

# Pre-Implantation Genetic Diagnosis for Sex Selection

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# Learning Objectives

- To review the methods to produce offspring of a specific sex
- To review the Ethics Document of the American Society of Reproductive Medicine concerning use of Pre-Implantation Genetic Diagnosis for Sex Selection

# Boy versus Girl : Genetic Sex

- Females:
  - 44 autosomes (# 1 – 22, 1 set from each parent)
  - 2 X chromosomes = 46 XX
- Males:
  - 44 autosomes (#1 – 22)
  - 1 X + 1 Y chromosome = 46 XY
- All eggs carry 1 X chromosome
- Sperm, “half” carry an X, half carry a Y
- Male determines child sex

# Sex Determination Methods

- Sperm Sorting
- Determine Sex of Embryo
  - Biopsy embryo, then Pre-implantation Genetic Diagnosis (PGD):
    - Fluorescent In Situ Hybridization (FISH)
    - Gene amplification by Polymerase Chain Reaction (PCR)

# Sperm Sorting

- Cell sorting technique developed by the US Department of Agriculture (USDA) for separation of X- and Y-bearing sperm for the cattle industry
- X Chromosome is larger than the Y so that X bearing sperm have 2.8% more DNA than Y-bearing sperm.



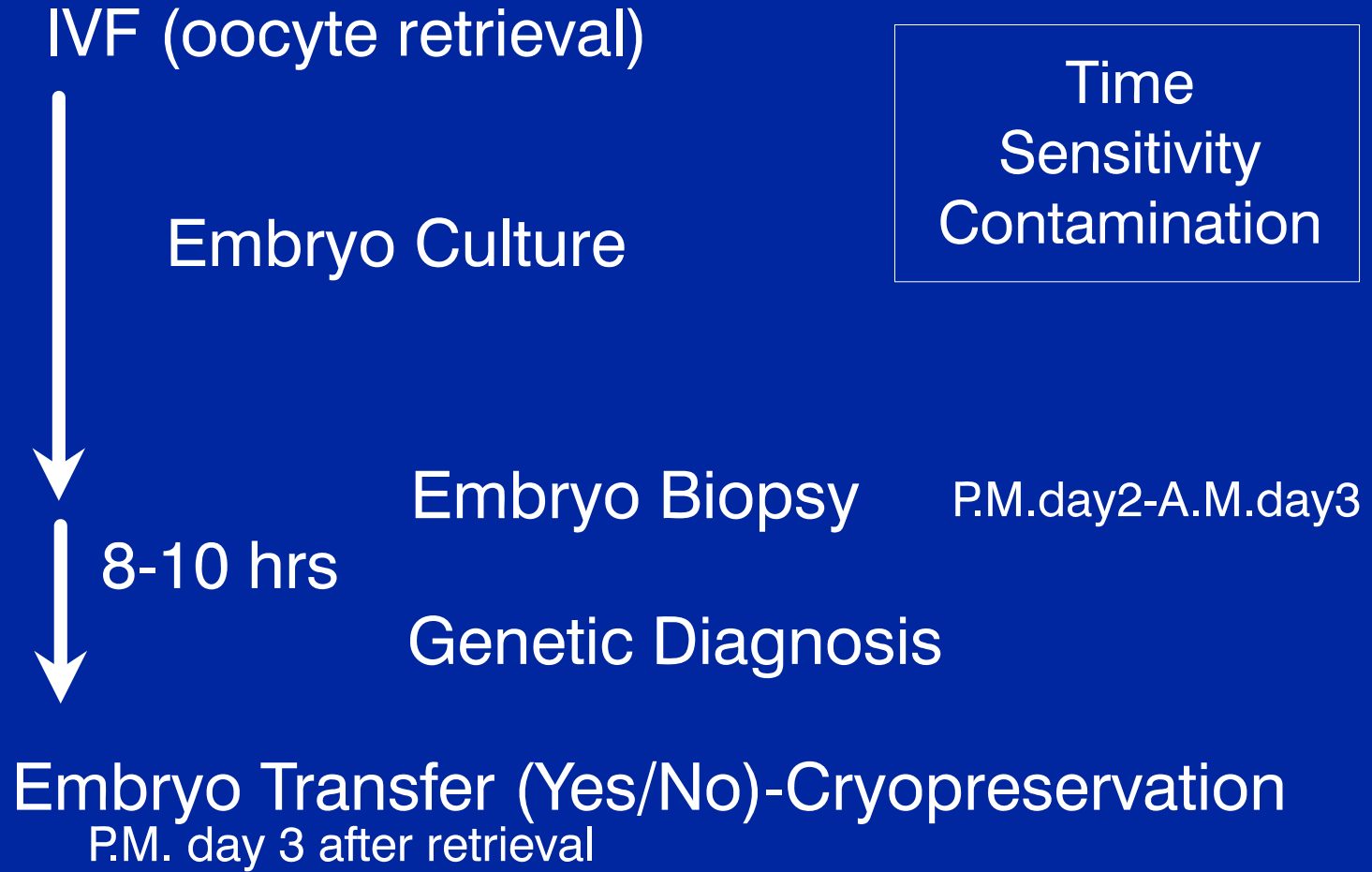
# Sperm Sorting

- Efficiency of sorting technique
- Can move ration of 50:50 boys:girls in semen to
  - 12:88 boys:girls, or
  - 70:30 boys:girls
- Technique better for selecting for girls
- Then use sperm as part of
  - Intrauterine insemination (non-operative)
  - IVF (operative)
- Accept outcome

# Embryo Sexing

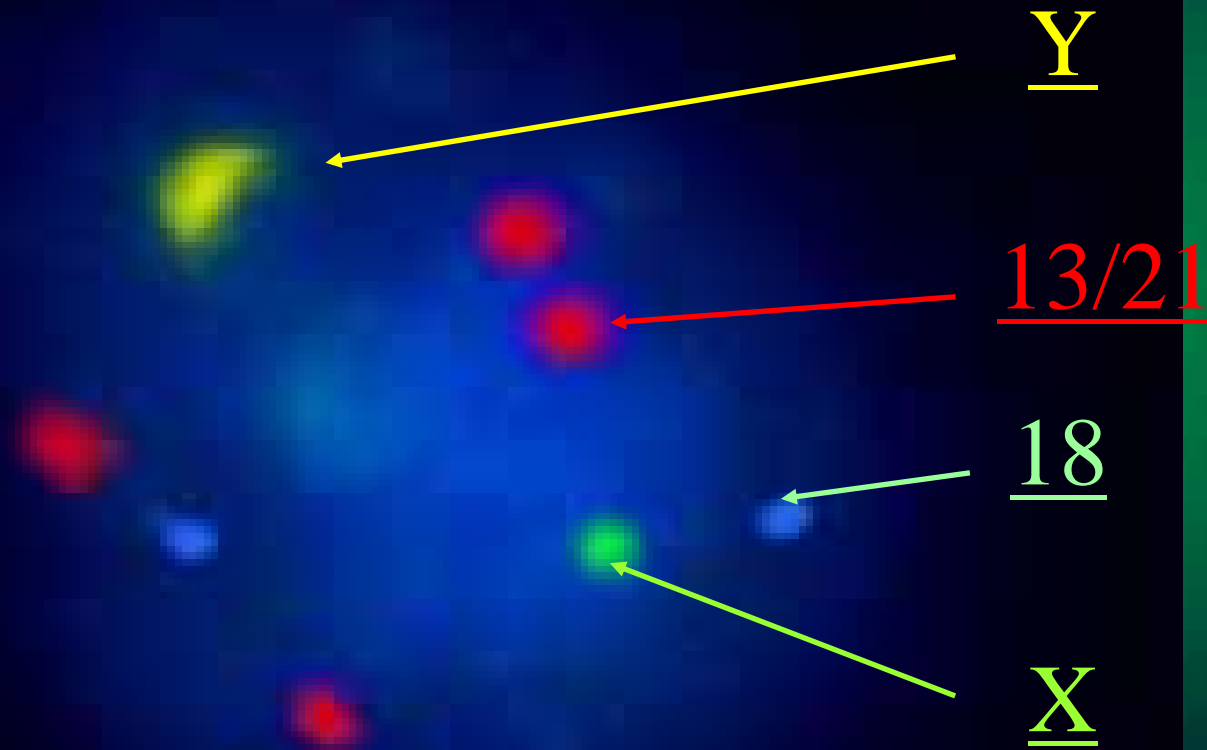
- After fertilization using In Vitro Fertilization and after the embryo has begun dividing, it is biopsied and one or two cells are removed from an 8-cell embryo and the DNA analyzed by PGD.
- DNA analysis:
  - FISH
  - PCR

