PGD: Genetic Testing of Embryos in the United States

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Preimplantation Genetic Diagnosis

Genetic testing of embryos before implantation:

- In vitro fertilization
- Embryo biopsy
- DNA analysis
- Embryo selected for transfer
PGD

Indications (to date)

• Avoid known risk for single gene disorders or chromosomal abnormalities
• Aneuploidy screening in those undergoing IVF (may be called PGS or Preimplantation Genetic Screening)
• HLA matching
  ➢ for sibling, and avoiding disease (Fanconi Anemia)
  ➢ for sibling, but not a genetic disease (leukemia)
• Sex Selection
  ➢ Where X-linked diseases
  ➢ For “family balancing”
The search for data on PGD in the U.S.

PGD data are collected by ESHRE – but few U.S. centers participate.

IVF data are collected by CDC – but PGD data are not required.

In 2007 SART, the IVF clinics’ organization, began collecting very limited PGD data.
What we wanted to know about PGD:

• How often
• By whom
• Accuracy
• For what purposes/indications
• With what outcomes
Why we wanted to know it:

• Concern about US regulation “lite” of both reproductive medicine and genetic testing.
• Questions about success rates and health outcomes of (how many?) babies.
• Consider how data and public opinion interact.
• Data can drive appropriate oversight.
Survey of IVF Clinics


- 415 ART clinics contacted April/May 06 (SART/CDC)
- Directors at clinics offering IVF
- 186 respondents
- 45% response rate
Results

- Nearly three-quarters (74%) of IVF clinics provide PGD.
- Approximately 3,000 PGD cycles in 2005.
- We estimate 4-6% of IVF cycles include PGD.
IVF Clinics Offering PGD?

- Offer and provide PGD
- Offer it, but no patient has requested
- Would like to offer PGD, but resources unavailable
- Do not offer for other reasons
Types of PGD provided by clinics

- Aneuploidy: 93%
- Autosomal disorders: 82%
- Chromosomal rearr.: 67%
- X-linked diseases: 58%
- To avoid adult-onset disease: 28%
- Non-medical sex selection: 42%
- HLA typing: 24%
- HLA typing w/o single gene: 6%
- To select for a disability: 3%
PGD performed in-house

- Percent of IVF-PGD clinics who perform in-house

- Any: 14
- Aneuploidy: 14
- Autosomal disorders: 10
- Chromosomal rearrangement: 8
- X-linked diseases: 3
Safety and Accuracy

• 21% of clinic directors are aware of inconsistencies between PGD and later genetic testing.
Types of PGD provided by clinics

- **Aneuploidy**: 93%
- **Autosomal disorders**: 82%
- **Chromosomal rearr.**: 67%
- **X-linked diseases**: 58%
- **Non-medical sex selection**:
  - HLA typing: 42%
  - HLA typing w/o single gene: 9%
- **To avoid adult-onset disease**: 28%
- **HLA typing**: 24%
- **HLA typing w/o single gene**: 6%
- **To select for a disability**: 3%
Clinic policies on sex of embryos

- **35%** inform, comply with parental preferences.
- **15%** inform, comply with parental preferences only for second or subsequent children.
- **30%** will reveal the sex and transfer embryos of desired sex if asked, but do not volunteer the information.
- **8%** transfer the best embryo without regard to sex.
- **10%** never reveal sex of the embryos in absence of an X-linked disorder.
- **8%** transfer the best embryo without regard to sex.
- **35%** inform, comply with parental preferences.
Types of PGD provided by clinics

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Practice of PGS in the U.S.

- 93% of IVF clinics offering PGD, and 68% of all IVF clinics offer PGS.
- Opinions of the effectiveness of PGS vary widely, even among those who offer it. i.e. 79% of those offering for AMA felt it was valid.
- 85% of clinic directors of clinics providing PGS believe more data are needed to determine whether and to whom it should be offered.
In their own words

“Obvious benefits of improving delivery rates by reducing miscarriage rates.”
“Literature evaluations say to do it.”

“There is no data that shows PGD for aneuploidy is helpful.”
“PGD is a waste of money and resources.”
PUBLIC OPINION ABOUT PGD
GPPC Public Opinion 2004

Do you think there should be limits set for acceptable and unacceptable uses of reproductive genetic testing?

Yes  88%
No  12%
Types of PGD provided by clinics

- **Aneuploidy**: 93% of PGD clinics have provided this service, accounting for 66% of all PGD cycles.
- **Autosomal disorders**: 82% of PGD clinics have provided this service, accounting for 12% of all PGD cycles.
- **Chromosomal rearr.**: 67% of PGD clinics have provided this service, accounting for 9% of all PGD cycles.
- **X-linked diseases**: 58% of PGD clinics have provided this service, accounting for 3% of all PGD cycles.
- **Non-medical sex selection**: 42% of PGD clinics have provided this service, accounting for 9% of all PGD cycles.
- **To avoid adult-onset disease**: 28% of PGD clinics have provided this service, accounting for 6% of all PGD cycles.
- **HLA typing**: 24% of PGD clinics have provided this service, accounting for 6% of all PGD cycles.
- **HLA typing w/o single gene**: 6% of PGD clinics have provided this service, accounting for 3% of all PGD cycles.
- **To select for a disability**: 3% of PGD clinics have provided this service, accounting for 3% of all PGD cycles.
For What Purpose?
GPPC Public Opinion 2004

% Who Approve

Purpose of PGD

Fatal Disease 68
HLA 66
Adult Risk 58
Sex Selection 40
Regulating PGD: Distribution of opinions among Americans

- Ban
- Regulate safety
- Regulate ethics & safety
- Regulate ethics
- Do not regulate
- No questions answered
Regulating PGD:
Distribution of opinions among Americans

- Ban: 19%
- Regulate ethics: 16%
- Regulate ethics & safety: 36%
- Regulate safety: 59%
- Do not regulate: 1%
- NA: 5%
Is There a Role for Additional Oversight?

Federal rule
- Ban or limit
- Congress or Agency

State Laws and Regulation

Professional Oversight
Options for Oversight:

Federal Government:
• CLIA
• FDA

Professional guidelines:
• ESHRE, PGDIS, ASRM
• RLAP/CAP certification
Who do you think should set limits?

- Leave the decision to individual patients and their doctors. 48%
- Professional medical societies develop guidelines for acceptable uses. 29%
- Federal or state government makes regulations that determine acceptable uses. 16%
- Patient groups develop guidelines for acceptable uses. 7%
Clinic Directors’ Views on Oversight

95% of directors agree that professional societies are best suited to create standards and guidelines relating to PGD.

85% agree that there should be more professional guidelines relating to PGD.

21% agree that there should be more government oversight related to PGD.
The Continuing Quest: A U.S. PGD Registry

“The registry should identify and take action on “outlier” centers just as the CDC registry does.”

“Successful collection and publication of center-specific ART results validate professional self-regulation in the United States as effective and responsive.”

“We submit that self-regulation is the most appropriate policy in the United States.”

Lingering Questions:

• PGD for aneuploidy (PGS) and the “take-home baby” rate?
  – Mastenbroek et al, NEJM 2007
  – ASRM Practice Committee Opinion
  – Question about techniques, embryo loss, patient groups.

• PGD for sex selection in the United States

• How do the babies do?
Genetics and Public Policy Center

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