WHAT IS GENETIC COUNSELLING AND WHY IS IT IMPORTANT?

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WITH SPECIAL THANKS TO SALLY BRECSONI, THE GENE MACHINE AND JUDITH TSIPIS FOR SHARING THEIR SLIDES FOR THIS TALK
HOW MANY GENES TO WE HAVE IN OUR GENOME?

• 20,000-25,000 GENES

HOW MANY GENETIC DISORDERS ARISE FROM CHANGES IN ONE OR MORE OF THESE GENES?

• AS OF APRIL 4, 2018, OMIM REPORTED 3,890 GENES KNOWN TO CAUSE A GENETIC DISORDER
HOW MANY GENETIC DISEASES OR DISORDERS CAN BE TESTED FOR?
INCIDENCE/PREVALENCE OF SOME GENETIC CONDITIONS

• 0.3% OF LIVEBORNS ARE ANEUPLOID
• DOWN SYNDROME = TRISOMY21
  • (1/600-700 LIVE BIRTHS)
• SEX CHROMOSOME ANEUPLOIDIES
  • FEMALE 47XXX 1/1000
  • MALE 47XXY 1/500-1000
  • FEMALE 45X0 1/2500
INCIDENCE/PREVALENCE OF SOME GENETIC CONDITIONS (CONT.)

- CYSTIC FIBROSIS (1/2500 CAUCASIAN AUSTRALIANS; 1 IN 25 ARE CARRIERS)
- FRAGILE X SYNDROME (1/1,000 MALES HAVE FXS, AND 1/260 FEMALE ARE “CARRIERS” WITH 30% HAVING ID)
- SPINAL MUSCULAR ATROPHY (4/1000 BIRTHS; 1 IN 90 AUSTRALIANS OF ANGLOSAXON ANCESTRY ARE CARRIERS; 1 IN 50 OF GERMAN ANCESTRY)
- HAEMOCHROMATOSIS (1/200-400 INDIVIDUALS; 1 IN 9 AUSTRALIANS OF ANGLOSAXON ANCESTRY ARE CARRIERS)
- BREAST CANCER (1/8 WOMEN OF WHICH 5-10% OF WILL HAVE A INHERITED GENETIC PREDISPOSITION)
OTHER STATISTICS

• 50% OF INTELLECTUAL DISABILITY HAS A GENETIC BASIS

• 5-10% OF ALL CANCERS ARE RELATED TO AN INHERITED SUSCEPTIBILITY GENE AND 100% OF ALL CANCERS ARE GENETIC

• 10% OF THE CHRONIC HEALTH CONDITIONS (INCLUDING HEART DISEASE, LATE-ONSET INSULIN DEPENDENT DIABETES AND ARTHRITIS) HAVE A GENETIC COMPONENT
GENETIC TESTING AND GENETIC COUNSELLING

• 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 WILL YOU TELL AND WHO SHOULD KNOW?

• WHO CAN HELP YOU MAKE THE BEST DECISIONS FOR YOU?
GENETIC COUNSELLING

• GENETIC COUNSELLING IS THE PRACTICE OF HELPING INDIVIDUALS AND FAMILIES UNDERSTAND THE MEDICAL, PSYCHOLOGICAL, SOCIAL AND REPRODUCTIVE IMPLICATIONS OF GENETIC AND CONGENITAL CONDITIONS.
INDICATIONS FOR GENETICS REFERRAL

- A family history of a known genetic condition, birth defect or developmental delay.
- Increased risk on first trimester screening, non-invasive prenatal test.
- Anomalies observed on ultrasound scan.
- Abnormal CVS or amniocentesis result.
- Increased risk from teratogens.
- Consanguinity.
- Recurrent miscarriages.
- Parental bloods indicate thalassaemia.
GENETIC COUNSELLING PROVIDES:

- INFORMATION AND SUPPORTIVE COUNSELLING REGARDING THE DIAGNOSIS AND RISK FOR A GENETIC CONDITION IN THE FAMILY

- DIAGNOSTIC, CARRIER, PREDICTIVE AND PRESYMPTOMATIC GENETIC TESTING WHERE APPROPRIATE (INCLUDING PRENATAL)
ELEMENTS OF THE PRACTICE OF GENETIC COUNSELLING INCLUDE:

1. **ASSESSMENT** OF THE CHANCE OF 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

3. **COUNSELLING 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
GENETIC COUNSELLOR PROVIDERS & WORK SETTINGS

- PRENATAL CLINICS
- PAEDIATRIC CLINICS
- SPECIALTY CLINICS
- ADULT GENETIC CLINICS
- CANCER CLINICS
- GENERAL GENETICS CLINICS

- MASTERS-LEVEL GENETIC COUNSELLORS
- CLINICAL GENETICISTS
- GENETIC NURSE CLINICIANS
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, GENETIC EXAMINATIONS
  • MEDICAL LITERATURE
  • DEATH CERTIFICATES
  • FAMILY PHOTOS
DIRK BRINGS HIS FAMILY TREE TO CLASS.
COMMON INFORMATION OBTAINED IN A 3 GENERATION PEDIGREE

