Genetic Counseling:
What is it?
Who does it?

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Genetics
THE FUTURE IS NOW
New breakthroughs can cure diseases and save lives, but how much should nature be engineered?
ONCE YOU UNFOLD ONE OF THESE THINGS, IT'S NEVER THE SAME.
How many genes do we have in our genome?

About 25,000
How many genetic disorders arise from changes in one or more of these genes?

~5,000
How many genetic diseases or disorders can be tested for?
Incidence/prevalence of some genetic conditions

- 0.3% of liveborns are aneuploid

- Down syndrome = Trisomy 21
  (1/600-700 live births)

- Sex chromosome aneuploidies
  47 XXX, 47 XXY, 47 XO

- Rare translocations, large deletions, insertions, etc

- Alcorp.com
  Hassold and Hunt Nature Review Genetics 2001
Incidence/prevalence of some genetic conditions (cont.)

- Cystic fibrosis (1/2500 Caucasian Americans; 1 in 25 are carriers)
- Fragile X syndrome (1/1,000 males have FXS, and 1/260 female are “carriers” with 30% having MR)
- Sickle cell disease (1/500 of African American births; 1 in 12 are carriers)
- Tay Sachs disease (1/3,000 birth of Ashkenazi Jewish heritage; 1 in 30 are carriers)
- Hemochromatosis (1/450 individuals)
- Breast cancer (1/8 women of which 5-10% of will have a inherited genetic predisposition)

http://www.kumc.edu/gec/prof/prevalence.html
Other statistics

- 50% of mental retardation has a genetic basis

- 5-10% of all cancers are related to an inherited susceptibility and 100% of all cancers are genetic

- 10% of the chronic conditions (including heart disease, late-onset insulin dependent diabetes, and arthritis) have a genetic component
Genetic testing and genetic counseling

Why would anyone want to undergo genetic testing?

If you did want to get tested, how would you get tested? Who would provide you with information before getting tested and obtain consent?
Look, lady - you’re the one who asked for a famous movie Star with dark hair, strong nose and deep set eyes.....
Who will tell you your test results and (hopefully) interpret them for you?

What will you do with the results of the genetic test?

Who can help you make the best decision for you?
Genetic Counseling is the practice of helping individuals and families understand the medical, psychological, social and reproductive implications of genetic and congenital conditions.
Elements of the practice of genetic counseling include:

1- **Assessment** of the chance for recurrence or occurrence of a condition, after **information gathering** and **establishing/verifying the diagnosis**

2- **Education** (information giving) about inheritance, natural history, testing options, medical management, prevention, social support and research, and

3- **Counseling** and psychological support to help clients adapt to their situation and choices, and to the psychological, familial and social issues that stem from the risk or condition in the family.
Providers of genetic counseling

- Masters-level genetic counselors
- MD geneticists
- Genetic nurse clinicians
- Other genetic sub-specialists (PhD geneticists, etc.)
Genetic counselor work settings: Clinical

- prenatal clinics
- pediatric clinics
- specialty clinics
- adult genetic clinics
- cancer clinics
- general genetics clinics
Genetic counselor work settings: Non-clinical

- research/clinical trials
- diagnostic laboratories
- biotech/pharmaceuticals
- public health/health policy organizations
- education
- infertility clinics/cryobanks
Information gathering: many types of information

To verify/confirm the dx and assess an accurate genetic risk:

- family history/pedigree
- medical records: lab reports, pathology reports, genetics exams
- medical literature
- death certificates
- family photos
Dirk brings his family tree to class.
Common information obtained in a 3-4 generation pedigree

Any relatives (including proband) who have:
- congenital anomalies (e.g. cleft lip, deafness, heart defect, etc.)
- chronic conditions (e.g. lung infections, immunological problems, etc.)
- psychiatric disorders (e.g. schizophrenia, manic depression, etc.)
- mental retardation, developmental delays
- dysmorphic features (e.g. low set ears, unusual shape of head, etc.)
- cancers (especially having an early age of onset)
- other notable health concerns
- stillbirths, multiple miscarriages or infertility
- consanguinity
- ancestry/ethnic background
Sample 3-generation pedigree

Key:
- Pyloric Stenosis
- CF carrier (delta F508)
Risk Assessment

- Mendelian risk- Using degree of relatedness to assess risk of inheriting a trait that is inherited in a Mendelian fashion (AR, AD, XL)

- Bayesian Analysis- Using Bayes theorem to adjust a Mendelian risk by taking into account other information from different sources (age of onset, enzyme levels, number of healthy children etc.)

- Empiric Risk- Using population statistics of similar families to assess risk
Sample pedigree for risk assessment

Genetic:
- AMA: 36 yo
- Recurrent miscarriage
  ?translocation carrier
- CF
  Risk of carrier: 1/2 & 1/25
- Pyloric stenosis
  ~1% based on empiric risk

Psychosocial:
- Mother’s SAB pattern
Traditional Jewish law instructs that if a woman’s first two sons bleed to death following circumcision, subsequent sons shall not be circumcised. Similarly, if the first sons of three sisters so die, subsequent sons of all sisters shall not be circumcised.


