

GENETIC COUNSELING, FAMILY PLANNING, IVF AND PGD

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August 18, 2012

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

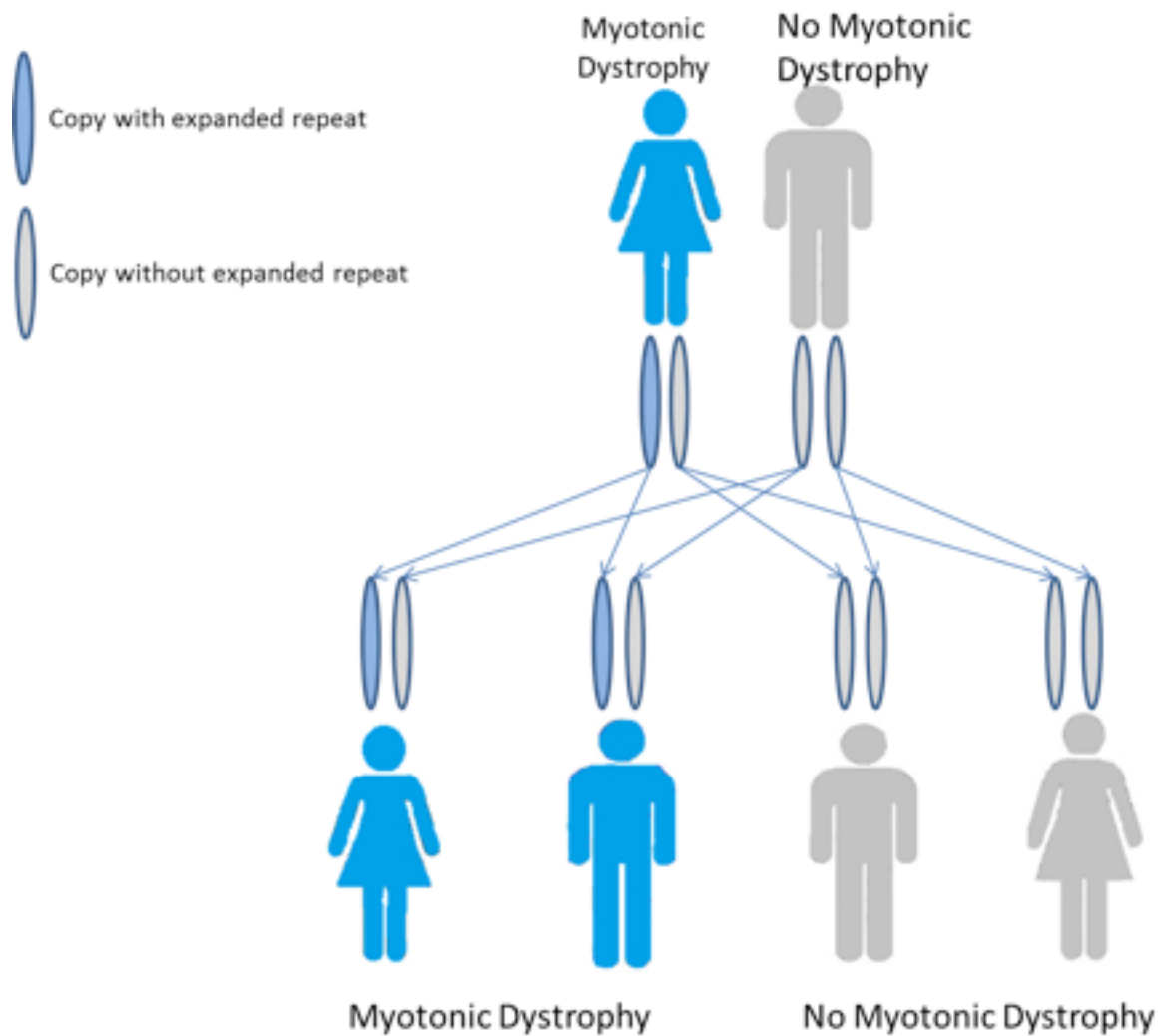
- What information will I get?
 - Information about the genetic disorder
 - How it is inherited
 - Recurrence risk (how it is passed on)
 - Testing options
 - Genetic and non-genetic
 - The pros and cons of testing
 - Informed consent

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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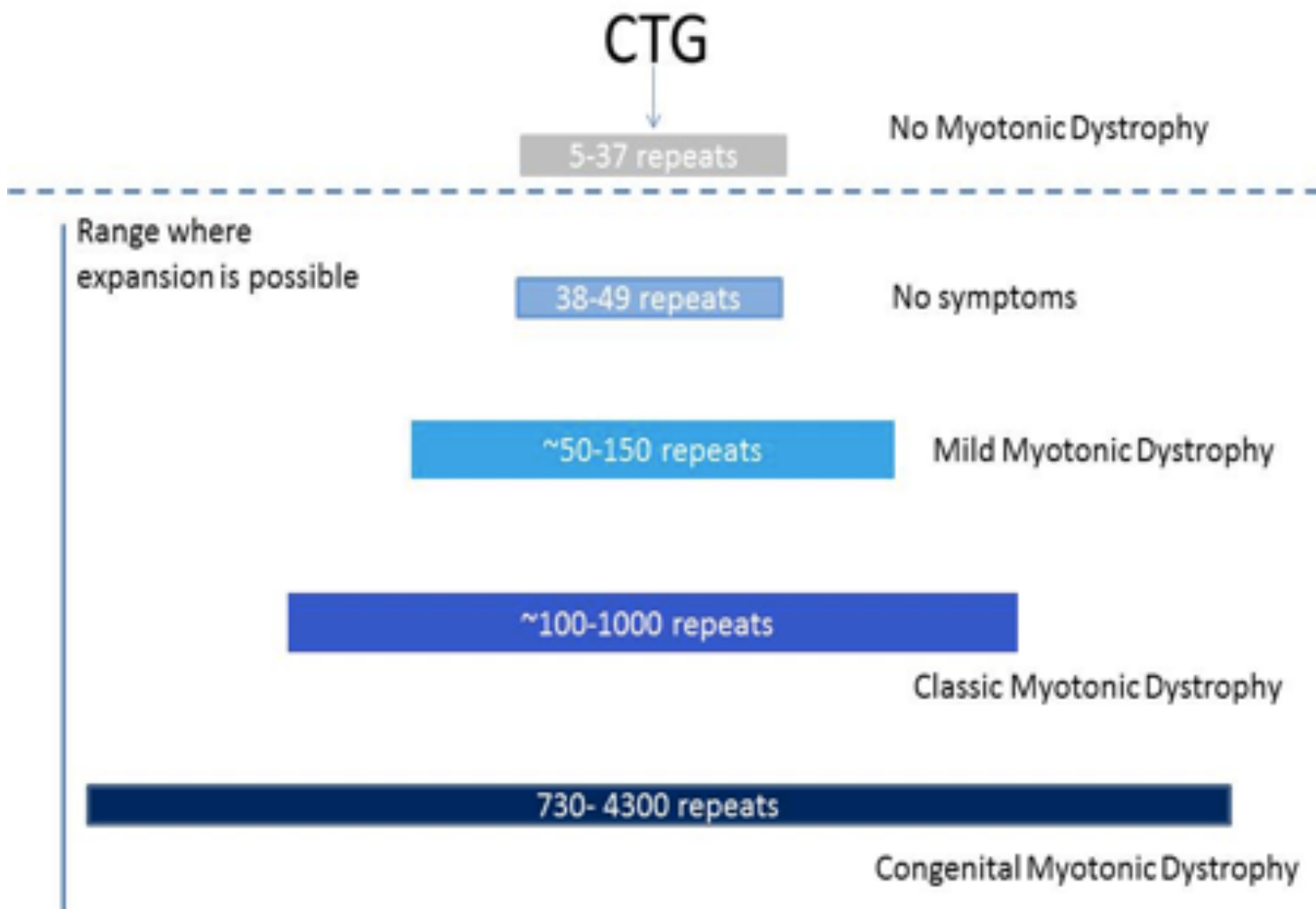


