# PGDIS 2024

**21ʳˢᵗ International Conference on Preimplantation Genetics**

**Kuala Lumpur, Malaysia, May 5 - 8, 2024**

*Session 8: Patient management and genetic counselling*
*– IVF Clinician, Clinical Geneticist, and Genetic Counselor*

Tuesday, 7 May 2024, 16:00 – 16:20

## PGT-A an <u>ethical</u> dilemma?
## What should clinicians be <u>discussing</u> with patients?

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# First Talk (60')
## Diagnosis – Proposal - Information

## 1. Diagnosis (20'): <u>> <span style="color:red">30</span> "clinical mosaic stones"</u>

- age, cycle length, contraception

- uterus, tubes, ovaries, ovarian reserve

- sperm

- waiting time, pregnancies, children

- previous ART: response, follicles, oocytes, maturity, morphology, fertilization, development, transfer

- obesity, smoking, diseases, economic and social background, values, possibilities

# First Talk (60')

## 2. Proposal (20')

- wishes, values, preferences
- **alternatives**, specialist assessment
- shared decision, reflection

# First Talk (60')

## 3. Information (20')

- Procedure

- Chance

- Risks

- Alternatives

- Costs


- New clinical **investigations**

# Informed Consent (2 x 15')

## 1. Medicine

Information:

- results, differential diagnosis and therapy
- suggestion, shared decision, plan, reflection

Consent:

- literature, **unknown reason** for success and failure in individual cases
- freedom of therapy, art of healing, intuition, experience, deviation from rules, will of the patient, physician responsibility, highly personal decision, "off label" treatment

# Informed Consent (2 x 15')

## 2. Law

bodily harm, information, consent

## 3. Ethics

- **Patient:** preferences, non-directive, intellect, education, mentality

- **Physician:** recognized procedures, minority opinions, **personal** assessment, Helsinki Declaration WHO

# PGT-A Aims and Indications

## 1. Aim

- Improve chance of **pregnancy**
- Shorten time to pregnancy
- Reduce risk of miscarriage, multiples, malformation, pointless ART

## 2. Indication

- Advanced Maternal Age
- Repeated Implantation Failure
- Repeated Miscarriages
- Severe Male Factor
- Will of the patients!

*Schmutzler, Eur J Med Genet. 2019*

# PGT-A: two stage decision

E. g. indication "increase chance of pregnancy":

- **before start of the cycle:** selection advantage?

- **before biopsy:**  selection **advantage?**

# Patient Properties
## 137 couples, 263 cycles

| Lower Chances | |
|---|---|
| no previous pregnancy | 57 % |
| advanced maternal age | 54 % |
| AMH < 2 | 50 % |
| PCO | 30 % |
| previous miscarriage | 27 % |
| smoking | 25 % |
| AMH >= 4 ng/ml | 24 % |
| overweight | 13 % |
| transfer of three embryos | 12 % |
| repeated implantation failure | 8 % |
| **Higher Chances** | |
| >= 6 fertilized oocytes | 36 % |

# Main Criteria for a
# Balanced Therapy Proposal

## Chances

- **age**, ovarian reserve, BMI, smoking
- diseases, pregnancies

## Background

- children, ART cycles, outcome in vitro
- wishes, values, preferences

# Primary Indication for PGT-A:
## (1.) Increase Chance of Pregnancy per Cycle

- 40 y, low income, AFC 5, 1. OR:

  **no!**

- 3. OR, AFC 10, > 3 fertilized:

  **yes!**

- 35 y, 3. OR, plan 2 embryos for transfer,

  2 fertilized: **no!**

- 6 fertilized, 6 biopsied, 4 aneuploid, 2 unknown:

  **transfer 2 unknown**

# Primary Indication for PGT-A:
# (2.) Shorten Time to Pregnancy

41 years, 8 antral follicles, high income, 1. ICSI

**yes!**

# Primary Indication for PGT-A:
# (3.) Reduce Risk of Miscarriages

35 years, got 2 miscarriages, 10 antral follicles, middle income, 1. ICSI

**yes!**

# Primary Indication for PGT-A:
# (4.) Reduce Risk of Multiples

- 35 years, got twins, 10 antral follicles, 1. ICSI,

  low income

  **no!** (SET)


- middle income

  **yes!** (SET)

# Primary Indication for PGT-A:
# (5.) Reduce Risk of Malformation

- 35 years, got interruption trisomy 12, 10 antral follicles, 1. ICSI,

    low income

    **yes!**

# Primary Indication for PGT-A:
# (6.) Reduce Senseless ART

- 38 years, got 4 ICSI, no pregnancy

    low income

        **no!** (transfer 3 day 2 or 3)


-         middle income

        **yes!**

# Game Changer: niPGT, -omics, AI?

**niPGT-A**

most probably no harm

all embryos checked, if not too expensive

**Genomics, Transcriptomics, Proteomics, Metabolomics, AI ("PGDIS to PDIS"?)**

mathematical algorithms

  for PGT-A indication

  for embryo selection

# Conclusions PGT-A Indication

## Personalized Medicine

- "clinical mosaic stones"
- no ethical dilemma
- no green table or lab decision
- **two-stage** decision:

  before start of cycle, before biopsy
- new techniques: less harm, higher precision
- own limitations
- future: -omics + AI

# Summary PGT-A Consent

## Diagnosis, Therapy Proposal

- assemble "clinical mosaic stones": facts and preferences
- aim, indication
- information, alternatives, open for new approaches

## Informed Consent

- shared decision, reflection, personal choice
- shared responsibility, highly personal decision
- **<u>two</u>-stages**