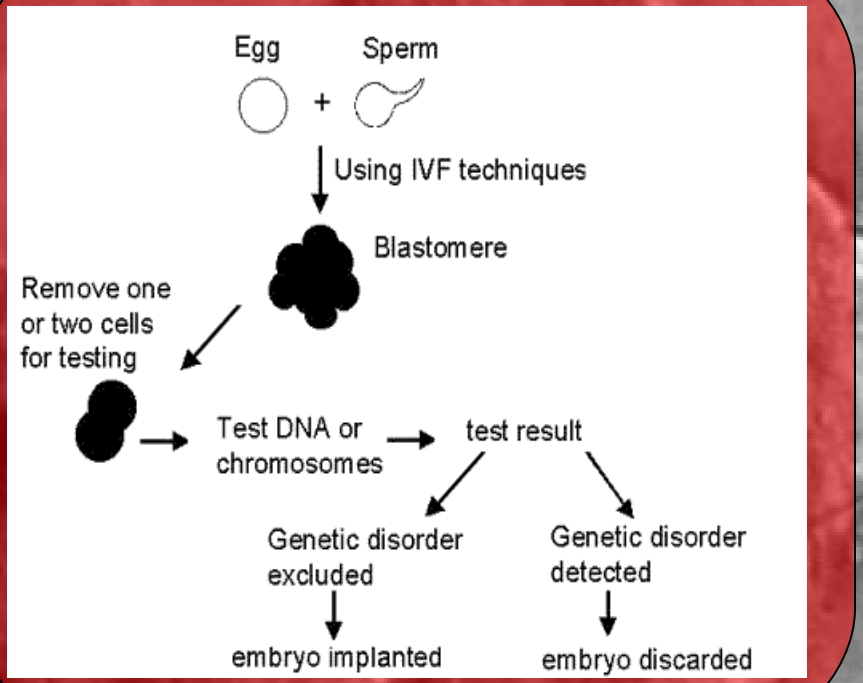
The Ethical Implications of Preimplantation Genetic Diagnosis (PGD)

"The great challenge to mankind today is not only how to create, but to know when to stop creating."

Lord Emmanuel Jacobvitz,
former chief rabbi of Britain

Elizabeth Kersten
June 4, 2008

What is PGD?

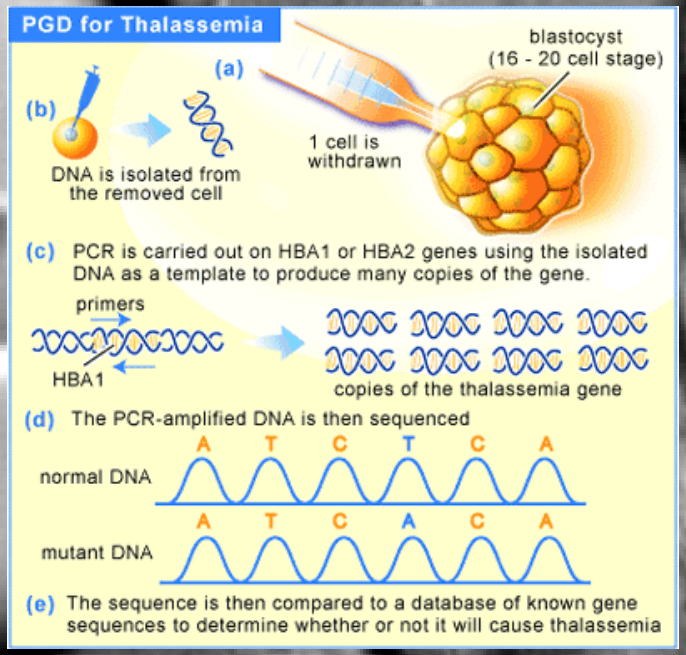


Technology used in conjunction with in vitro fertilization to screen embryos for genetic conditions prior to transfer:

- **Remove a cell from a 3-day old embryo fertilized in vivo**
- **Analyze cells for specific genetic or chomosomal abnormalities (PCR or FISH)**

What is PGD?