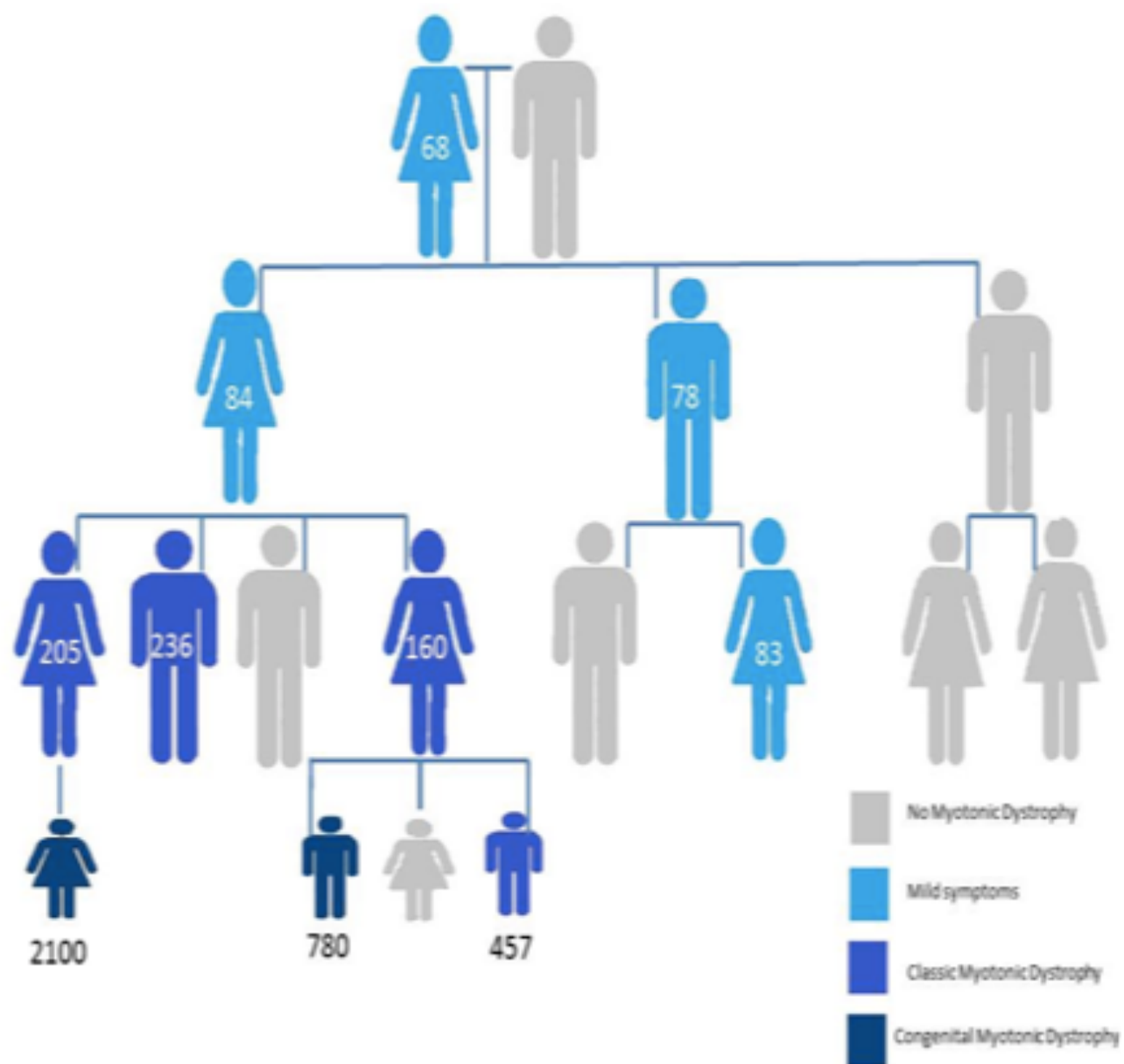
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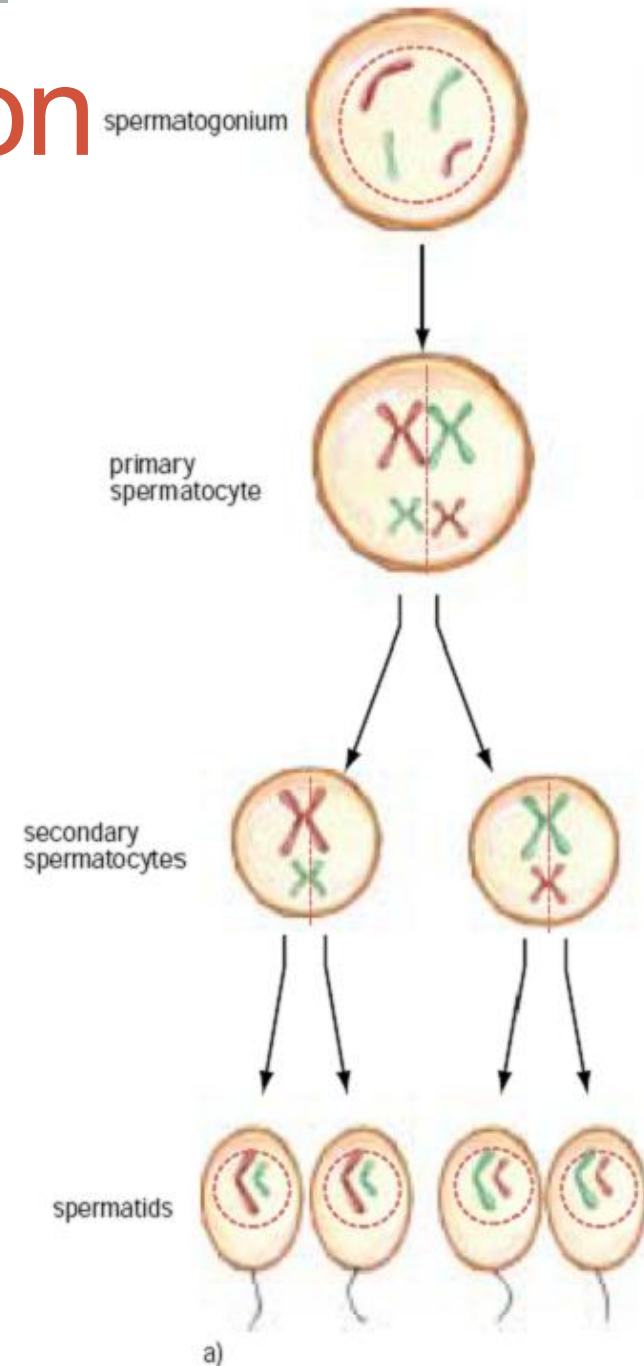
Myotonic Dystrophy Type 1





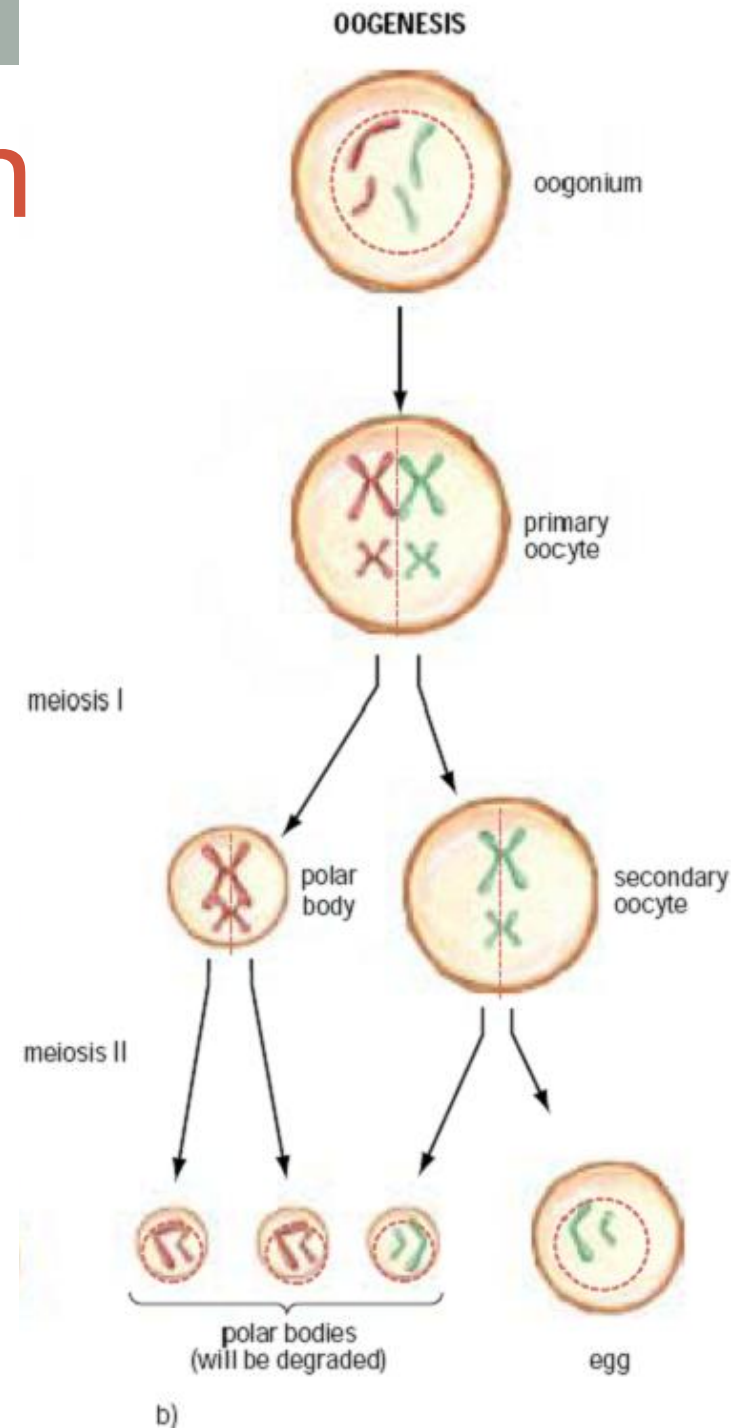
Sperm repeat expansion

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



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)



Dean et al. Fertil. Steril. 2006;86:98-105

<http://oscscs-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



Santelli et al, The Measurement and Meaning of Unintended Pregnancy, *Perspect. On Sex and Reprod Health* 2003: 32(2), 94

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

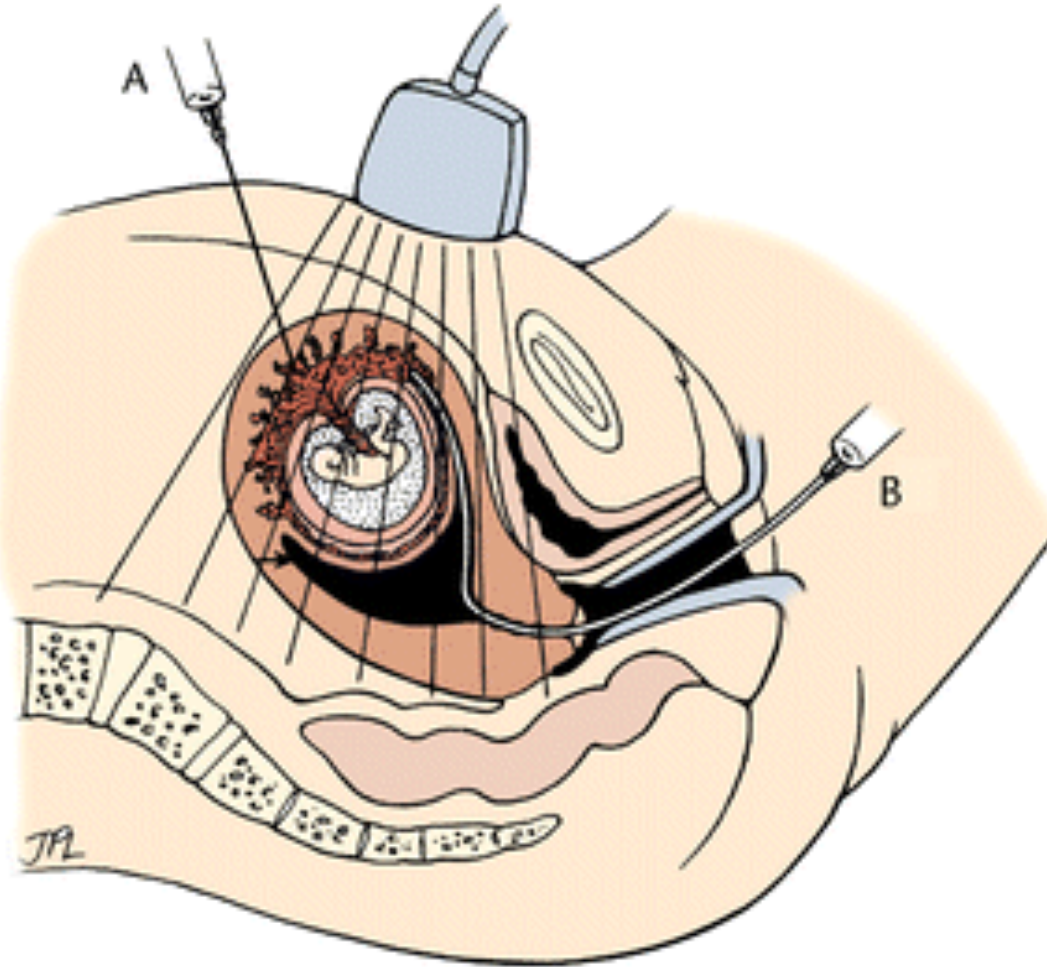
- Reversible
 - Diaphragm or cervical cap
 - IUD (intrauterine device)
 - Hormonal contraceptives
 - Oral contraceptive pill
 - Contraceptive patch
 - Contraceptive shots
 - Contraceptive implants
 - Rhythm method
- Irreversible
 - Tubal ligation

