REPRODUCTIVE OPTIONS IN HEREDITARY CONIDTIONS

Jacqui Russell

Genetic and Metabolic Nurse Practitioner

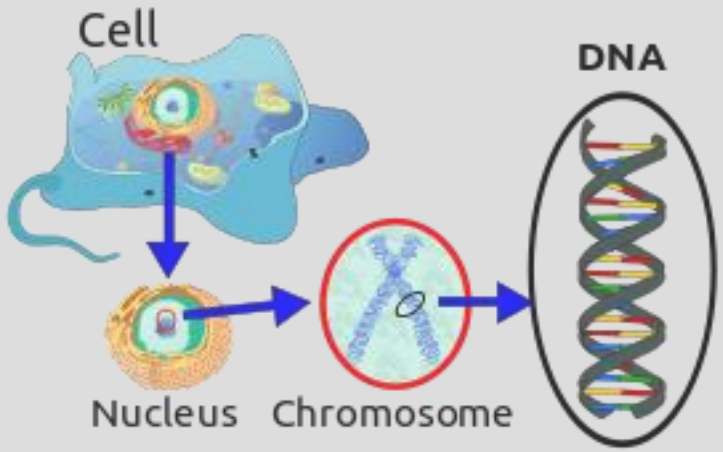
Sydney Children's Hospital Randwick

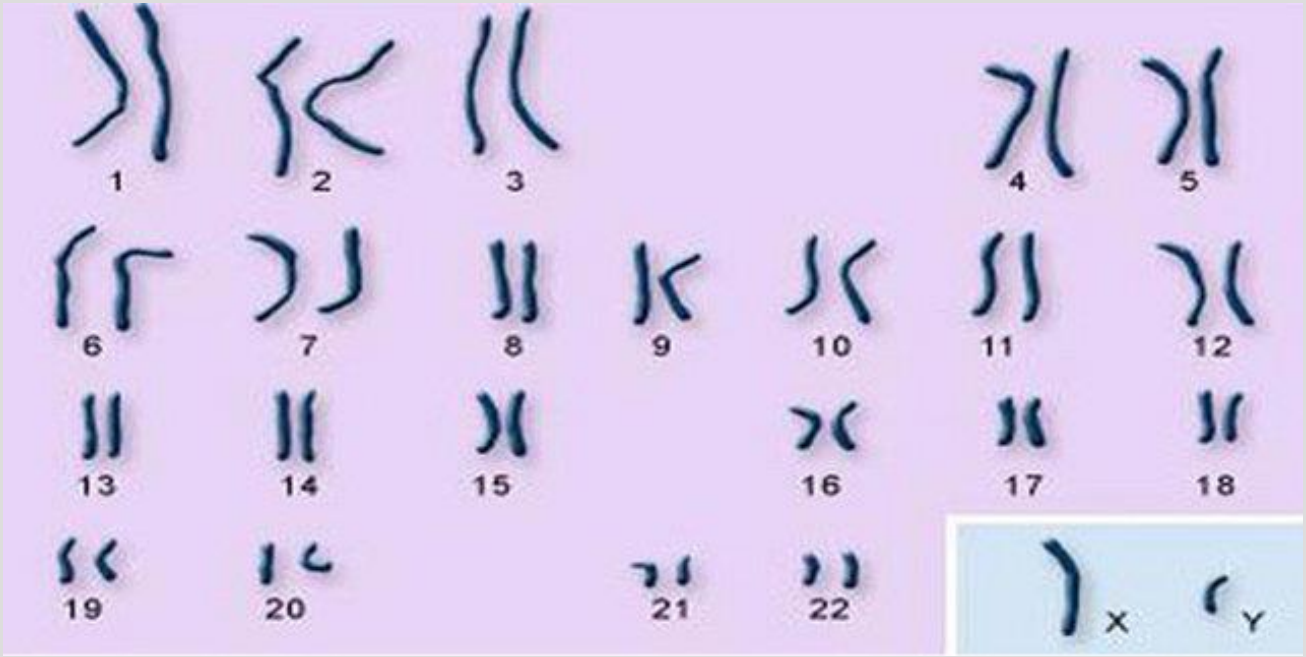
DNA

- The blueprint of life
- Recipe to make us who we are
- Inherited from our parents
- Shared with our relatives
- Sometimes the code is wrong
- Two types
  - Nucleic
  - Mitochondrial