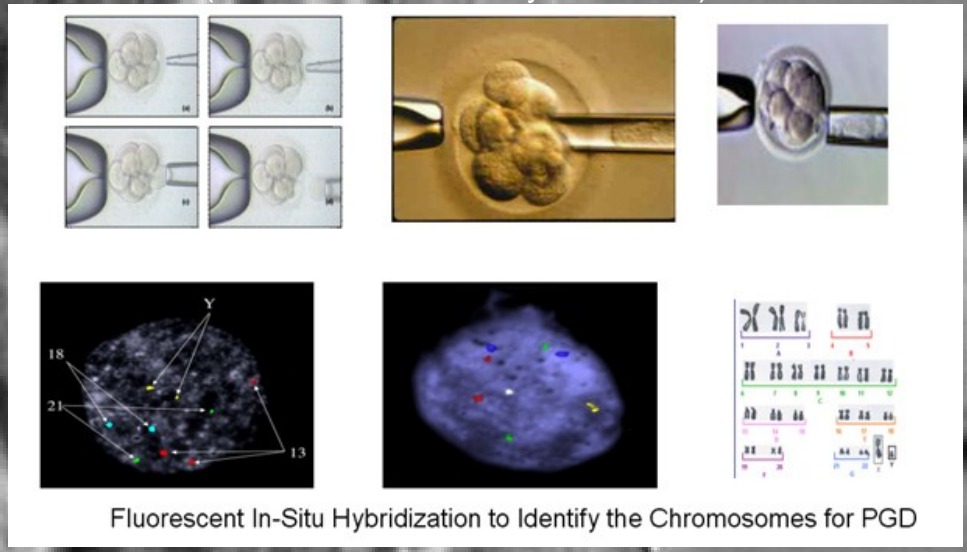
…using PCR



- Single gene defects in autosomal disease
- Single gene defects in male infertility
- Identification of sex in X-linked diseases

…using FISH

(Fluorescence in situ hybridization)



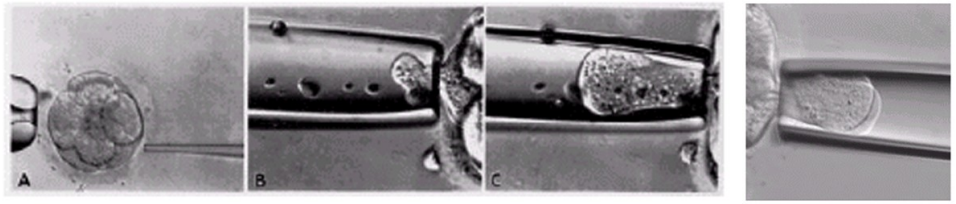
Fluorescent In-Situ Hybridization to Identify the Chromosomes for PGD

- Aneuploidy screening in women of advanced maternal age
- Aneuploidy screening for male infertility
- Identification of sex in X-linked diseases
- Recurrent miscarriages caused by parental translocations

History of PGD

- 1990: PGD first used to screen against genetic mutation for cystic fibrosis
- Throughout 1990s: PGD used to screen mutations for severe, irreversible, genetic conditions
  - Sickle-cell anemia
  - Tay-Sachs Disease
  - Duchenne's Muscular Dystrophy
  - Beta-thalassemia
- As of 2003, the procedure was able to select against 100 different genetic conditions

"Soon PGD will be used as regularly as amniocentesis is now"



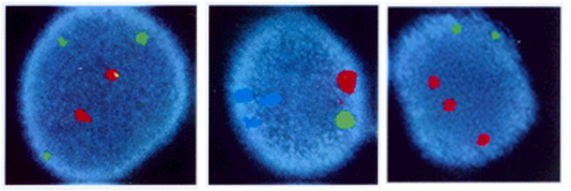
Removal of blastomere from 8 cell embryo (blastocyst)

PGD Uses

Traditionally:

- Single gene disorders
- Chromosomal structural abnormalities
- Aneuploidy screening (women over 37)
- History of recurrent miscarriage or failed assisted reproduction

Age, y	Embryos (Normal)	Embryos (Aneuploidy)	Other Abnormality
25-35	61%	8%	31%%
36-37	60%	10%	30%
38-39	47%	18%	35%
40-41	43%	26%	31%
42-44	39%	30%	31%