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

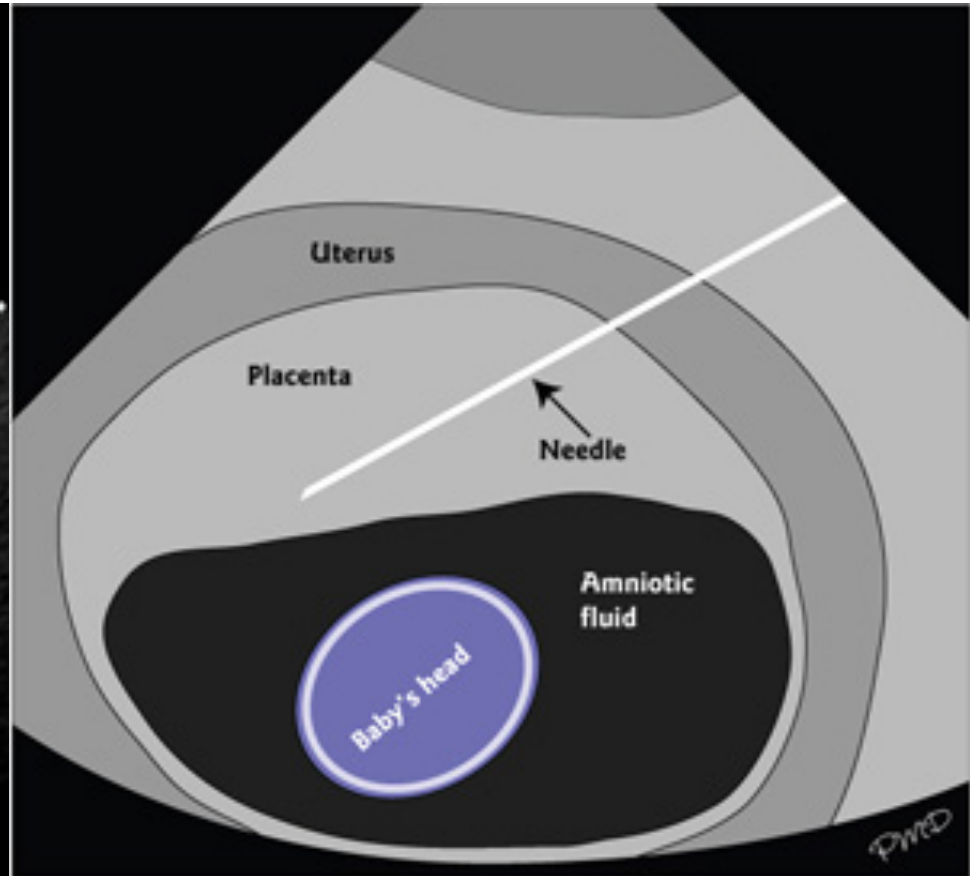
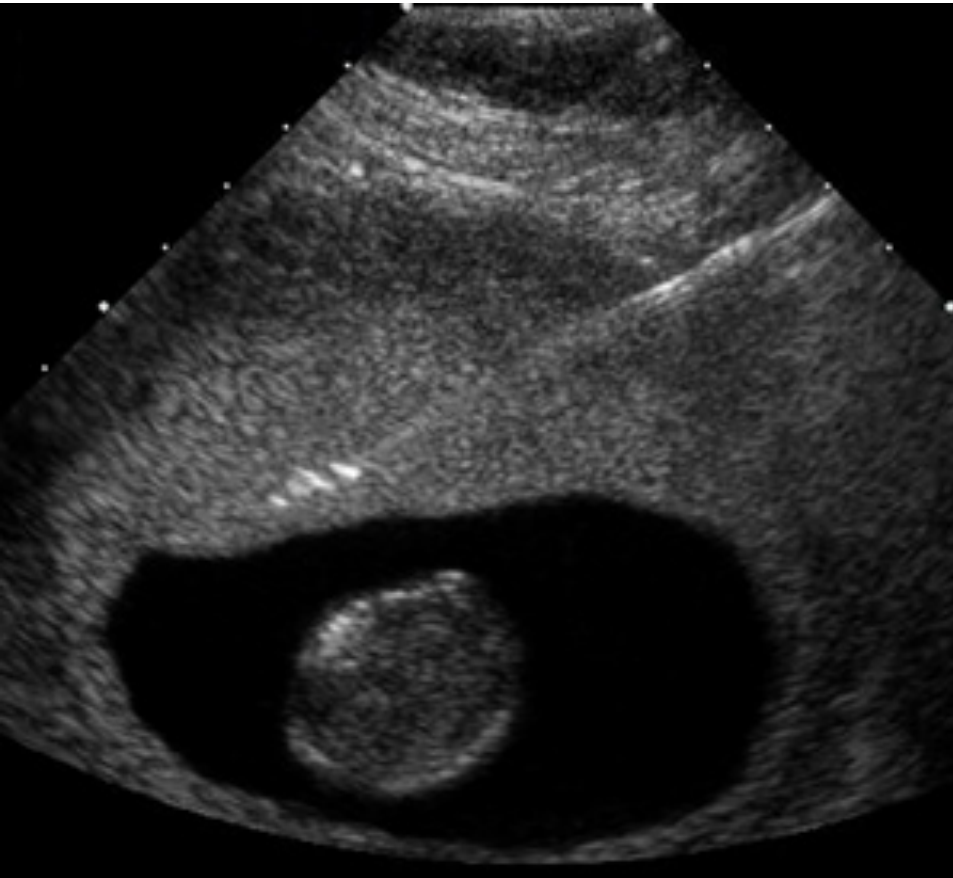
Prenatal Genetic testing