NUCLEAR DNA

- Found in the nucleus
- Half from mum, half from dad
- Packaged as chromosomes
- 23 pairs
  - 22 pairs autosomes
  - 1 pair sex chromosomes
- 20,000 pairs of genes
- Pathogenic variants can cause neuromuscular disorders
- We all have 10-15 pathogenic variants


Cell
DNA
Nucleus
Chromosome


1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
X
Y

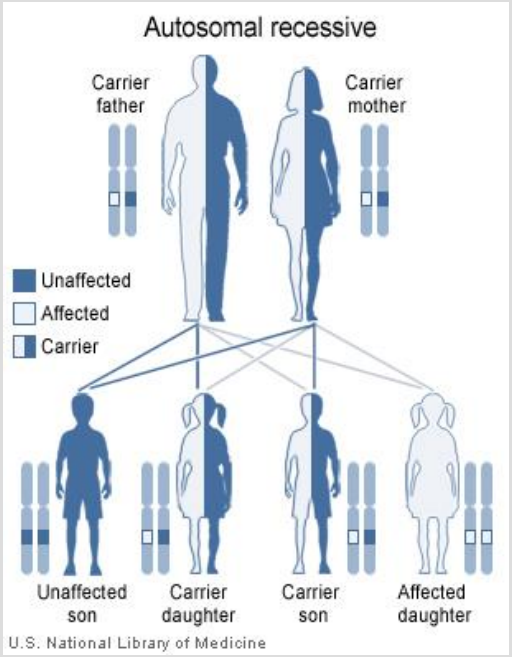
INHERITANCE OF NM DISORDERS

- Can be caused by pathogenic variants in the nuclear DNA
- Can be caused by different types of inheritance
- Can be genetic but not inherited
- Need to know the exact genetic change for accurate genetic counselling

AUTOSOMAL RECESSIVE INHERITANCE

- Need pathogenic variants in both copies of the gene to have the disorder
- Parents are both healthy carriers
- Equally likely for boys and girls to be affected
- 25% recurrence risk
- Usually no family history

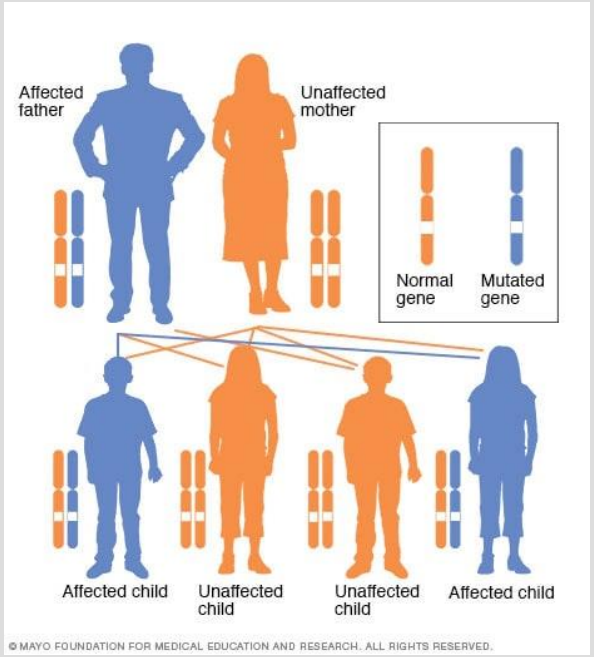
AR INHERITANCE



AUTOSOMAL DOMINANT INHERITANCE

- Need a pathogenic variant in only one copy of the gene (pathogenic variant is *dominant* over the good copy)
- Usually one parent is affected or can be a new mutation (de novo)
- Equally likely for boys and girls to be affected
- Up to 50% recurrence risk
- Often a family history