# Pre-Implantation Genetic Diagnosis

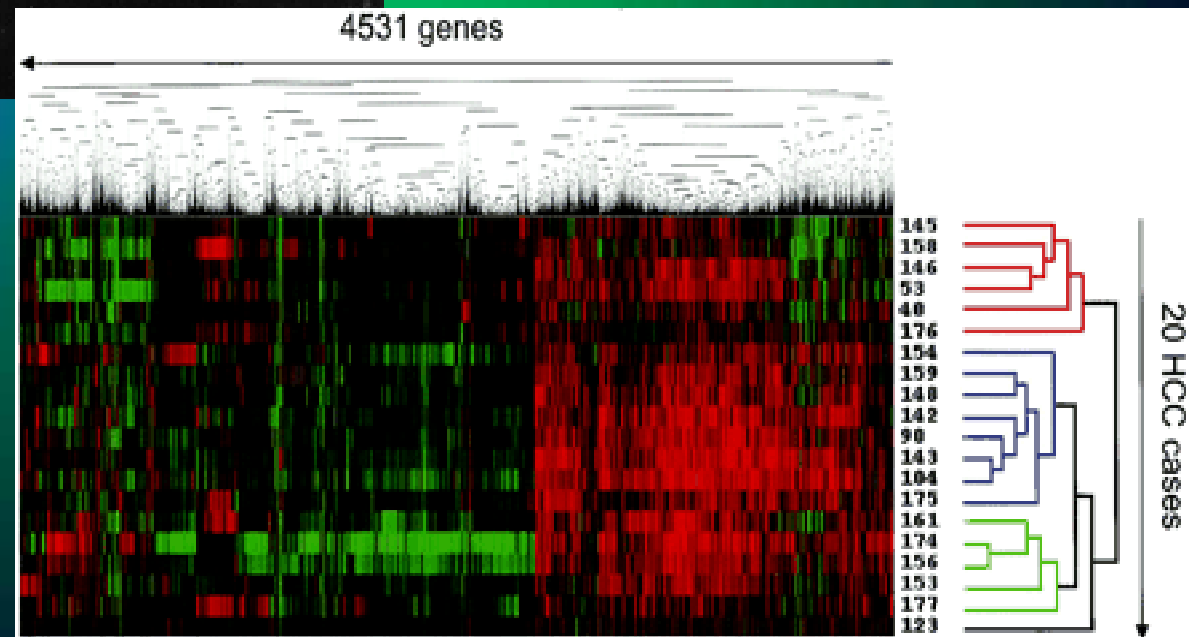
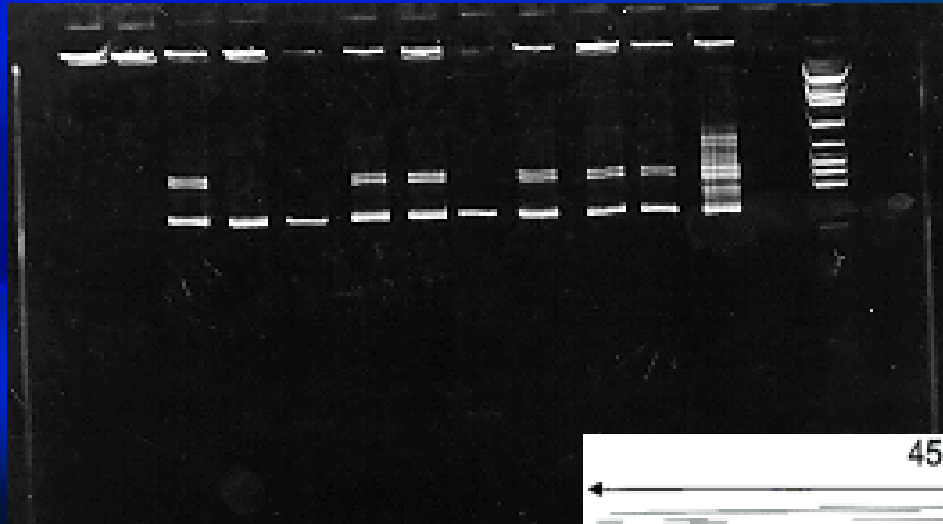