- 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

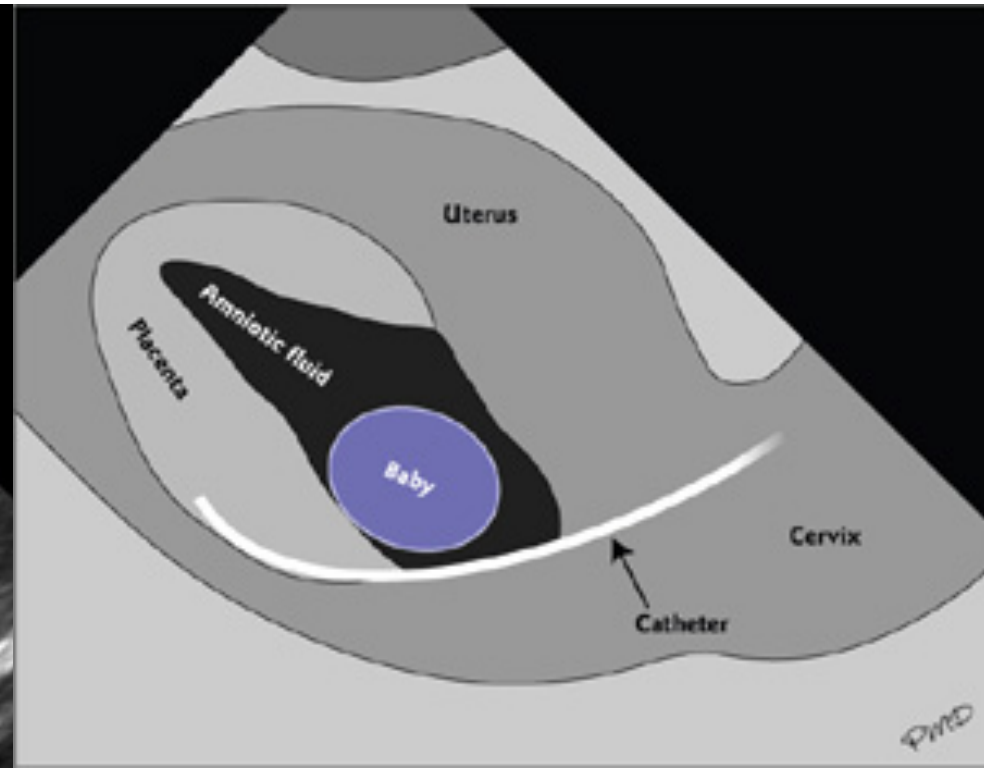
Chorionic Villus Sampling



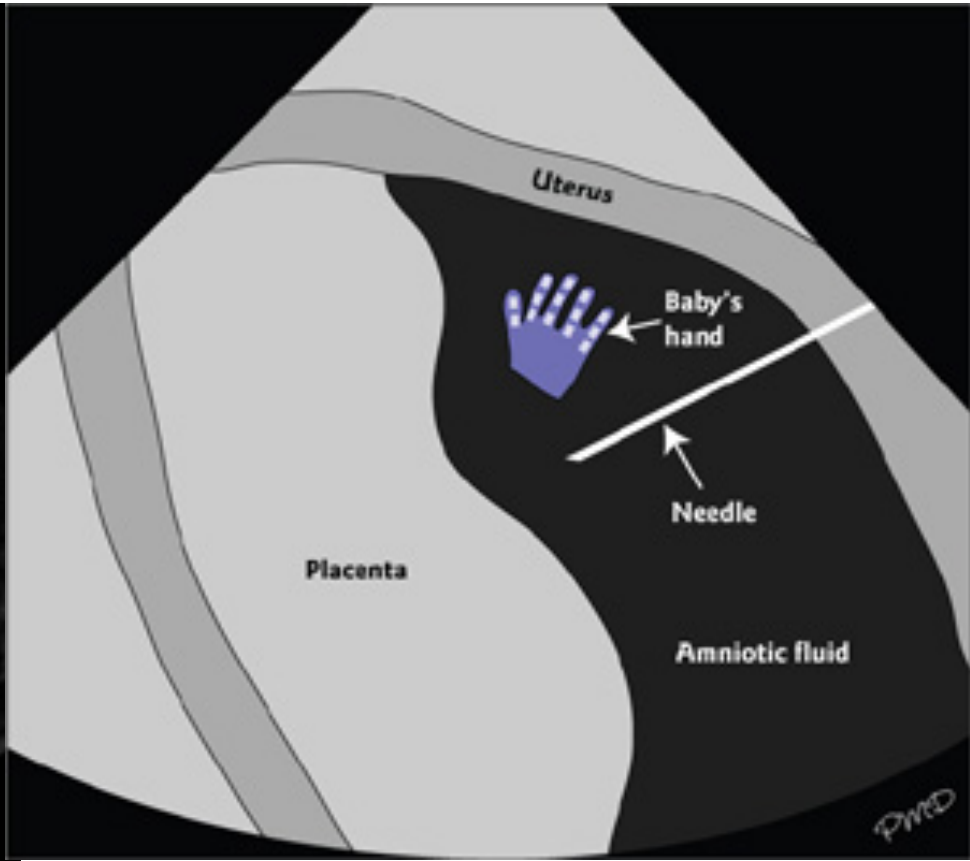
Chorionic villus sampling



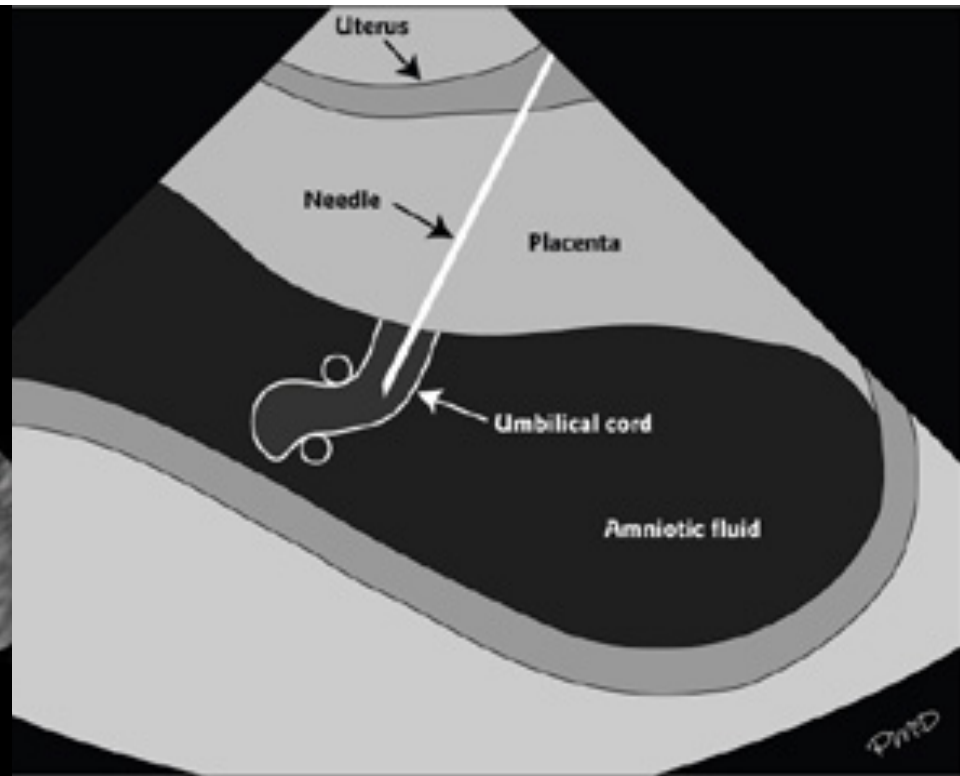
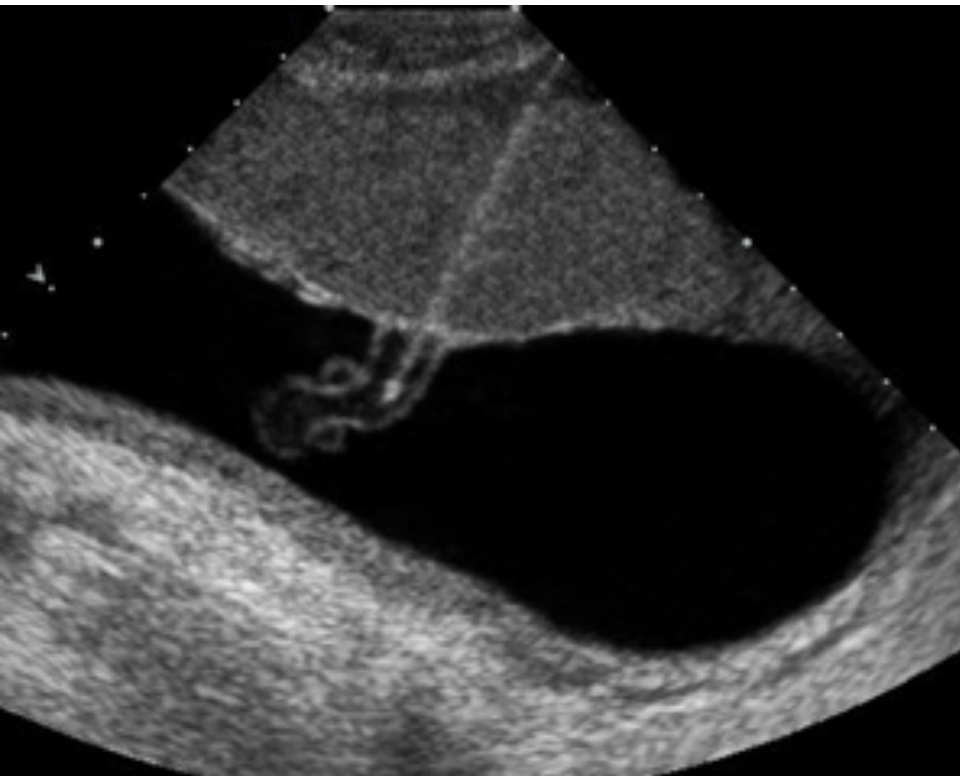
Chorionic villus sampling