- ANY RELATIVES WHO HAVE:
  - CONGENITAL ANOMALIES (Eg. CLEFT LIP, DEAFNESS, HEART DEFECT, ETC)
  - CHRONIC CONDITIONS (Eg. HEART PROBLEMS, ANEURYSM, CANCER, ETC.)
  - PSYCHIATRIC DISORDERS (Eg. SCHIZOPHRENIA, DEPRESSION ETC.)
  - INTELLECTUAL DISABILITY, DEVELOPMENTAL DELAY, ASD
  - DYSMORPHIC FEATURES (Eg. LOW SET EARS, UNUSUAL HEAD SHAPE, SINGLE PALMER CREASE, EXTRA FINGERS OR TOES)
  - OTHER HEALTH CONCERNS
  - STILLBIRTHS, MULTIPLE MISCARRIAGES OR INFERTILITY
  - CONSANGUINITY
  - ANCESTRY/ETHNIC BACKGROUND
BASIC GENETICS & BACKGROUND ON GENETIC TESTING

ONCE YOU UNFOLD ONE OF THESE THINGS, IT'S NEVER THE SAME.
DNA, CHROMOSOMES & GENES
DNA – GENETIC BLUEPRINT

• DEOXYRIBONUCLEIC ACID (DNA)

• LOCATED IN THE NUCLEUS

• RAPPED UP IN STRUCTURES CALLED CHROMOSOMES.
46 Chromosomes - 23 Pairs in every cell

CHROMOSOMES
DNA IS MADE OF SEGMENTS CALLED NUCLEOTIDES

• THE BUILDING BLOCKS OF DNA ARE NUCLEOTIDES.

• THERE ARE 4 DIFFERENT NITROGEN BASES IN DNA AND THEY CAN VARY FROM ONE NUCLEOTIDE TO THE NEXT A G T C

• THE ALTERNATING BASES PROVIDE THE CODE
IN HUMANS, THE DNA MOLECULE IN A CELL, IF FULLY EXTENDED, WOULD HAVE A **TOTAL LENGTH OF 1.7 METRES**. IF YOU UNWRAP ALL THE DNA YOU HAVE IN ALL YOUR CELLS, YOU COULD REACH THE MOON ...6000 TIMES!
WHAT IS A GENE?

• A PART OF THE DNA THAT CODES FOR A PROTEIN.

• NOT ALL THE DNA CODES FOR PROTEINS.

• 25,000 GENES IN THE HUMAN GENOME.
GENETIC ALTERATIONS

• De novo
  • New change occurring at conception
  • Passed from a parent
  • May be variable
ABNORMAL NUMBER OF CHROMOSOMES

TRISOMIES - 3 COPIES RATHER THAN 2 COPIES OF A CHROMOSOME

MONOSOMIES – 1 COPY RATHER THAN 2
CHROMOSOMAL ABNORMALITIES

- **DELETION**: A SECTION IS MISSING
- **DUPLICATION**: AN EXTRA SECTION OF CHROMOSOME
- **INVERSION**: A SECTION GETS SNIPPED OFF AND REINSERTED THE WRONG WAY AROUND.
- **TRANSLOCATION**: A SECTION SHIFTS FROM ONE CHROMOSOME ONTO ANOTHER
- **MOSAICISM**: THE PRESENCE OF TWO OR MORE POPULATIONS OF CELLS WITH DIFFERENT GENOTYPES IN ONE INDIVIDUAL, WHO HAS DEVELOPED FROM A SINGLE FERTILIZED EGG.

The large number of autistic individuals with unaffected family members may result from spontaneous structural variation — such as deletions, duplications or inversions in genetic material during meiosis.
UNIQUE – UNDERSTANDING RARE CHROMOSOME DISORDERS

WE ARE UNIQUE!

Unique supports, informs and networks with families living with a Rare Chromosome Disorder or some Autosomal Dominant Single Gene Disorders associated with learning disability and developmental delay, among other symptoms. Sound like your family? Come and join us to help our understanding of these rare disorders. Just click on the Join Us button below.

JOIN US

https://www.rarechromo.org/
INHERITANCE

- All cells (apart from egg/spERM cells) have 46 chromosomes (23 pairs).