Trisomy 13 Trisomy 18 Trisomy 21

Abnormalities of chromosomes 13, 18, 21

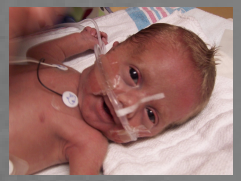
PGD Benefits

PGD is preferable to alternatives for Mendelian disorders:

- Don't have children
- Use donor gametes
- Conceive→ prenatal testing→ if positive may abort

The Magliocco's first son died at 8 weeks from Spinal Muscular Atrophy

When scaled up to society level, "This will represent a significant reduction of physical and emotional stress related to care for an affected family member and a significant reduction of medical expenses to society"



The Ethics of PGD

Objections on the grounds of need to create and select embryos, then discard those not selected

- Embryo is a life→ no PGD
- Embryo is a potential life deserving of respect→ only PGD for medical purposes

Objections on grounds of selection itself

- Deontological: reproduction as a gift
- Consequentialist: PGD will lead to eugenic world of designer children

Further Concerns…

- Reminiscent of Eugenics
- Increased inequality

  "…while wealthy parents are able to select traits for happiness, creativity and physical talents, disorders such as obesity, heart disease, alcoholism and mental illness will be left to "drift randomly among the families of the underclass."
- Restriction, rather than extension, of choice
- Disability discrimination claim

  "…the danger lies in how this testing could promote further stigmatization of and discrimination against people with "genetic impairments" or their parents. Indeed, testing could entrench a culture of prevention and perfectionism and promote a culture of intolerance."

Avoidance of late-onset diseases

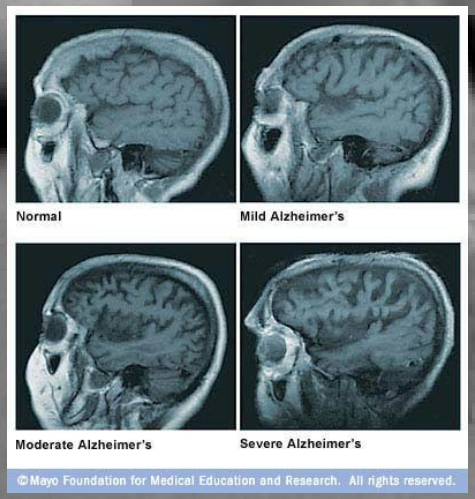
Proponents:

- Enables avoidance of horrible condition
- Time of onset is not morally significant
- Case stronger for this than susceptibility

Concerns:

- Treatment may be developed in the interim
- Ability of affected parent to raise the child
- Age of onset, seriousness of disorder must be considered

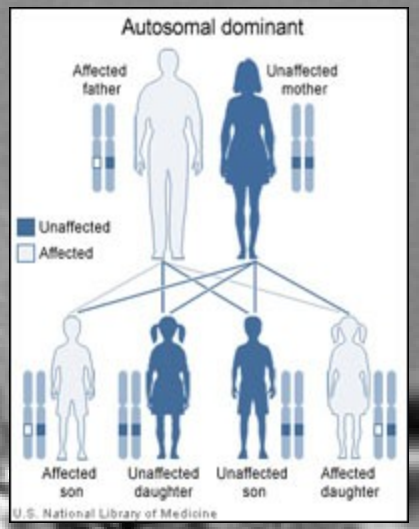
A new study from Nancy Wexler, in Venezuela in the 1990s with a boy with Huntington's disease, suggests there may be ways to delay the onset of the disease.



"PGD has also been used by a woman who carried a gene for early onset Alzheimer's disease (AD), and who wished to have a child that would be free of that condition. In that case the woman was 31 years of age, had an older sister who had already experienced early onset Alzheimer's, and had herself tested positive. She requested PGD to be sure that any fetus that she carried did not also have that gene. PGD was carried out, and she gave birth to a child free of that condition"

Susceptibility conditions

(diseases with variable or incomplete penetrance)



Concerns:

- Similar to late-onset, but harder case because of lower penetrance

- Many potentially treatable
  - BRCA1 and BRCA2 mutations
  - Hereditary non-poly colorectal cancer, etc.