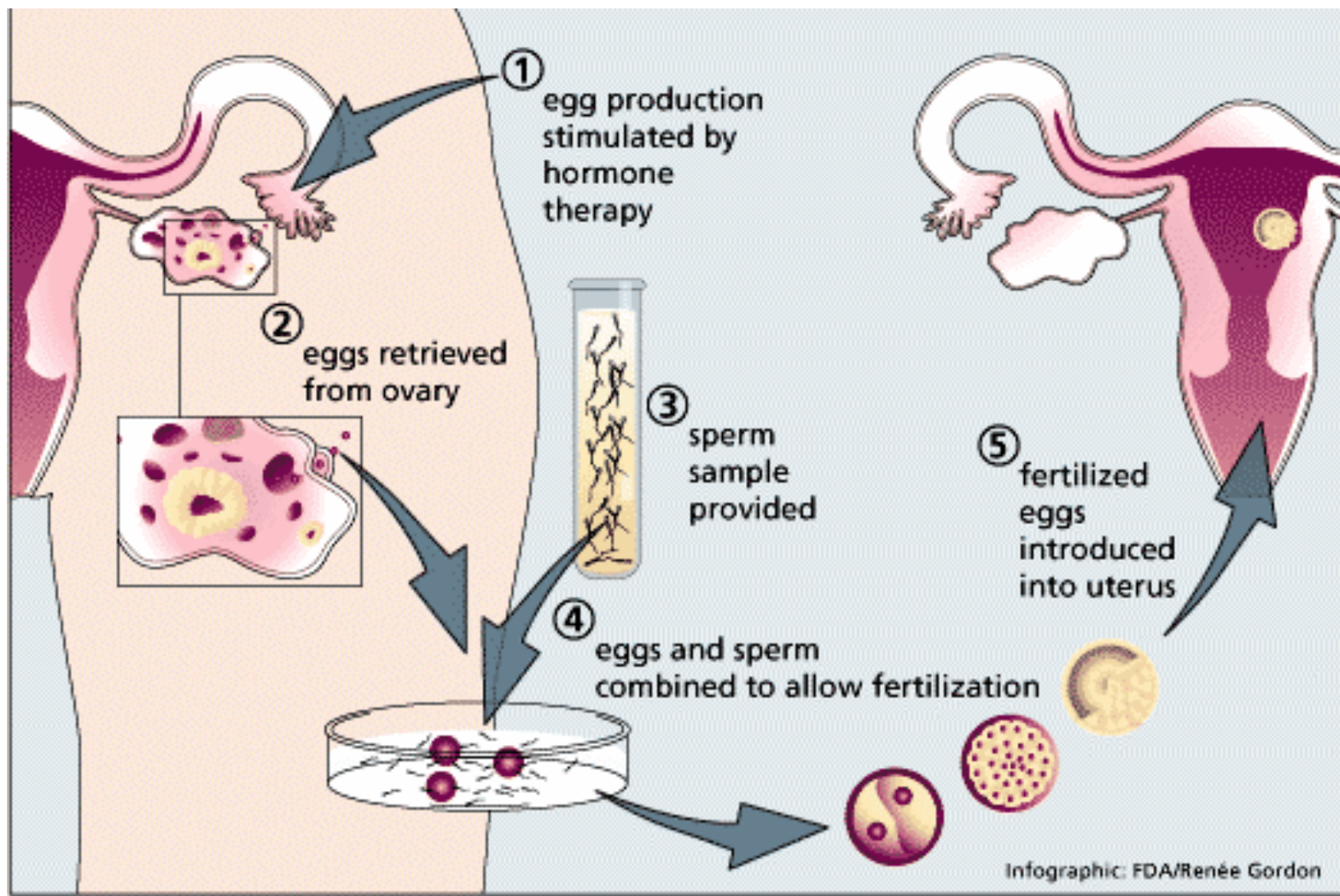
Amniocentesis



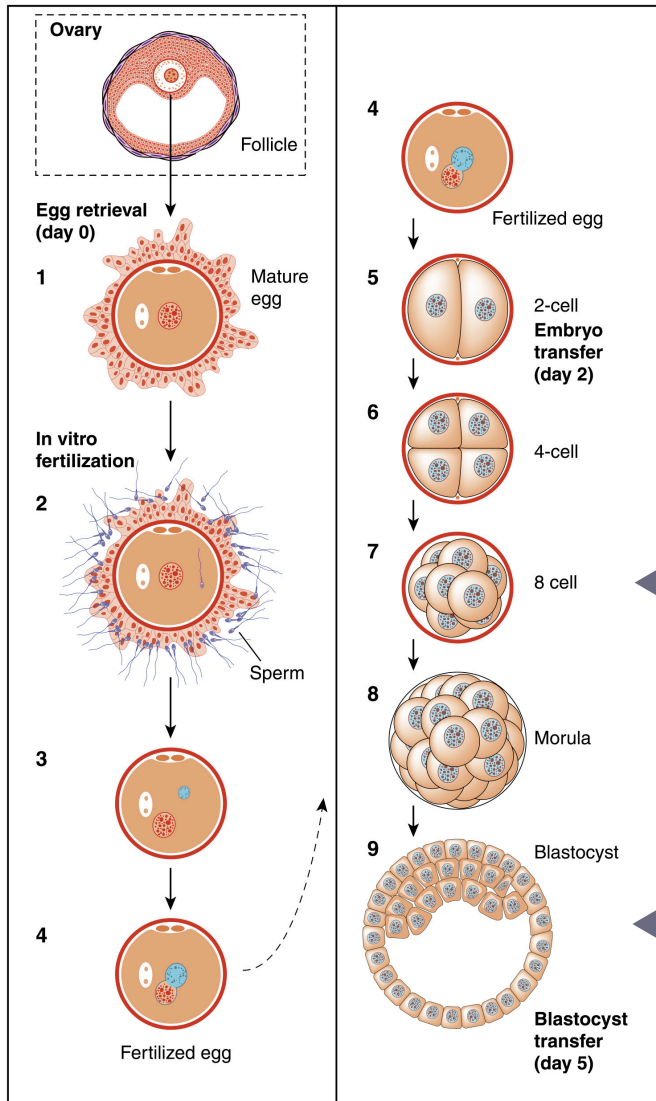
Umbilical blood sampling



In vitro fertilization



Pre-implantation Genetic Diagnosis



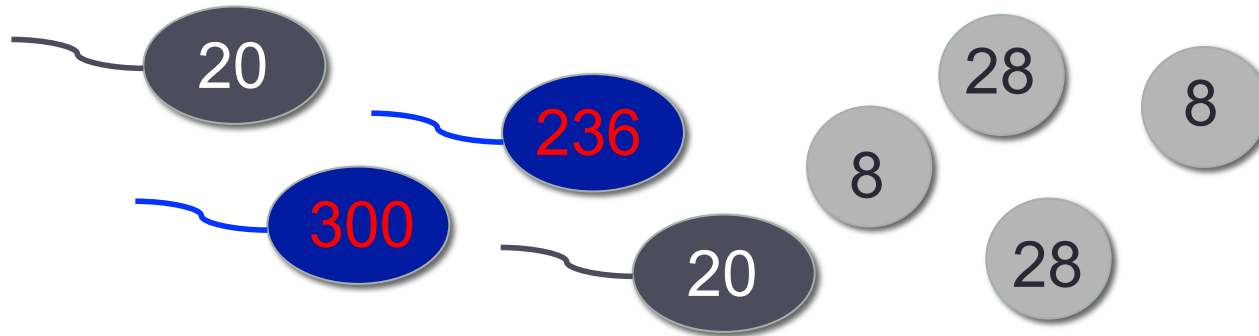
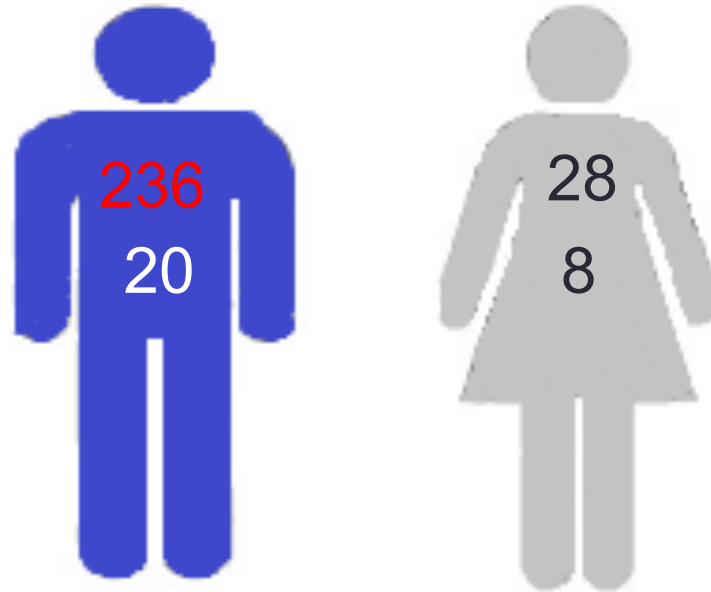
- 1-2 cells from each embryo are removed
- Each tested by PCR (polymerase chain reaction)
- Can freeze embryos while awaiting gene test results

Preimplantation Genetic Diagnosis

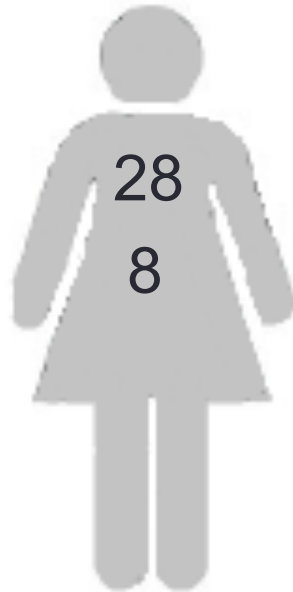


<http://www.xtimeline.com/evt/view.aspx?id=101848>

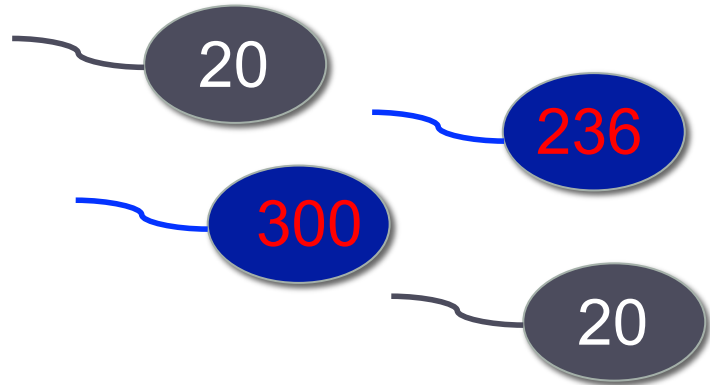
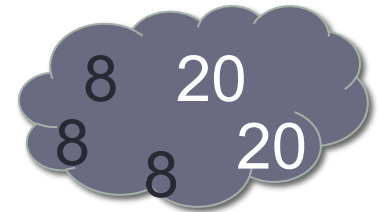
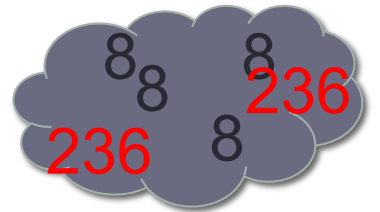
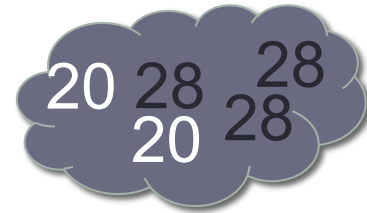
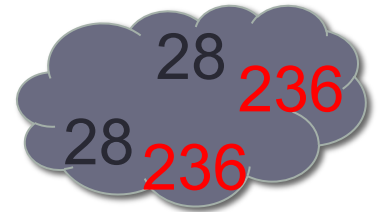
Preimplantation genetic testing



