GENETIC COUNSELING, FAMILY PLANNING, IVF AND PGD

Jacinda Sampson MD PhD
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Genetic Counseling

• What is genetic counseling?
  • Dialogue between you and counselor
    • Counselor can be:
      • Physician with experience with genetic disorders
      • Genetic counselor
Genetic Counseling

Who is it for?

- ANYONE with questions about a genetic disorder
  - With or without symptoms
  - With or without a definite diagnosis
  - At risk for a genetic disorder
  - At any age
  - Planning a family at this time
  - Not planning a family at this time
  - Whether or not interested in genetic testing
  - JUST CURIOUS
Genetic Counseling

- What information will I get?
  - Information about the genetic disorder
  - How it is inherited
  - Recurrence risk (how it is passed on)
  - Testing options
    - Genetic and non-genetic
  - The pros and cons of testing
    - Informed consent
Genetic Counseling

- genetic testing discrimination risks
  - GINA act (Genetic Information Nondiscrimination Act -2008)
    - protects asymptomatic people from health insurance discrimination
    - Does not apply if symptomatic (pre-existing condition)
    - Does not apply to:
      - life insurance
      - long term disability insurance
Genetic Counseling

• How is it done?
  • Private, confidential
  • Non-directive
    • Will not make decisions for you
    • Will not tell you what to do
  • Supportive
    • Emotions and stress related to diagnosis and testing issues
    • Emotions and stress related to living with or caring for someone with a genetic disorder
Dominant inheritance

- 50% chance of inheriting abnormal gene
- 50% chance at each pregnancy
- Does not alternate or “even out”
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Myotonic Dystrophy Type 1

CTG
- 5-37 repeats: No Myotonic Dystrophy
- 38-49 repeats: No symptoms
- ~50-150 repeats: Mild Myotonic Dystrophy
- ~100-1000 repeats: Classic Myotonic Dystrophy
- 730-4300 repeats: Congenital Myotonic Dystrophy

Range where expansion is possible
Sperm repeat expansion

- Repeat expansions <100 are more unstable when inherited from the father’s side
- Even NORMAL repeat sizes show repeat number variation in sperm

http://oscss-biology.wikispaces.com/Images
Egg repeat expansion

- Occurred prior to fertilization
- Somatic mosaicism
  - Different tissues have different repeat sizes
  - Repeat size increases during development
  - Somatic expansion observed at 13-16 weeks (2nd trimester)

http://oscss-biology.wikispaces.com/Images
Myotonic Dystrophy type 2

CCTG

11-26 repeats  Normal repeat number

27-74 repeats  Borderline expansions

Range where expansion or contraction is possible

75-11,000 repeats  Myotonic dystrophy type 2
Family Planning

• Unplanned pregnancy
  • 49% in 1994
  • 57% in 1987

Planning options

• No planning (allowing nature to take its course)
• Not having children
• Adoption
• Using a sperm donor or egg donor
• Prenatal genetic testing and pregnancy termination
• Using in vitro fertilization (IVF) and preimplantation genetic diagnosis (PGD)
Myotonic Dystrophy and contraception

- Papers published = 0
- No information about effectiveness or side effects specific to myotonic dystrophy population
- Contraceptive methods only work if used
- Talk to your physician (family practice or OB/gyn) about specific types
Contraceptive options

**Men**
- reversible
  - Condoms
  - Spermicide
- Irreversible
  - vasectomy

**Women**
- Reversible
  - Diaphragm or cervical cap
  - IUD (intrauterine device)
  - Hormonal contraceptives
    - Oral contraceptive pill
    - Contraceptive patch
    - Contraceptive shots
    - Contraceptive implants
- Rhythm method
- Irreversible
  - Tubal ligation

**talk to your physician about what would be best for you**
Prenatal Genetic testing

- Chorionic villus sampling
  - >12 weeks

- Amniocentesis
  - 15-20 weeks

- Cordocentesis
  - >18 weeks

- Fetal skin biopsy
  - >18 weeks

- Results take 2-3 weeks
- Information for
  - Preparing for pregnancy or
  - Termination of pregnancy
Chorionic Villus Sampling

Phillips, S. E. 2001. Genetic Counselling. eLS.
Chorionic villus sampling
Chorionic villus sampling

http://hcp.obgyn.net/pregnancy-and.birth/content/article/1760982/1878411
Amniocentesis
Umbilical blood sampling

http://hcp.obgyn.net/pregnancy-and-birth/content/article/1760982/1878411
In vitro fertilization

1. Egg production stimulated by hormone therapy
2. Eggs retrieved from ovary
3. Sperm sample provided
4. Eggs and sperm combined to allow fertilization
5. Fertilized eggs introduced into uterus

Infographic: FDA/Renée Gordon
Pre-implantation Genetic Diagnosis

- 1-2 cells from each embryo are removed
- Each tested by PCR
- (polymerase chain reaction)
- Can freeze embryos while awaiting gene test results
Preimplantation Genetic Diagnosis

