Umm AL Qura University

PATTERNS OF INHERITANCE

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PATTERNS OF INHERITANCE

- Definition
- Family Studies
- Pedigree drawing and Terminology
- Mendelian inheritance
- Non-Mendelian inheritance
- Mitochondrial inheritance

PATTERNS OF INHERITANCE: DEFINITION

- Its the manner in which a particular genetic trait or disorder is passed from one generation to the next.

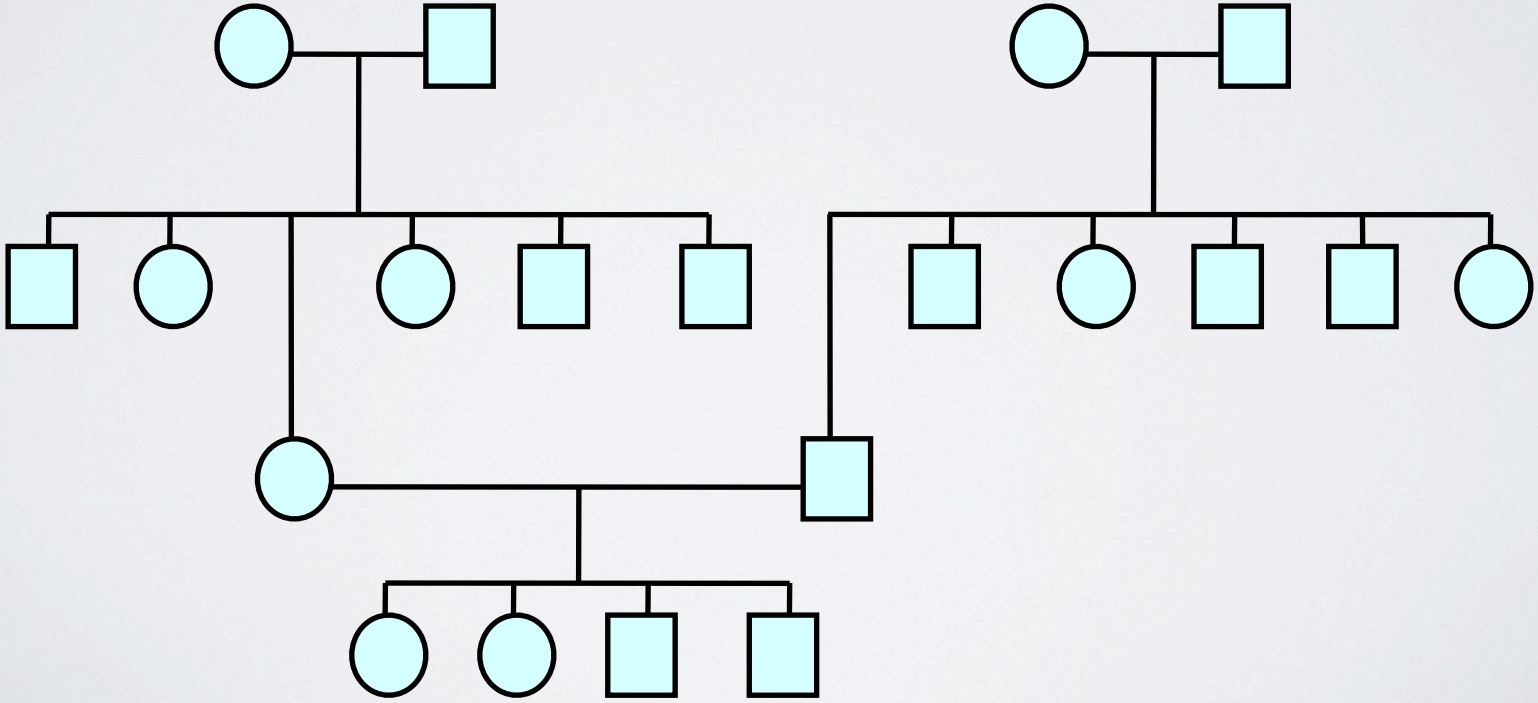
- Examples:
  - Autosomal dominant,
  - autosomal recessive,
  - X-linked dominant,
  - X-linked recessive,
  - multifactorail, and
  - mitochondrial inheritance.