# Evaluation of Chromosomal Aneuploidy by Fluorescent In Situ Hybridization (FISH)



# Polymerase Chain Reaction (PCR) DNA Analysis



# Sperm Sorting vs Embryo Analysis

- Sperm Sorting:
  - Sorting gametes (sperm), not embryos
  - Accept risk undesired result
- Embryo Analysis
  - “99+%” Effective
  - Discard embryos of unwanted sex (or donate to another couple or for research)

# Spectrum of "Debate"

- Jeffrey Steinberg, MD
  - Fertility Specialist with clinics in California and Mexico performing embryo sex selection
  - When asked about what he would tell couples would call requesting selection for eye color, etc. "I tell them we aren't able to do this now, call back in 5-10 years."
- Mark Hughes, MD
  - Geneticist who developed PGD techniques to screen for disease
  - "Sex is not a disease."

# American Society of Reproductive Medicine 1999 Ethics Committee Statement on PGD for Sex Determination

- John Robertson part of this committee
- Evaluated the spectrum of Assisted Reproduction/IVF leading into PGD, i.e. degree of invasiveness for female partner
- Listed the 'arguments' pro and con for performing PGD

# Spectrum of ART leading to PGD

Embryo sex identification by preimplantation genetic diagnosis for nonmedical reasons.

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(a) Patient is undergoing IVF and PGD.

Patient learns sex identification of embryo as *part of*, or as a *by-product of*, PGD done for other medical reasons.

(b) Patient is undergoing IVF and PGD.

Patient requests that sex identification be *added to* PGD being done for other medical reasons.

(c) Patient is undergoing IVF, but PGD is not necessary to treatment.

Patient *requests PGD* solely for the purpose of sex identification.

(d) Patient is not undergoing either IVF or PGD (for the treatment of infertility or any other medical reason).

Patient *requests IVF and PGD* solely for the purpose of sex identification.

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# Ethics Committee Statement: "Pro" Sex Selection

- Western Societies "strong presumption in favor of reproductive choice"
- Sex selection a "logical extension" to reproductive choice, particularly to prevent disease
- Gender balance
- Parental companionship preferences
- Lesser evil than abortion
- Parents don't need to continue reproducing until get wanted child of particular sex

# Ethics Committee Statement: "Against" Sex Selection

- Gender discrimination
- Inappropriate control over nonessential characteristics of children, trivialize reproduction
- Unfair use of limited medical resources
- Stress on sex-selected offspring due to inappropriate expectations
- Marital conflict over decisions
- Reinforcement of societal gender bias
- Altered sex ratios: China

# Ethics Committee Statement

- Pros and cons have arguable contexts
- Weighted in light of spectrum of effort/invasiveness, i.e. non-invasive sperm selection without embryo destruction more 'defensible' or added decisions about embryo sex in cases where IVF with PGD is already being done versus initiating IVF for sex selection alone (maternal risks of procedure).

# Ethics Committee Conclusions

- PGD used for sex selection to prevent disease is ethically acceptable
- Patients undergoing IVF for other medical reasons as in (a) through (c) holds some risk of gender bias, harm to individuals and society, and inappropriate medical use and should not be encouraged.
- IVF with PGD solely for sex selection holds even greater risk and should be discouraged.

# Ethics Committee Conclusions

- Ethical caution regarding PGD for sex selection calls for the study of this practice. Such study should include cross-cultural as well as intracultural patterns, assessment of competing claims for medical resources, and reasonable efforts to discern changes in the level of social responsibility and respect for future generations.