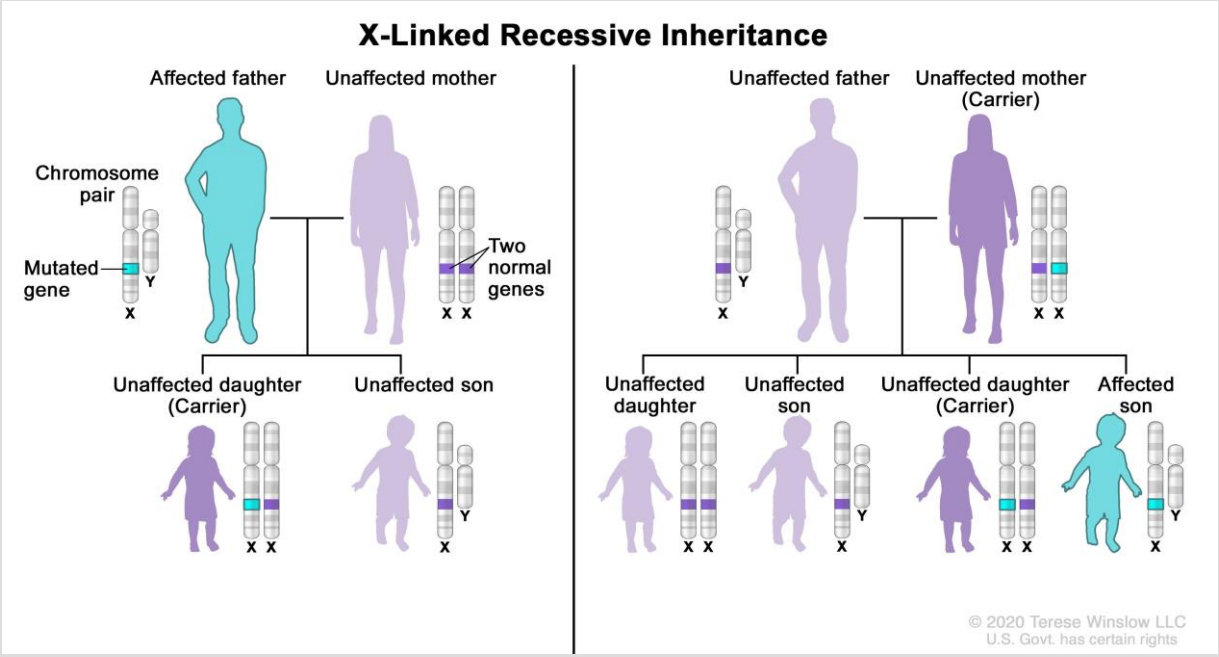
AD INHERITANCE



X-LINKED RECESSIVE INHERITANCE

- Pathogenic variants found in genes on the X chromosome
- Females have two copies, males have one copy
- Females usually carriers, males affected
- Some females can be affected
- Recurrence risk can be 50% in boys
- No male to male transmission