(Taken from Weil, J. Psychosocial Genetic Counseling. Oxford University Press, New York, 2000)
Information giving/education

May include:

- what the diagnosis is and how the diagnosis was made
- what the genetic risk is and how it was assessed
- the natural history of the condition
- the inheritance pattern of the condition
- recurrence risks and risks to other relatives
- treatment/management options
- testing options (prenatal, carrier, confirmation) and results
- research options
- resources
It's like this, Mrs. Cameron. The results are negative, but that doesn't mean not positive, exactly. Nor is it not negative, we wouldn't want a double negative there, would we ...
Counseling + psychosocial support

Psychological dilemmas, emotions, and reactions commonly encountered in genetic counseling:

- anger
- denial
- disbelief
- grief & mourning
- shattered expectations of normality
- intellectualization
- displacement (blame)
- anxiety
- guilt
- shame
- fear
- helplessness
- rationalization
- hopelessness
- fatalism

"This is your side of the family, you realize."
Psychological implications

- change in perception of self
- change in family belief systems
- challenge to religious beliefs
- change in social functioning
- marital/relationship discord
- search for meaning
Other issues to consider in genetic counseling

- Timing of genetic counseling
- Dysfunctional or complex family dynamics
- Client culture
- Language
- Client age and educational level
- Client learning styles
Common ethical issues for families

- Right to know/right *not* to know
- Sharing of information
- Coercion
- Privacy
- Reproductive decision making
- Testing of minors
Cases

The genetics may be straightforward, but addressing the family concerns may not be...
Indications for genetic counseling: Adult

Individuals concerned about their risk of:

- having a genetic condition (child of parent with HD)
- having a predisposition to a genetic condition (family history of breast cancer)
- carrying a genetic condition (sister of male with FraX)
A 50 yo woman, LM, was referred to genetic counseling because she has a family history of Huntington disease and is interested in pre-symptomatic testing (she had no symptoms).

The genetic counselor met with the LM and took a 3-generation genetic family history. Her mother and maternal grandmother are diagnosed with HD.
Case 1: Timing of testing
Huntington Disease: A brief review

- A progressive disorder of motor, cognitive and psychiatric disturbances that is inherited in an autosomal dominant fashion, with anticipation seen in paternal transmissions.

- Is found in all populations and has a prevalence between 1-15/100,000

- Generally has an adult age of onset (mean age of onset is between 35 and 44 years)

- The median survival time after symptoms appear is generally between 15 and 18 years.
Why have testing now?

Studies show that people who have pre-symptomatic testing often have it at times of family transitions (getting married, starting a family, planning for retirement, etc.)

LM is 50yo and states that she wants her test results to be her son’s (SM) wedding gift.

LM states that she is certain that she did not inherit it because she resembles her father’s side of the family.
What does the GC do?

-gently dispel the notion that if you resemble a family member you share his/her genetic fate.

-reiterate LM’s risk of 50% and encourage her to “plan for the worst” by taking her through all of the possible testing result scenarios, including a positive test result for an HD mutation.
Outcome

LM processed the information and reconsidered her options.

She decided to delay testing until after her son’s wedding, saying that it would be important information for him to have before he started his family, but that his wedding day was about celebrating his marriage.
Case 2: Adult re. family communication

SH, a 30 yo Caucasian woman has genetic counseling because she is concerned about her cancer family history.

A 3-generation cancer genetic pedigree is taken. It is noted that her mother died of breast cancer at age 48 years and her maternal grandmother died of ovarian cancer at age 36 years. In addition a maternal aunt has breast cancer that was diagnosed at age 50 y.

Early onset (< 50 y) breast and/or ovarian cancer suggests a familial predisposition to breast/ovarian cancer.
Case 2: Pedigree

[Pedigree diagram showing relationships and ages of individuals, with certain family members marked as deceased (d. ov ca 36 y) and having breast cancer (dx br ca 50 y).]
Predisposition to breast/ovarian cancer: a brief review

- All cancers arise from genetic alterations

- About 5% to 10% of cancer is due to an inherited predisposition

- Certain hereditary or “germline” alterations increase cancer risk

- For family histories of breast and ovarian cancer, BRCA 1 and 2 testing is available. If a familial BRCA1 or 2 mutation is identified, BRCA testing can clarify lifetime cancer risk in asymptomatic relatives.
Testing for BRCA 1 and BRCA 2

- Ideal to test the individuals who have breast and/or ovarian cancer in a family to maximize likelihood of identifying a familial mutation (if one is present).

- SH’s maternal aunt is the best individual to test first- unless samples are available on either SH’s mother or maternal grandmother.

- No samples appear to be available on either SH’s mother or maternal grandmother. Testing SH’s maternal aunt is proposed.
Requesting testing

- SH’s aunt lives in Australia and SH has not been in touch with her for many years— not since SH’s mother died. They don’t have any relationship to speak of.

- SH is unsure how she would approach her aunt, a stranger, with this request.
- Discuss what SH is most worried about re: reconnecting with her aunt.

