Preimplantation genetic diagnosis of genetic kidney diseases in Paris

Dr Julie STEFFANN
Genetic Laboratory
Necker-Enfants Malades Hospital
Preimplantation genetic diagnosis (PGD)

Stimulation, ponction, and fertilisation by ICSI

Embryonic biopsy (Day3)

Genetic diagnosis
- FISH (chromosomal)
- PCR (monogenic)
  12 à 24 hours

Uterin transfert
Day 5
(1 to 3 healthy embryos)
French PGD regulations

- **Law n° 94-654 (29/07/94):**
  - PGD is authorized in exceptional circumstances for couples at high risk to have a child affected by a serious and non-curable genetic disease.
  - Genetic defects should be identified in at least one member of the couple.
  - Consent.
  - Restricted to the detection of the specific genetic defect.
  - Multidisciplinary center.
  - Certification and licence (Biomedecine Agency).

- **Decree (24/03/98)**
Certifications for PGD activities

• Embryonic biopsy (11 practitioners)

• Single-cell FISH analysis (8 practitioners)

• Single-cell PCR analysis (9 practitioners)
French PGD Organization

4 licensed PGD centers

• Paris (Necker/Béclère Hospital)
  • Strasbourg
  • Montpellier
  • Nantes
NECKER
Genetics
Pr Munnich
Dr Steffann
Dr Monnot
Cytogenetics
Pr Vekemans
Pr Romana
Dr Maurin

BECLERE
Obstetrics and Gynecology
Pr Benachi
Coordinating midwife: L. Grunfeld
Reproductive medicine unit
Pr Tachdjian
Pr Achour-Frydman
PGD Pluridisciplinary Center
(geneticist, gynecologist, biologist, psychologist)
250 request/year

Step 1: PGD request

Multidisciplinary center
Feasibility of gynecologic treatment
Feasibility of genetic diagnosis

ok (n=180)

Pluridisciplinary consultation
No feasibility of ovarian stimulation+++/Genetic diagnosis

no (n=70)
Paris PGD couples (2000-2012)

PGD Couples (n=2590)

Started PGD cycles (n=1364)

Long and expensive procedure…
Step 2: Assisted Reproductive Technology

Ovarian stimulation and monitoring
254 cycles

Paris PGD activity
In 2013, 133 couples have started a PGD cycle

Ponction
n=185
2155 oocytes

Fertilization
ICSI
1231 embryos

Embryonic biopsy
n=722
Step 3: Genetic Diagnosis

199 PGD in 2014

**FISH PGD (n=94)**
- Chromosomal translocations n= 90
- X-linked disorders n=4

**PCR PGD (n=105)**
- Autosomal dominant n=47
  - 33% Steinert
  - 26% Huntington
- Autosomal recessive n=33
  - 56% cystic fibrosis
- X-linked n=23
  - 30% Fragile X
- mtDNA n=1
Molecular PGD of kidney diseases

<table>
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<tr>
<th>DISEASES</th>
<th>GENES</th>
<th>COUPLES</th>
<th>PGD CYCLE</th>
<th>PREGNANCIES</th>
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<td>TSC2</td>
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<td>Joubert syndrome</td>
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<td>TOTAL</td>
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<td>46</td>
<td>9</td>
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</table>

If there is a maternal renal disease, it can complicate the PGD procedure (pregnancy)

Gigarel et al., Reprod Biomed Online. 2008
Step 4: uterin transfer and follow-up

In 2013:
133 transfers (177 embryos)
41 pregnancies
41 deliveries
50 healthy babies
How likely am I to get pregnant if I use PGD?

- Only 57% of the couples will have a uterin transfer
- 30% evolutive pregnancy after embryo transfer
- Baby take home rate: 17%

Frydman et al., Bull Acad Natl Med, 2011
How long will the process take?

**FISH PGD**
9 months

1 month
5-6 months
3-4 months

**PCR PGD**
18 months

1 month
12 months
4-6 months
PGD for renal diseases: conclusions

- PGD is an alternative to prenatal diagnosis
- PGD is a long process
- With limited efficacy
- Maternal renal disease should be carefully investigated before, during and after the PGD procedure
Paris PGD team

Molecular Genetics
• A Munnich
• S Monnot
• J Steffann

Cytogenetics
• M Vekemans
• S Romana
• M-L Maurin

• R Borghèse (genetic counsellor)
• M Flis Treves (psychiatrist)

Assisted Reproduction
• G Tachdjian
• L Hesters
• N Frydman

Obstetrics and Gynecology
• A Benachi
• N Ahdad

• L Grunfeld (midwife)

Hôpital Necker-Enfants Malades
Hôpital Antoine-Béclère