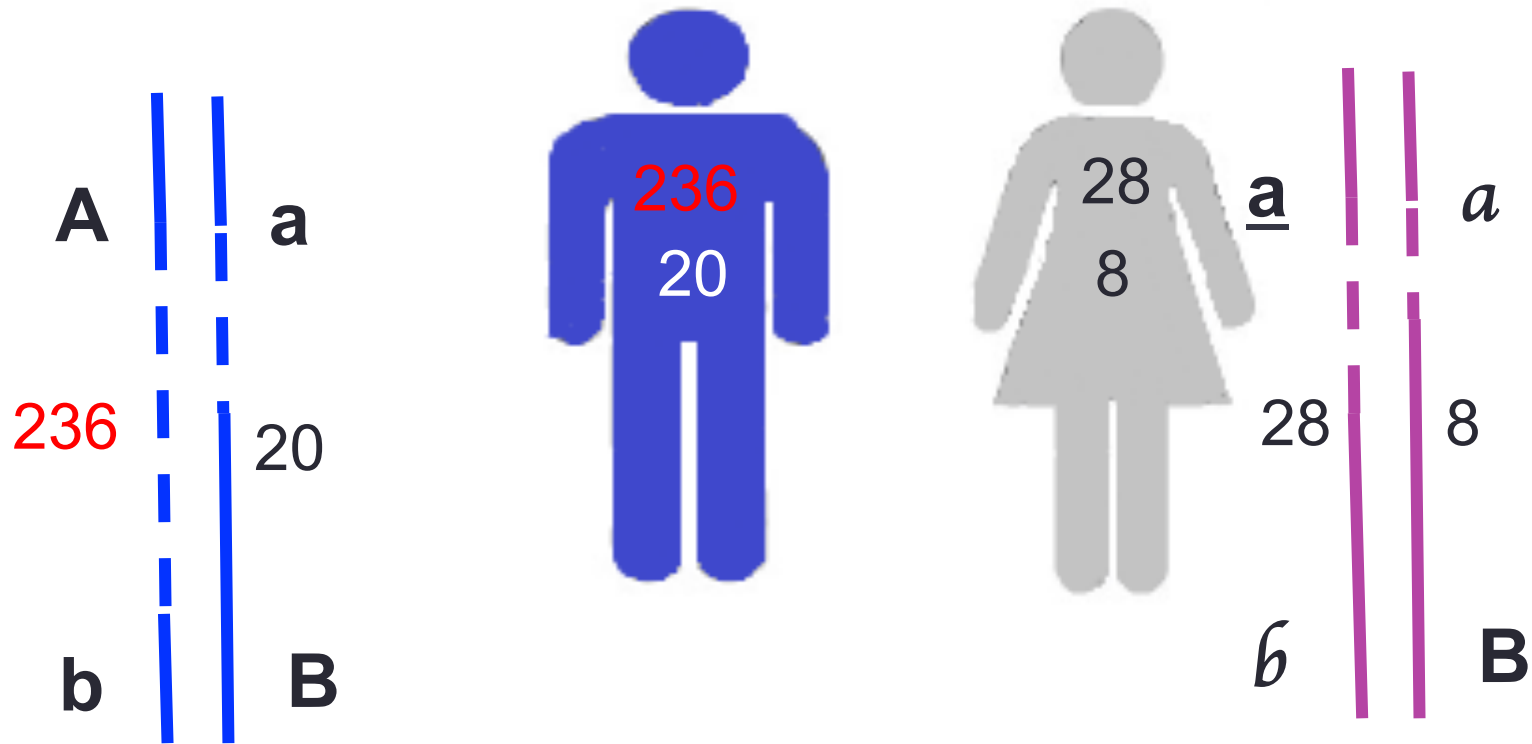
Preimplantation genetic testing



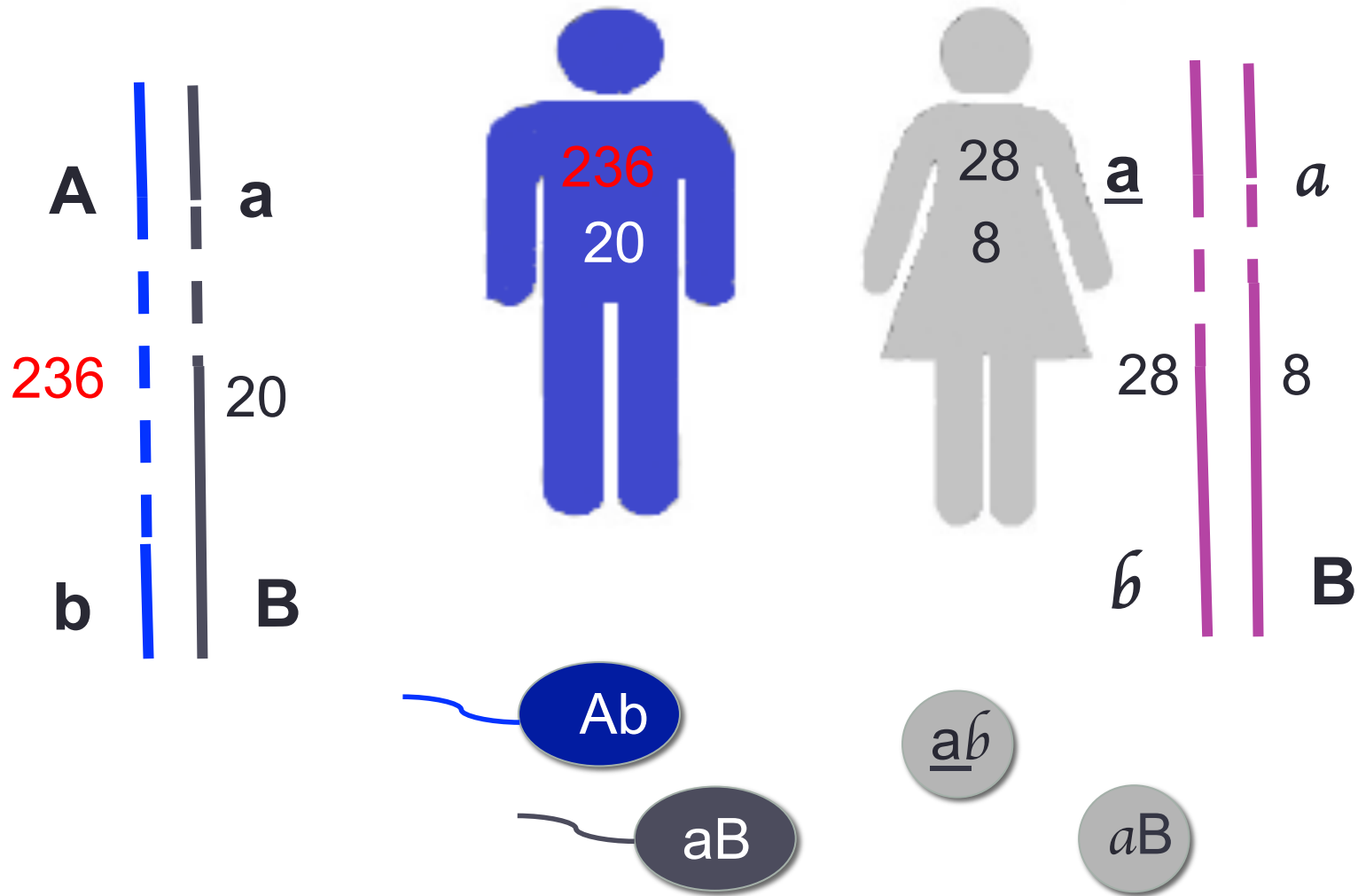
PCR
amplification
→



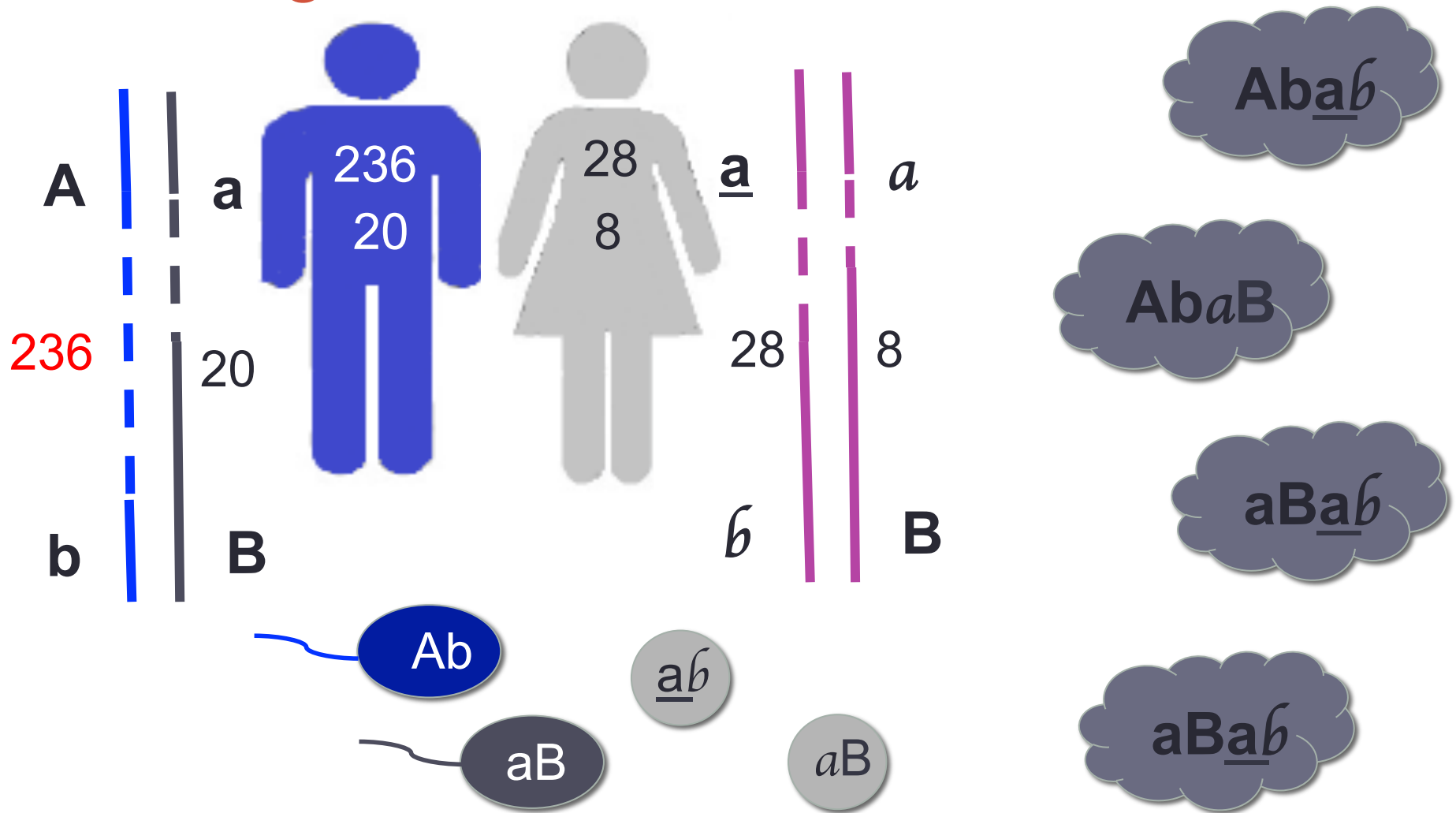
Preimplantation genetic testing



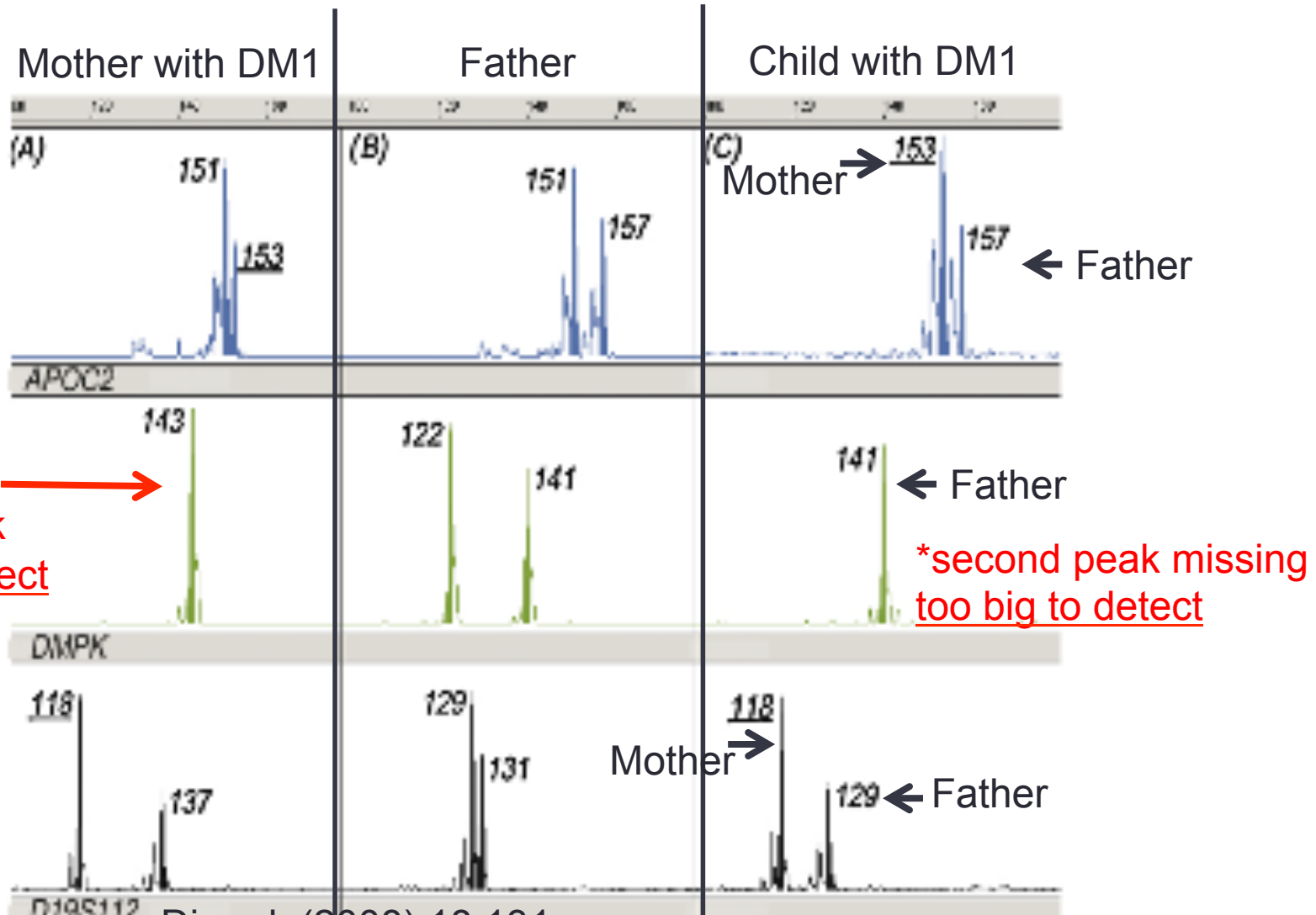
Preimplantation genetic testing



Preimplantation genetic testing- flanking markers

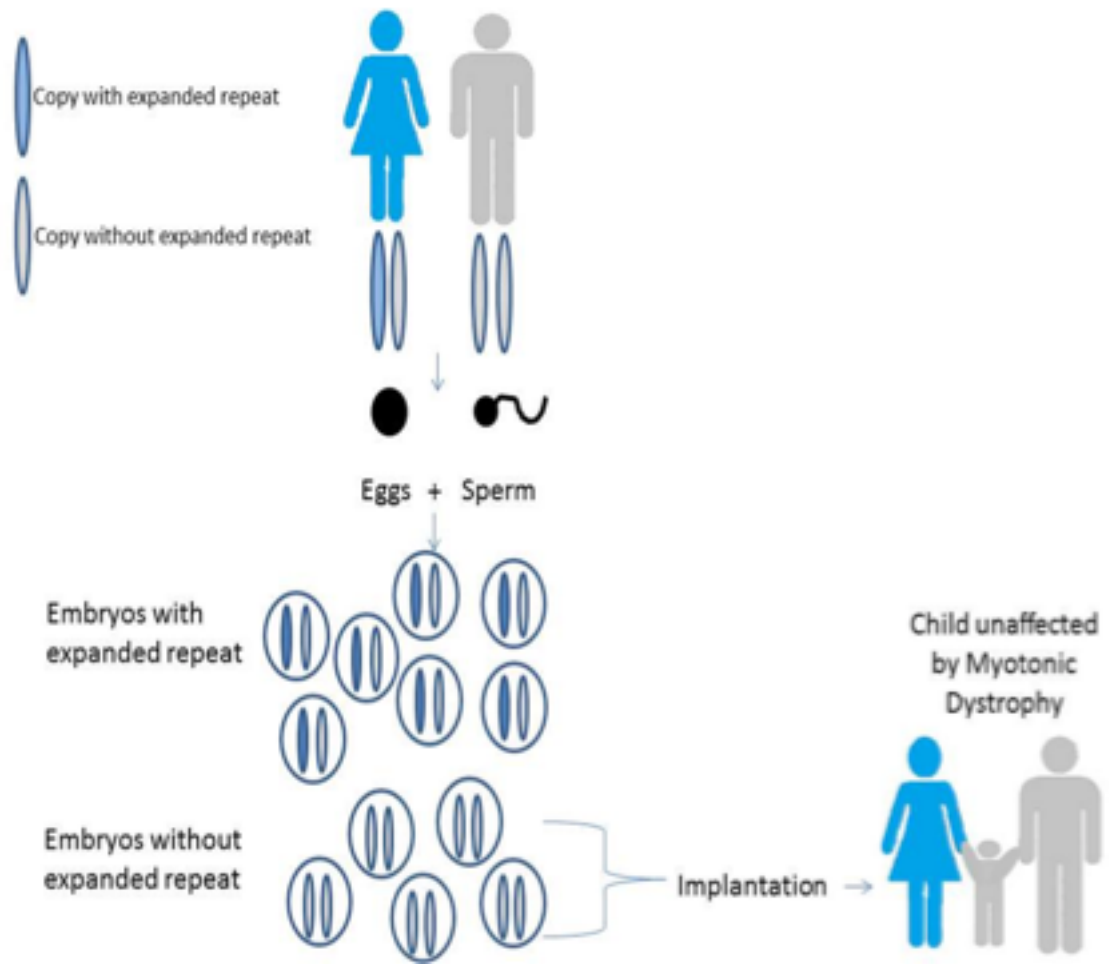


Example of PCR for flanking markers



Only 1 peak →
*second peak
too big to detect

*second peak missing
too big to detect



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)

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.

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%

Awater et al Eur J of Ob. & Gyn. & Reprod Biol. 2012; 162:153

Rudnick-Schoneborn et al. Neurology 2006;66; 579

Myotonic Dystrophy Type 2 and pregnancy risks

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

Awater et al Eur J of Ob. & Gyn. & Reprod Biol. 2012; 162:153

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>

<http://www.fertilitylifelines.com/payingfortreatment/state-mandatedinsurancelist>.

IVF- 34 years of progress



A DM blog <http://apgdblog.blogspot.com>

The screenshot shows a Blogger blog page with a blue header. The main title is "A PGD blog". Below the title is a paragraph: "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!". A navigation menu contains buttons for Home, Contact me, About me and my blog, IVF History/key posts, Myotonic Dystrophy, My symptoms, PGD, Disclaimer, Infertility links, Disability links, Counselling, and Blogroll. A short