Preimplantation genetic testing
Preimplantation genetic testing

PCR amplification
Preimplantation genetic testing

A  a

236  20

b  B

28  8

a  a

b  B
Preimplantation genetic testing
Preimplantation genetic testing-flanking markers
Example of PCR for flanking markers

Mother with DM1  Father  Child with DM1

(A) 151  (B) 151, 157  (C) 153

Mother  Father  Mother  Father

APCC2

143  122  141

Father  Father  Father

*second peak missing too big to detect

DMPK

118  129

Mother  Father

Only 1 peak  *second peak too big to detect

Copy with expanded repeat

Copy without expanded repeat

Eggs + Sperm

Embryos with expanded repeat

Embryos without expanded repeat

Child unaffected by Myotonic Dystrophy

Implantation

[Diagram showing the process of how an expanded repeat gene can be passed from parent to child, leading to unaffected offspring and one affected child.]
In vitro fertilization in DM1

• No difference in:
  • Number of follicles (maturing eggs)
  • Endometrial thickness (lining of the womb)
  • Estrogen response

• Differences in:
  • Slower response to ovarian stimulation medications
    • Later human chorionic gonadotropin (hCG) administration
  • Higher doses of stimulating medications needed
    • follicle stimulating hormone (FSH)
    • human menopausal gonadotropin (HMG)

Feyereisan, Hum. Reprod. (2006); 21(1):175
Embryo implantation in DM1

- No differences in:
  - Implantation rate
  - Pregnancy rate (22% per embryo transferred)

- Differences in:
  - Higher number of cycles of implantation for a pregnancy
    - In this series, no successes on first cycle.

Feyereisan, Hum. Reprod. (2006); 21(1):175
IVF+PGD- Case series Belgium

- 78 couples. Technique changed over time
  - Sperm injection
  - Implantation of up to 4 embryos
- Cycle 1: 49% implantation
- Cycle 2: 28% implantation
- Overall, 20%/cycle resulting in a live birth
- Overall, 78 couples -> total of 151 cycles ->49 children
- Pregnancy complications (8): preterm bleeding, failure to progress, premature rupture of membranes, eclampsia
- 8 babies admitted to NICU (5 briefly observed, 2 due to prematurity)

IVF+PGD- Case series UK

- 17 couples, total of 22 IVF cycles, 6 children
- 12 cycles resulted in unaffected embryos for transfer
- Genetic testing inconclusive or failed in 24%
- 15 of the 17 couples had a family member affected by DM1
- 7 already had a child with DM1
- 2 had lost a child to congenital myotonic dystrophy
- 5 had already tried prenatal genetic testing and elective pregnancy termination
- 4 had infertility

Myotonic Dystrophy Type 1 and pregnancy risks

- Ectopic pregnancy
- Hypertension/eclampsia
- Preterm vaginal bleeding
- Urinary tract infections
- Premature rupture of membranes
- Placenta problems 11%
- Preterm labor delivery 31%
- Failure to progress in labor
- Cesarean delivery 37%
- Non-vertex presentation 35%

Rudnick-Schoneborn et al. Neurology 2006;66; 579
Myotonic Dystrophy Type 2 and pregnancy risks

- preterm labor (12.6-50%)
- Preterm delivery (27%)

Rudnick-Schoneborn et al. Neurology 2006;66; 579
Insurance and Fertility treatment

- 15 states mandate private insurance coverage for fertility treatment
  - Excludes self insured, small businesses
- BUT, only AK, CN, HI, IL, MD, MA, NJ, TX mandate IVF
- Conditions
  - May require failure to get pregnant by “less expensive means”
  - May exclude use of sperm or egg donor
  - Only covered for specific conditions (i.e., not necessarily myotonic dystrophy)
  - Genetic testing often not covered
  - Cryopreservation (freezing) of embryos may not be covered
- Out-of-pocket cost could range from $20,000-83,000

http://ivfcostcalculator.com/index.html
IVF - 34 years of progress
A DM blog  http://apgdblog.blogspot.com

A PGD blog
I have Myotonic Dystrophy type 1, so my husband and I chose to do IVF with PGD in order to have a baby without passing on the condition. Six cycles later we now have two healthy children!

When my husband and I started on this journey in 2006, I found it was easy to research the science of PGD, but what I really wanted to hear was the patient’s perspective.

Our Complete Family

FRIDAY, 6 JULY 2012

Trying to crawl

Tabitha is now seven and a half months old and so much fun. She is so smiley! Here is a picture of her lovely smile. She often has her tongue bent over in that strange way. She has got her bright blue eyes from her dad.
Conclusions- ask your medical team

You have the right to have information to make decisions about your health and family planning

• Genetic counseling
• OB/Gyn
• Primary care physician
• Neuromuscular physician
• Local resources for IVF and PGD if you are interested
Acknowledgements

- Allie Copeland- artwork, brochure
Repeat expansions

New triple primer PCR method

2 copies of 5 repeats

2 copies of 12 repeats