TIMELINE TO EMBRYO TRANSFER



PGD CYCLE TO CREATE EMBRYOS



Down regulation & ovarian stimulation together



Egg collection

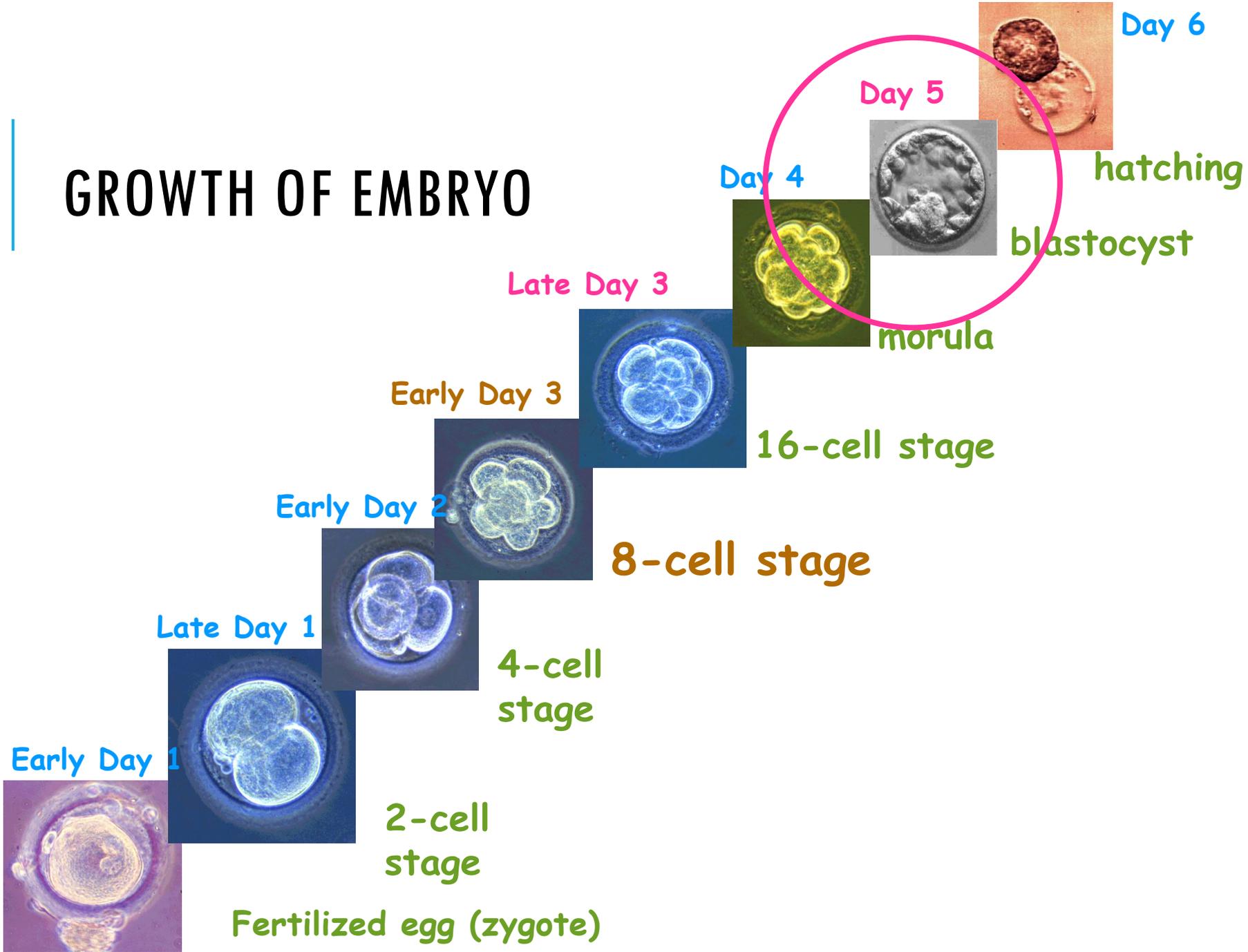


Fertilisation with ICSI



3 weeks

GROWTH OF EMBRYO



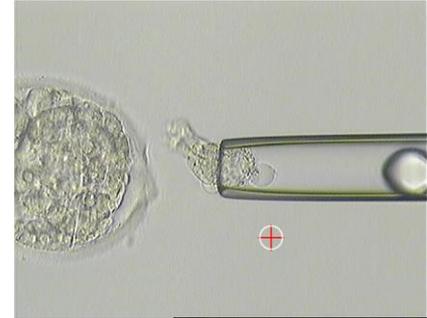
BLASTOCYST BIOPSY



Blastocyst held in position



Trophectoderm cells extruded through breach of zona



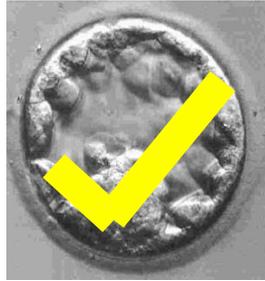
Cells removed for testing



FREEZE ALL EMBRYOS



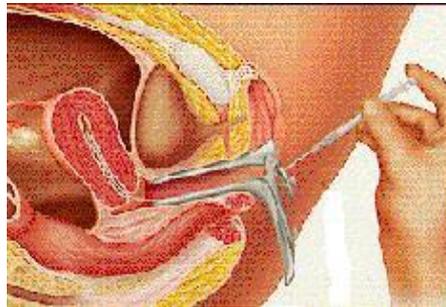
EMBRYO RESULTS



EMBRYO TRANSFER



Down regulation and
womb lining preparation



Embryo transfer



Pregnancy test-
Positive or negative



7-8 weeks

KEY ISSUES

Average number of embryos for biopsy

4

Average number of embryos for transfer

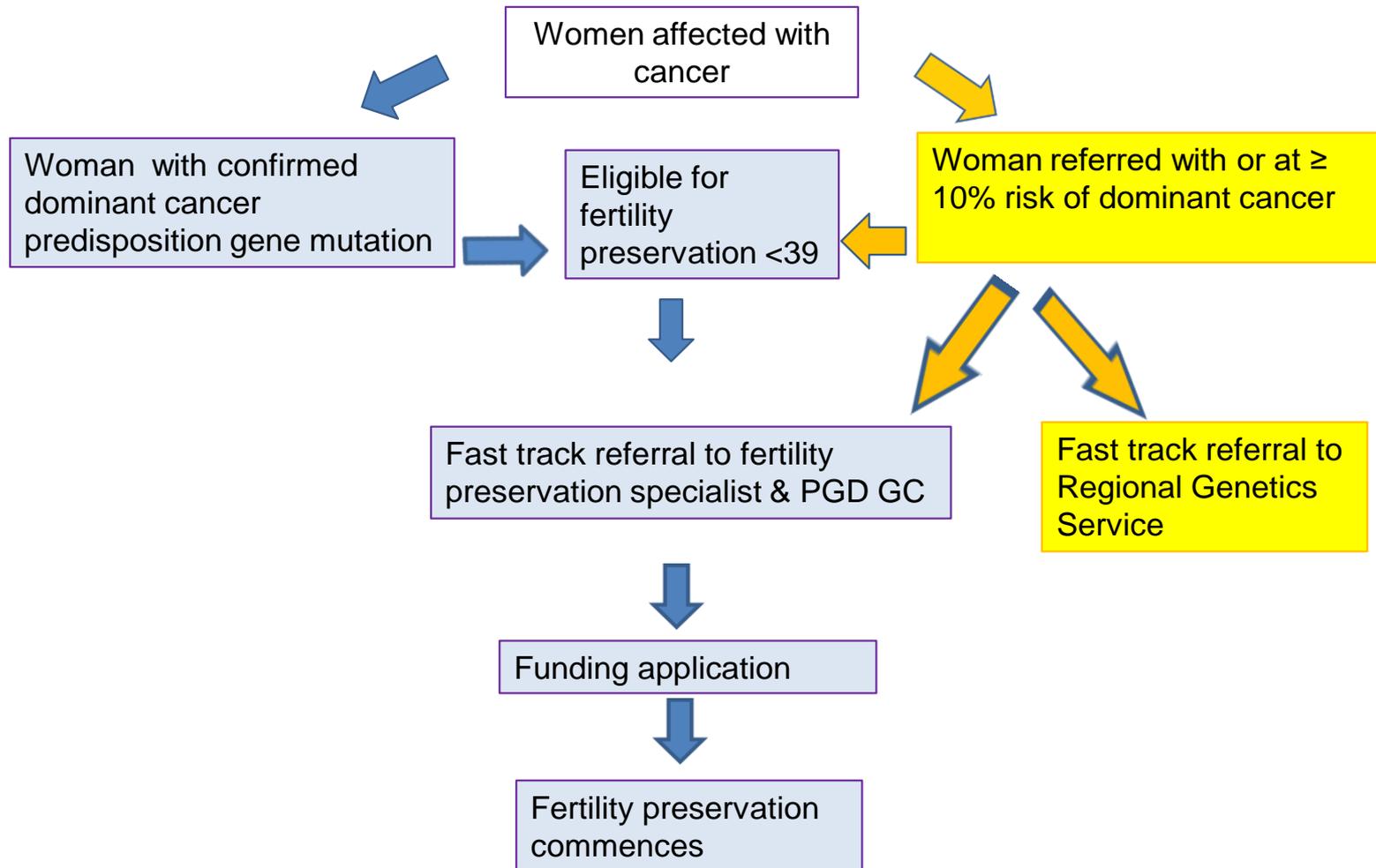
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Over 800 babies born through PGD at Guys!!

WHAT ABOUT YOUNG CANCER PATIENTS WHO NEED CHEMOTHERAPY BUT HAVE NOT HAD A FAMILY YET?

-Fertility preservation

Fertility preservation pathway



PROS AND CONS OF PGD

Pros

Avoids the need to TOP

More acceptable for variable phenotypes

Avoids repeated high risk pregnancies

Early knowledge of pregnancy status

Fully NHS funded in England if eligible

Cons

Limited success

Complex invasive procedure

Lengthy time to prepare for treatment

Expensive if NHS funding not available

WE MUST NOT FORGET.....

There are still other options:

- Take a chance
- No children/no further children
- Gamete donation
- Adoption

Surrogacy



THANK YOU!
ANY QUESTIONS