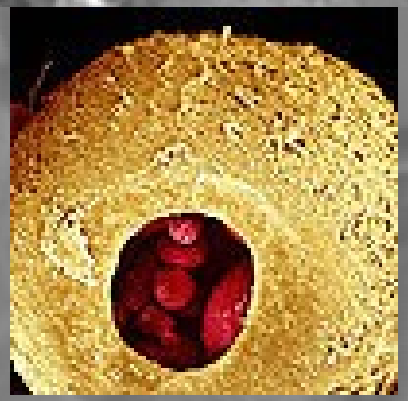
Hereditary Nonpolyposis Colon Cancer (Lynch Family Syndrome)

Type of Mutation: Autosomal Dominant

Lifetime Risk: 70-82% lifetime risk (vs. 5% in population without mutation)

Average Age of Diagnosis: 45 (vs. 60-70 in population without mutation)

Tissue-typing to save the life of another child



Concerns:

- Long-term psychological consequences for "savior sibling"
- Instrumentalization of a child (violates Kantian imperative)

Proponents:

- Unlikely to treat the new child poorly
- No intrusions on new child (umbilical cord blood)
- If transplant fails, will be another child to love in place
- Better than alternatives:
  - –No transplant→ first child likely to die
  - –Non-sibling match→ much less safe, much less effective
  - –Couple conceive coitally to get a match
    - May undergo prenatal diagnosis and abort if not match
    - May give child up for adoption if not match

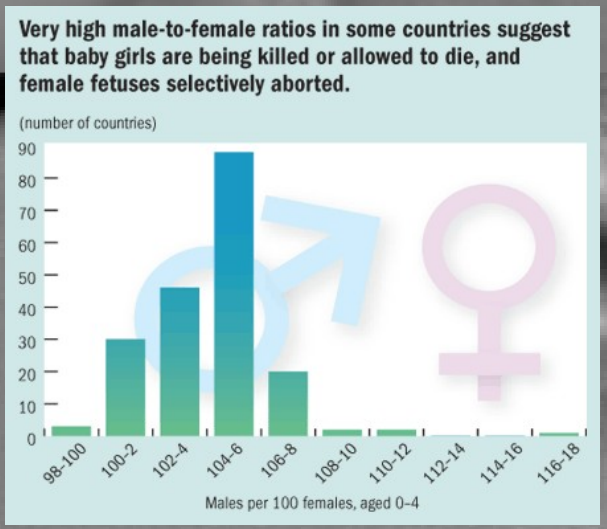
Non-medical sex selection

Two types:

- First child sex selection
- Gender balancing

Concerns:

- Slippery slope
- Discriminatory
- Could lead to great disparities

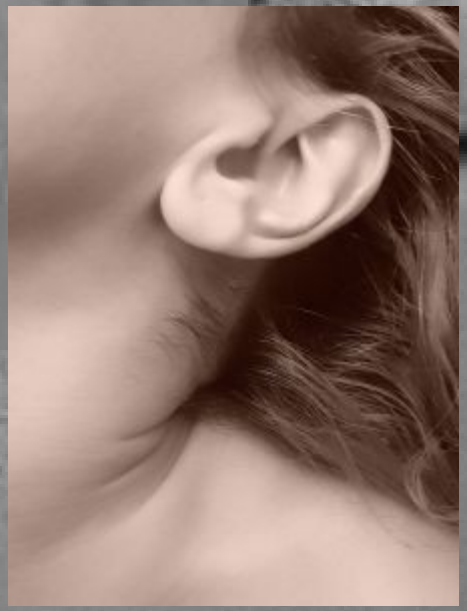


Proponents:

- Alternative is abortion
- Gender balancing doesn't necessarily entail devaluing one sex over the other
- Certain cases acceptable
- Contributes to population control
- Desire for parental companionship by raising child of same gender

Nonmedical Traits

- Hearing
- Sexual Orientation
- Height
- Beauty
- Intelligence
- And on and on…



Where to Draw the Line?

- Avoidance of Late-Onset Diseases
- Susceptibility Conditions
- Tissue-typing to Save Life of Other Child
- Non-medical Sex Selection
- Other non-medical traits

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