paragraph follows: "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." The main content area features a post dated "FRIDAY, 6 JULY 2012" titled "Trying to crawl". The post text reads: "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." Below the text is a photograph of a baby with bright blue eyes sticking its tongue out. To the left of the post is a sidebar with a photo of a family and the text "OUR COMPLETE FAMILY" and "Courtesy of Sheffield Telegraph". Below that is an "ABOUT ME" section with a photo of a woman and the name "Shona". To the right of the post is another sidebar with a "Top Health Blogger" badge, a "WellSphere" logo, a search bar, and a "BLOG ARCHIVE" section listing months from 2012 to 2011.

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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!

Home Contact me About me and my blog IVF History/key posts Myotonic Dystrophy My symptoms
PGD Disclaimer Infertility links Disability links Counselling Blogroll

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



Courtesy of Sheffield Telegraph

ABOUT ME



Shona
In 2006, I found out I had got Myotonic dystrophy, Type 1. This blog is about coping with this bombshell and how

FRIDAY, 6 JULY 2012

Trying to crawl

Like Be the first of your friends to like this.

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.



Top Health Blogger

WellSphere

SEARCH THIS BLOG

Search

BLOG ARCHIVE

- ▼ 2012 (9)
 - ▼ July (2)
 - Trying to crawl
 - Dexter
 - ▶ June (1)
 - ▶ May (3)
 - ▶ March (1)
 - ▶ February (1)
 - ▶ January (1)

