Pre-implantation Genetic Diagnosis (PGD)

Kristi Jones  
Clinical Geneticist  
MBBS FRACP PhD  

Children’s Hospital at Westmead  
Westmead Hospital  
‘Genea – World Leaders in Fertility ’  
(formerly Sydney IVF)  
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Pre-implantation genetic diagnosis (PGD)

- When a serious genetic disorder affects a person or a family member
- Combine IVF with genetic testing of embryos prior to transfer to the uterus
- Choice for family planning
- Alternative to prenatal genetic testing on an ongoing pregnancy
History

- 1967 - successful sexing of rabbit blastocysts
- 1978 - 1st IVF child born
- 1980s - human IVF fully developed
- 1990 first births from PGD

Indications for PGD?

- Specific condition where a mutation/gene is known
  - eg Haemophilia, cystic fibrosis
- Chromosome rearrangement
- Screen for abn chromosome number
  - eg Down syndrome
- Cancer predisposition
- Gender selection
- Non-disclosure eg HD
- HLA matching
Genea - PGD
‘work ups’ to date

- Total work ups for single gene disorders = 547
  - Cystic fibrosis = 13%
  - Huntington disease = 10%
  - Fragile X = 5%
  - Neuromuscular Disorders = 16%
  - Haematological Conditions = 11%
    - eg. Thalassemia, Haemophilia

Process

- IVF
- ICSI (intracytoplasmic sperm injection)
  - Single sperm injected into each egg
  - To avoid the risk of contamination
Embryo development

Day 3
- Oocyte
- 8 cell

Day 5
- Zygote
- Morula
- Blastocyst

Biopsy at blastocyst stage
Day 5/6 post fertilisation

Biopsy.mpg
Genetic analysis

- Can only be done when the specific genetic mutation is known
  - or we are certain of the gene involved

- Usually have 20,000 - 100,000 cells
  - here only a few cells

- Molecular analysis using PCR
  - use two methods
    - Linkage +/- direct mutation
    - >99% accurate
Genetic analysis

- CGH (comparative genomic hybridisation)
- Detects abnormalities in the number of all the chromosomes
  - eg. Down syndrome
  - Improves chance of an embryo implanting

Pros and cons

- Risks of
  - IVF process for woman
  - IVF for baby
  - biopsy process
  - getting it wrong

- Alternatives – balance

- Chance of success?
  - Maternal age
Genetics of Haemophilia
X-linked recessive inheritance

**Legend:**
- $X$: recessive faulty gene on X chromosome
- $X^+$: working gene copy

<table>
<thead>
<tr>
<th>Mother</th>
<th>Father</th>
<th>Son 1</th>
<th>Son 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>$X^-$</td>
<td>$X$</td>
<td>$X^-$</td>
<td>$X^-$</td>
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<tr>
<td>$X^-$</td>
<td>$X^+$</td>
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</tbody>
</table>

Girls: 1 out of 4 chance 25%
Boys: 1 out of 4 chance 25%

Non-carrier father
Affected father with haemophilia

**Legend:**
- $X^-$: recessive faulty gene on X chromosome
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Girls: 1 out of 4 chance 25%
Boys: 2 out of 4 chance 50%

Non-carriers

**IVF/PGD**

Parental history of haemophilia.

<table>
<thead>
<tr>
<th>Generation</th>
<th>Gender</th>
<th>Haemophilia Status</th>
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<tbody>
<tr>
<td>1st</td>
<td>Male</td>
<td>Healthy</td>
</tr>
<tr>
<td>2nd</td>
<td>Female</td>
<td>Healthy</td>
</tr>
<tr>
<td>3rd</td>
<td>Male</td>
<td>Healthy</td>
</tr>
<tr>
<td>4th</td>
<td>Female</td>
<td>Healthy</td>
</tr>
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</table>

Affected male

IVF/PGD: In Vitro Fertilization/Preimplantation Genetic Diagnosis

**Key:**
- $X^-$: Faulty gene
- $X^+$: Working gene

**Chromosome:**
- XY: Male
- XX: Female

**IVF/PGD:**
- IVF: In Vitro Fertilization
- PGD: Preimplantation Genetic Diagnosis

Gene carrier for haemophilia: mother
Non-carrier father
Affected with haemophilia
Non-carrier mother
Affected father with haemophilia

Genetic carrier for haemophilia (mother)
Non-carrier father
Affected with haemophilia
Non-carrier mother
Affected father with haemophilia
PGD Assistance

About the PGD Assistance Program

Medicare rebate for expensive IVF treatment PGD sought by clinics

The Daily Telegraph
July 25, 2011
11:45PM