- One copy of each pair is inherited from the mother and the other from the father.
SEX CELLS

• SPERM AND EGG CELLS ONLY HAVE HALF THE NUMBER OF CHROMOSOMES (23)

• AT FERTILIZATION THE NUCLEUS OF A SPERM UNITES WITH THE NUCLEUS OF AN EGG TO PRODUCE A COMPLETE SET OF CHROMOSOMES (46).
INHERITANCE

- DOMINANT INHERITANCE
  - ONE COPY OF A GENE IS DOMINANT OVER THE OTHER

- RECESSIVE INHERITANCE
  - A GENE IS EXPRESSED ONLY WHEN BOTH COPIES ARE THE SAME

- X-LINKED INHERITANCE
  - A GENETIC FEATURE IS CARRIED BY THE X CHROMOSOME
    (FEMALES XX, MALES XY)
**SINGLE GENE DISORDERS**

**Single gene changes:** a small nucleotide change in a segment of the DNA that codes for a gene

- **AUTOSOMAL DOMINANT**
  - NEW VARIANT – DE NOVO
  - FAMILIAL

- **AUTOSOMAL RECESSIVE**
  - CONSANGUINITY

- **X-LINKED**
AUTOSOMAL DOMINANT INHERITANCE
CORNELIA DE LANGE SYNDROME

ACHONDROPLASIA

Peter Drinklage aka Tyrion Lannister
AUTOSOMAL RECESSIVE INHERITANCE

- Genetic carrier mother: Rr
- Genetic carrier father: Rr
- Eggs: R, r
- Sperm: R, r
- Non-carrier: RR
- Genetic carrier: Rr
- Affected: rr

1 out of 4 chance (25%)
2 out of 4 chances (50%)
1 out of 4 chance (25%)

Genealogical charts to illustrate autosomal recessive inheritance.
OCULO-CUTANEOUS ALBINISM
X-LINKED RECESSIVE INHERITANCE

Legend:
- $X^r$: recessive faulty gene on X chromosome
- $X^R$: working gene copy

Genetic carrier mother
- $X^r X^r$
- Eggs: $X^r$

Non-carrier father
- $X^R Y$
- Sperm: $X^R$

Genetic carrier
- $X^R X^r$
- Girls: 25% chance of having affected child

Non-carrier
- $X^R X^R$
- Boys: 25% chance of having affected child

Affected
- $X^r Y$

Pedigree 7. X-linked recessive inheritance.

1. I
2. 1
3. 2

II
1. 1
2. 2
3. 3
4. 4
5. 5
6. 6

III
1. 1
2. 2
3. 3
4. 4
5. 5
6. 6
COFFIN LOWRY SYNDROME
EXAMPLES OF GENETIC CONDITIONS

- ABNORMAL NUMBER OF CHROMOSOMES
  - DOWN SYNDROME, EDWARDS SYNDROME,
- DELETION
  - CRI DU CHAT, ANGELMAN SYNDROME
- SEX CHROMOSOME ABNORMALITIES
  - TRIPLE X SYNDROME, TURNER SYNDROME, KLINFELTER'S SYNDROME
- SINGLE GENE MUTATIONS
  - CYSTIC FIBROSIS, SICKLE CELL ANAEMIA, ANGELMAN SYNDROME, BREAST/OVARIAN CANCER SYNDROME
GENETIC TESTING FOR SPECIFIC CONDITIONS

1. TAKE A SAMPLE (BLOOD/AMNIOTIC FLUID, MOUTH SWAB)

2. USE STAINING OF CHROMOSOMES TO LOCATE ANY CHROMOSOME ABNORMALITIES

3. OR USE MATCHING DNA SEQUENCES TO DETECT GENE ABNORMALITIES
## TYPES OF TESTS

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<tr>
<th>Type</th>
<th>Description</th>
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<tr>
<td><strong>Diagnostic</strong></td>
<td>Used to confirm a diagnosis based on physical signs</td>
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<td>- GCH microarray – chromosome deletions or duplications</td>
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<td>- Genetic panels – single gene conditions</td>
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<tr>
<td></td>
<td>- Genomic testing – single gene conditions</td>
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<tr>
<td><strong>Predictive</strong></td>
<td>Used to detect gene variant associated with disorders that appear later in life</td>
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<td>- Variant must be known</td>
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<tr>
<td><strong>Carrier Identification</strong></td>
<td>Used by people with a family history of recessive genetic disorders</td>
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<td>- Variant must be known</td>
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<tr>
<td><strong>Prenatal</strong></td>
<td>Used to test a foetus when there is risk of bearing a child with mental or physical disabilities</td>
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<td>- Variant must be known</td>
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<tr>
<td><strong>Newborn Screening</strong></td>
<td>Used as a preventative health measure once the baby is born</td>
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<tr>
<td><strong>Research testing</strong></td>
<td>Used for finding unknown genes and identifying the function of a gene</td>
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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….
KEY ISSUES WITH GENETIC TESTING
COUNSELLING & PSYCHOSOCIAL SUPPORT

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

- ANGER
- DENIAL
- DISBELIEF
- GRIEF & LOSS
- SHATTERED EXPECTATIONS OF NORMALITY
- INTELLECTUALISATION
- DISPLACEMENT (BLAME)
- ANXIETY
- GUILT
- SHAME
- FEAR
- HELPLESSNESS
- RATIONALISATION
- 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
COMMON ETHICAL ISSUES FOR FAMILIES

• RIGHT TO KNOW/RIGHT NOT TO KNOW
• SHARING OF INFORMATION
• COERCION
• PRIVACY
• REPRODUCTIVE DECISION MAKING
• TESTING OF MINORS
"Eureka! I've discovered the gene that makes us think that everything's determined by genes!"