- Offer to draft a letter to the aunt/family outlining the issues and requesting testing, with the GC as the contact person.

- Offer to identify testing centers in Australia in anticipation of facilitating testing for the aunt.

- Try to identify samples from SH’s mother and grandmother in case any were overlooked for testing.
The Outcome

-SH and the GC drafted a letter together that SH sent to her aunt.

-SH’s aunt emailed SH and they reconnected. The aunt was happy to have testing; she had been thinking about it given her family history and thought the information would be useful to her son before he started his family.

-A BRCA1 mutation was identified in the aunt.

-SH had BRCA1 testing for the familial mutation.

-SH did not inherited the BRCA1 mutation in her family.
Indications for genetic counseling: Prenatal

Pregnant women (& their partners):
- who are over 35 years at delivery

- who have abnormal MSS results or ultrasound findings

- who have been exposed to a teratogen

- who are at risk for having a child with a genetic condition

- who are from an ethnic group that has a high prevalence of carriers of specific genetic conditions
Other indications for genetic counseling in a prenatal setting

Individuals & couples who are experiencing infertility or recurrent miscarriage.

Individuals who are consanguineous.

Individuals who are concerned about having a child with a genetic condition or birth defect.
Case 3: Prenatal case re. making difficult decisions

LP, a 35 yo G2P0 Caucasian woman of Northern European ancestry has genetic counseling because of her age related risks of having a pregnancy with a chromosomal condition. Her partner is a 36 yo Caucasian male, also of Northern European ancestry.

A 3-generation genetic pedigree is taken. Apart from the risk of being a cystic fibrosis carrier (given the Northern European ancestry) and the age related risk related to having a pregnancy with a chromosomal condition, there are no other significant genetic concerns noted.
Case 3: Pedigree

Northern European Ancestry

58 y  59 y

36 y  LP, 35 y  32 y

SAB
8 wk GA

16 wk GA  7 y  5 y
Genetic Risks

Northern European Ancestry:
- 1/25 CF carrier prevalence
- carrier screening for cystic fibrosis should be offered

Maternal age-related risks (at 35 y at delivery):
- 1/200 risk (at 16-18 weeks gestation) for a chromosomal condition
- prenatal screening (MSS) and/or testing (via amniocentesis) should be offered. The risk of miscarriage related to amniocentesis is 1/200.
Making a decision: to have screening/testing or not to

-LP is overwhelmed. The information that her pregnancy is considered to be at elevated risk for a chromosomal condition was unexpected and caught her off guard.

-LP states that this is a very wanted pregnancy. She had had a miscarriage 18 months earlier and was very happy to discover she was pregnant again.

-LP can’t decide what to do. Her risk of having a pregnancy with a chromosomal condition (1/200) is the risk of miscarrying the pregnancy due to having the amniocentesis

-LP goes back and forth listing the reasons to have testing and then listing the reasons not to have testing. She can’t make a decision and is going in circles.
What does the GC do?

- Confirm that LP is aware of all of the options available to her (their risks and limitations): MSS screening, prenatal testing via amnio, or no testing

- Explore with LP how important it is for her to know the chromosomal status of the pregnancy (what would she do with the information?)

- Explore with LP how she has made difficult decisions in the past (what coping strategies and resources does she have? Would discussing her options with someone she trusts—her partner or family—help her?)
- Explore with LP if there is a possible “compromise” strategy- perhaps doing screening (MSS and ultrasound) to gain some information, and then reassess the option of diagnostic testing later.

- Normalize LPs indecision- many people find it difficult to make these kinds of decisions. There is no “right” or “wrong” decision.
The outcome

- LP states that she likes the “compromise” strategy, and she makes an appointment for MSS and an ultrasound for the next week.

- LP states that if the MSS or Ultrasound show anything suggestive of a chromosomal condition, she and her partner will discuss having the amnio at that time- “she’ll cross that bridge when she gets to it.”

- LPs MSS results came back “negative” (meaning risk for trisomy 21, 18 and ONTD’s are below the cut-offs) and the ultrasound was “normal”-showed no abnormal findings.

- LP decided not to have an amniocentesis; she didn’t think the risk warranted getting the information.
-LP had a healthy boy born at term.
In summary

Genetic Counseling uses the ever-increasing information and technology of contemporary science and applies it to human experiences that are age-old in their impact on individuals and societies. The science is contemporary, but the hopes, fears, and anxieties surrounding genetic disorders and birth defects remain unchanged.

Jon Weil, 2001
Resources

- National Society of Genetic Counselors (www.nsgc.org)
- Canadian Association of Genetic Counsellors (www.cagc-acccg.ca)
- Organization for Support Groups & Information: Genetic/Rare Conditions: sss.kumc.edu/gec/support/grouporg.html
- American College of Medical Genetics (www.acmg.net)
- CDC Genomics and Disease Prevention (www.cdc.gov/genomics)
- GeneTests/GeneClinics (www.genetests.org)
- Alliance of Genetic Support Groups: www.geneticalliance.org
- National Coalition for Health Professional Education in Genetics (www.nchpeg.org)