Conclusions- ask your medical team

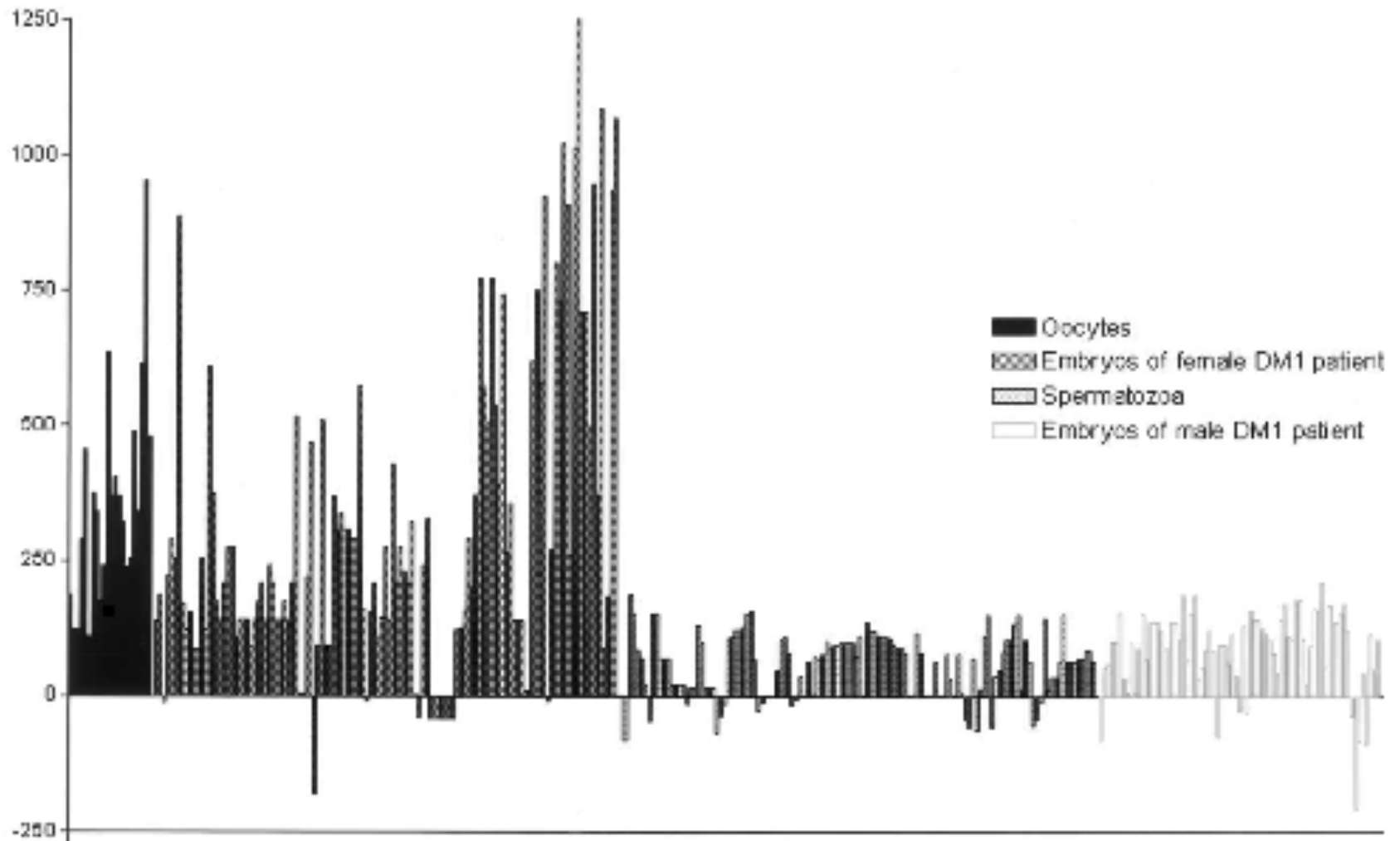
You have the right to have information to make decisions about your health and family planning

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

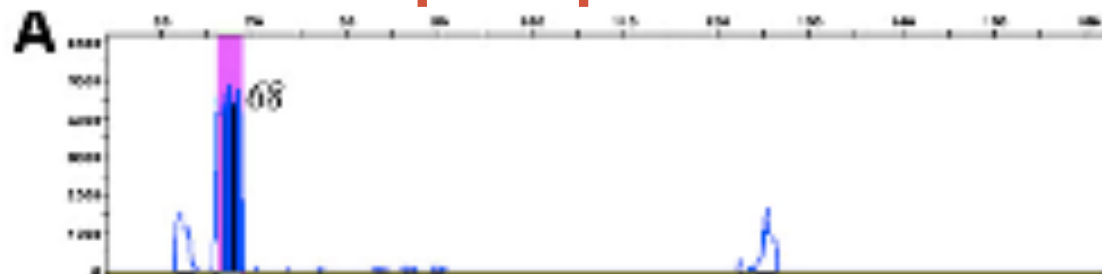
Acknowledgements

- Allie Copeland- artwork, brochure

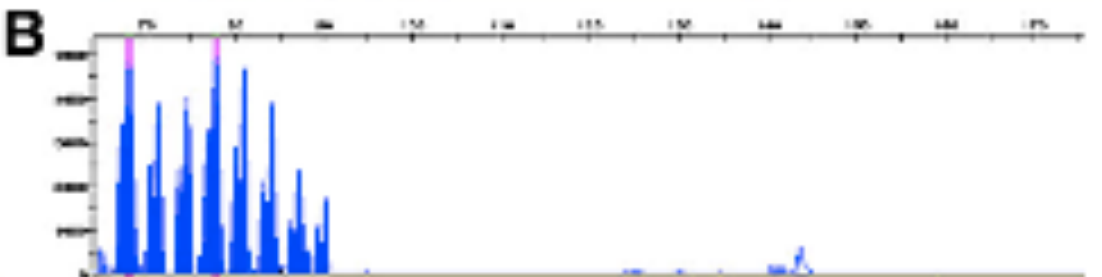
Repeat expansions



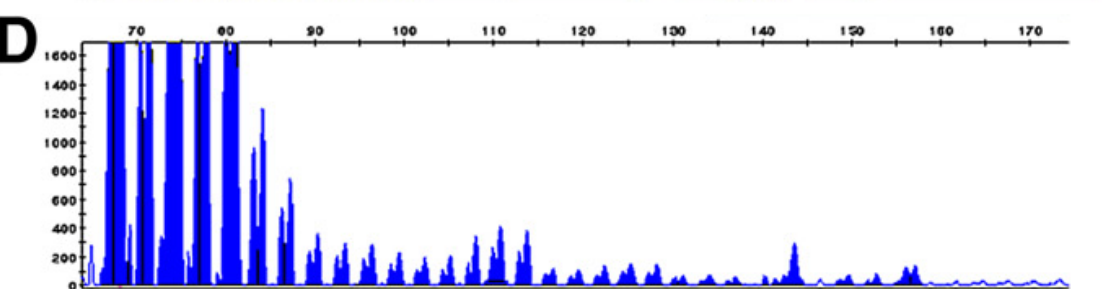
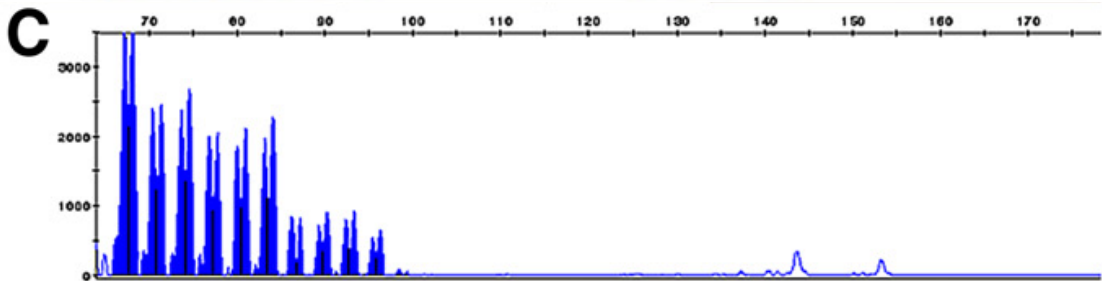
New triple primer PCR method

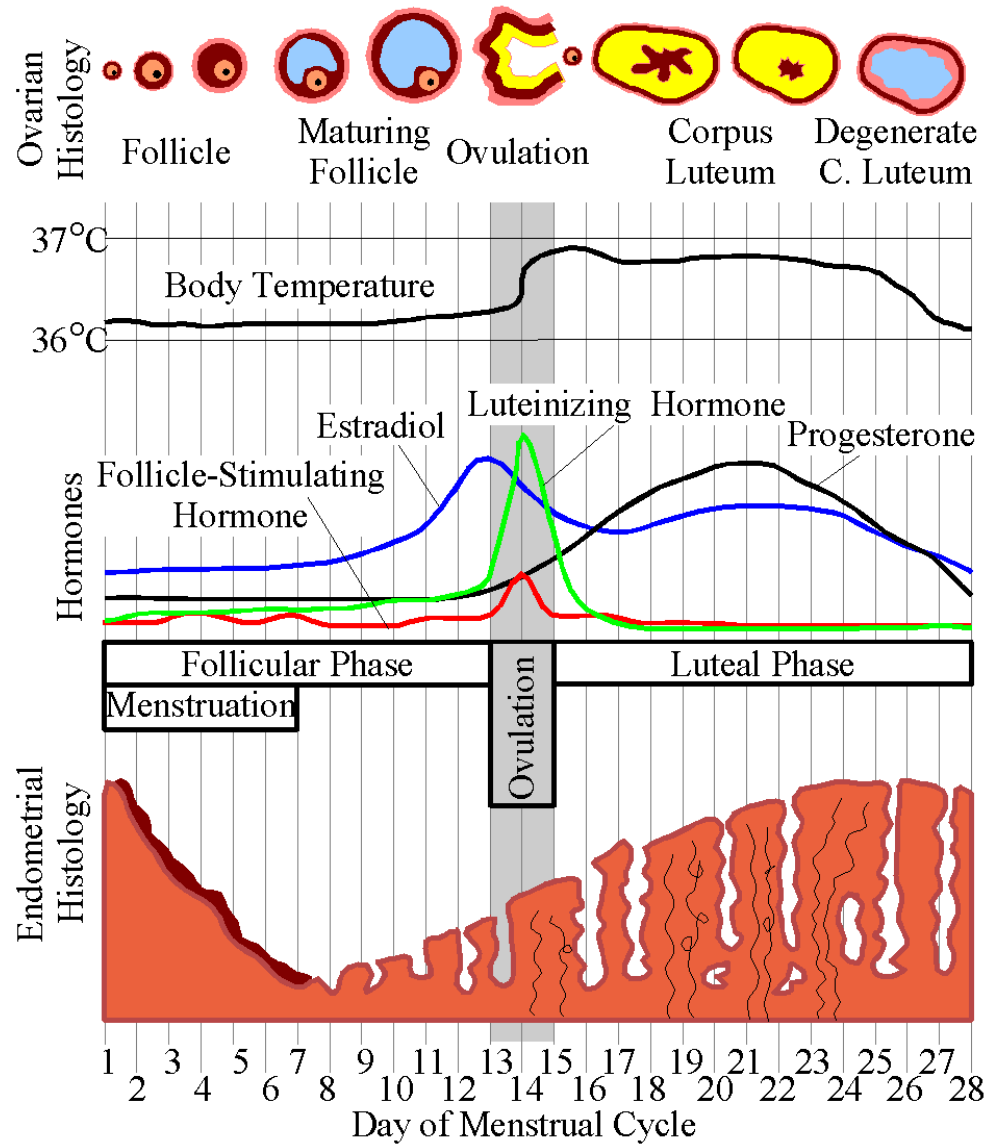


2 copies of 5 repeats



2 copies of 12 repeats





(Average values. Durations and values may differ between different females or different cycles.)