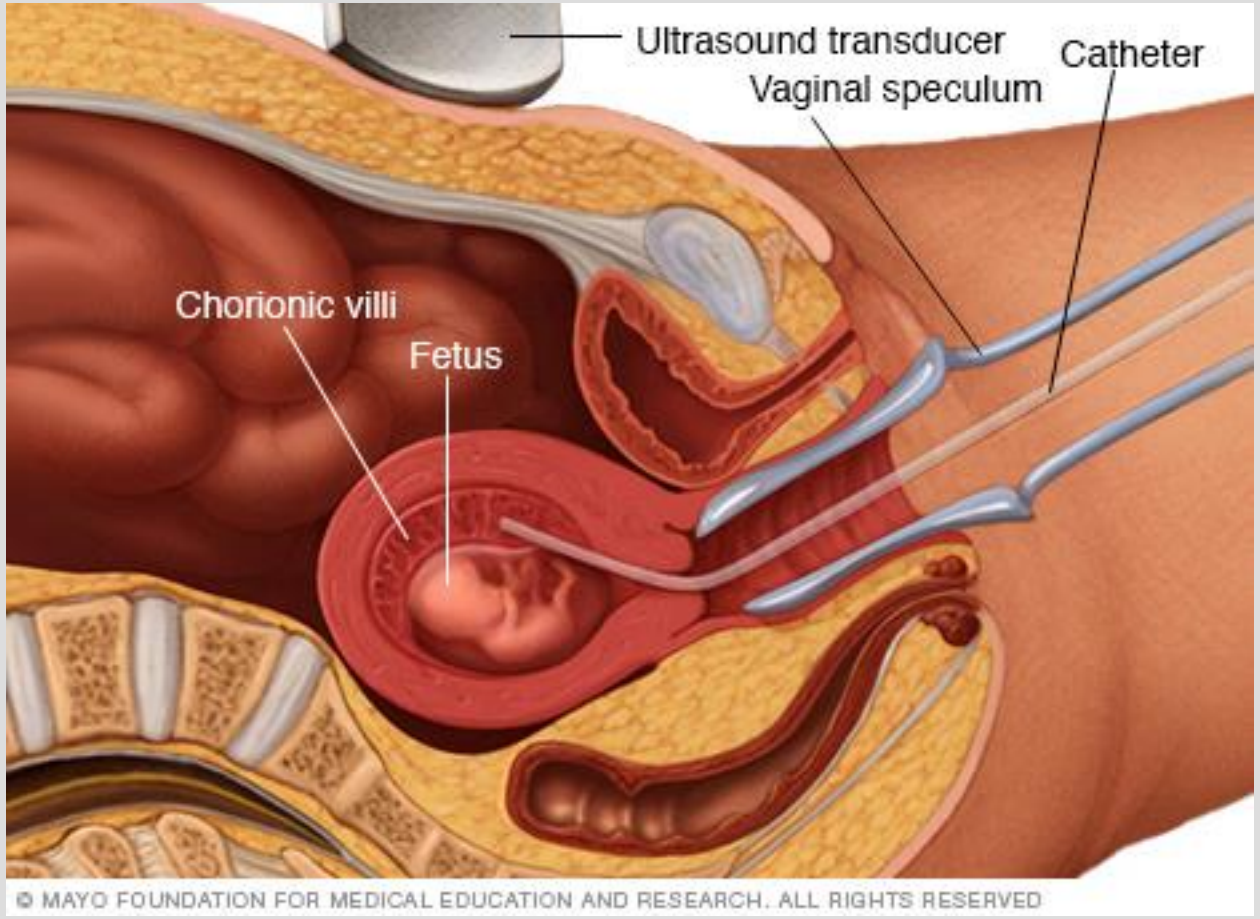
X-LINKED RECESSIVE INHERITANCE



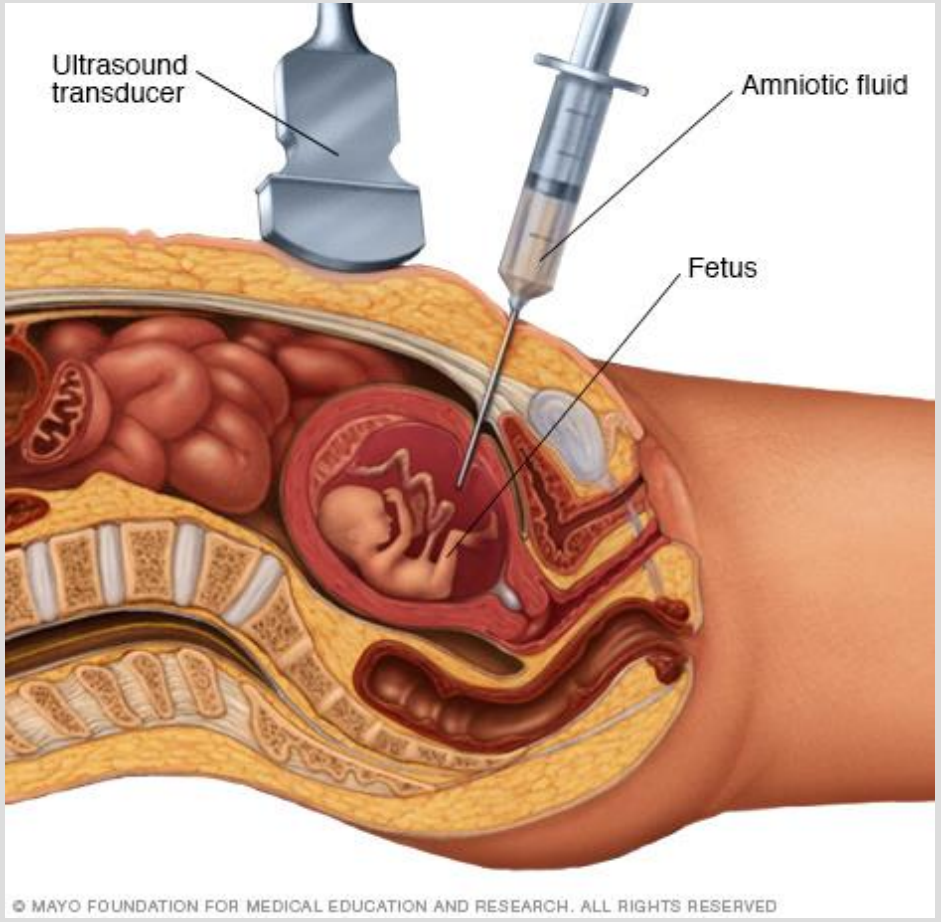
OPTIONS FOR FUTURE PREGNANCIES

- Natural Conception
  - Do nothing
  - Do CVS
  - Do amniocentesis
- IVF pregnancy
  - PGD
- Donor
  - Donor egg
  - Donor sperm

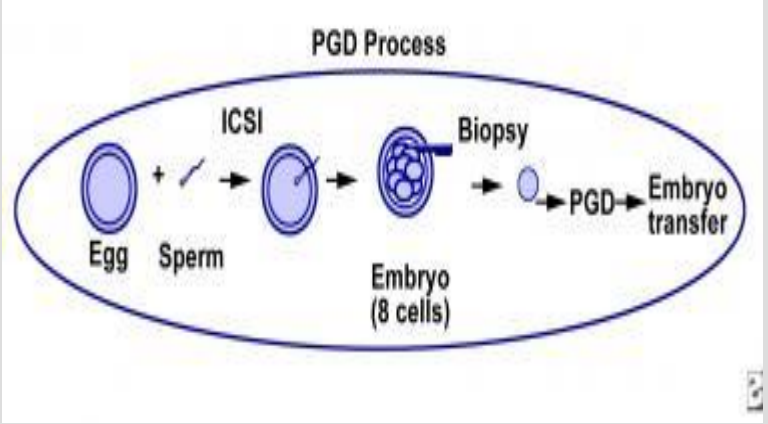
CHORIONIC VILLUS SAMPLING



AMNIOCENTESIS



PRE-IMPLANTATION GENETIC DIAGNOSIS



DONOR GAMETE

- Helpful for when you don't know the genetic mutation
- Easier to get sperm donor than egg donor
- Don't use a relative!
- Disadvantage is that one parent will not be a 'biological' parent

PRECONCEPTION CARRIER SCREENING

- We are all carriers for something
- Most people don’t even know
- Can screen before a pregnancy
  - Screen individually
  - Screen as a couple
- Only a screening test and not 100% accurate
- Currently only private
- Mackenzie's Mission

QUESTIONS

- ???