PATTERNS OF INHERITANCE

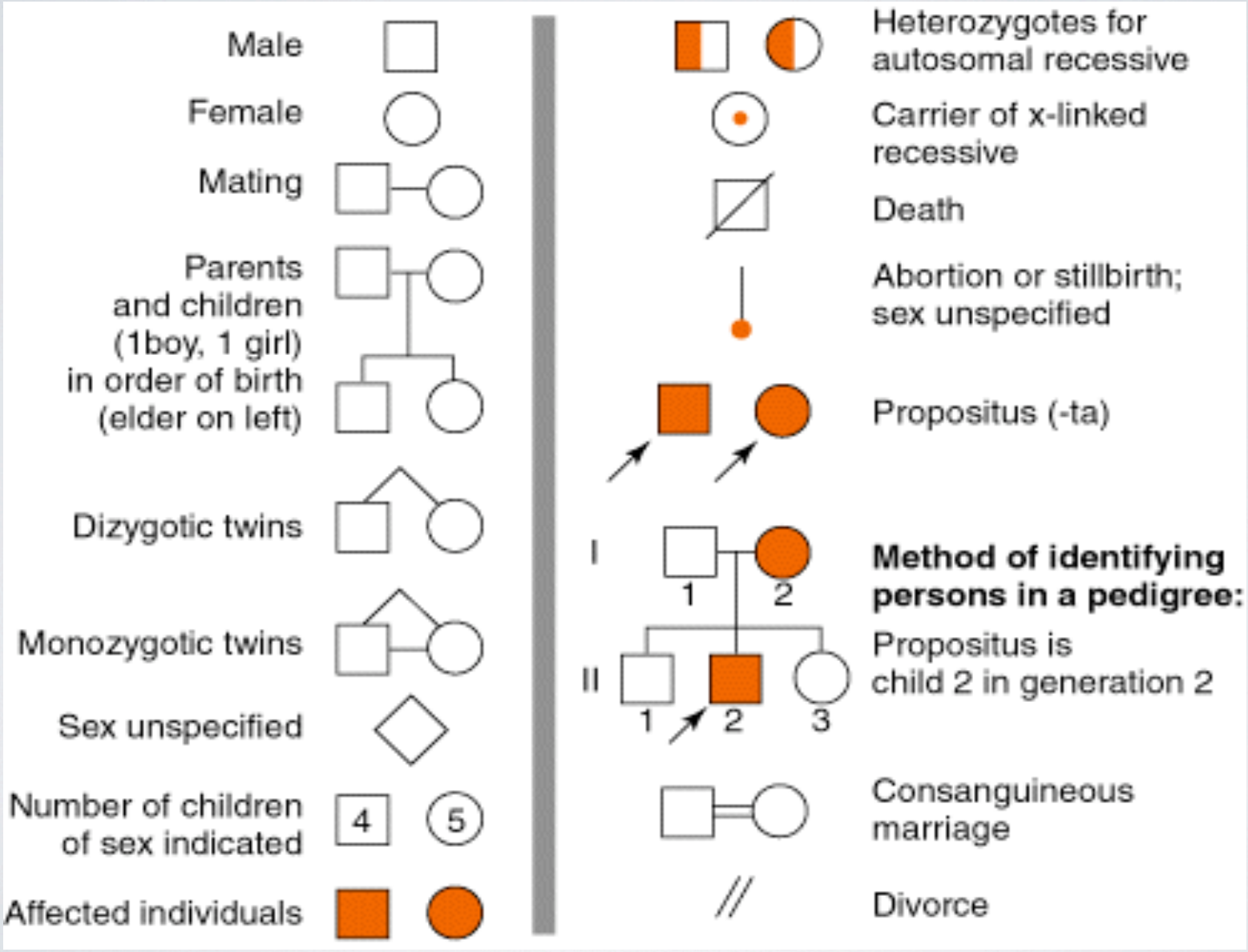
- The importance of studying the pattern of inheritance of disorders within families:
  - Genetic counseling: Advice to be given to members of a family regarding the susceptibility of their developing the disease OR.
  - Passing it on to their children.

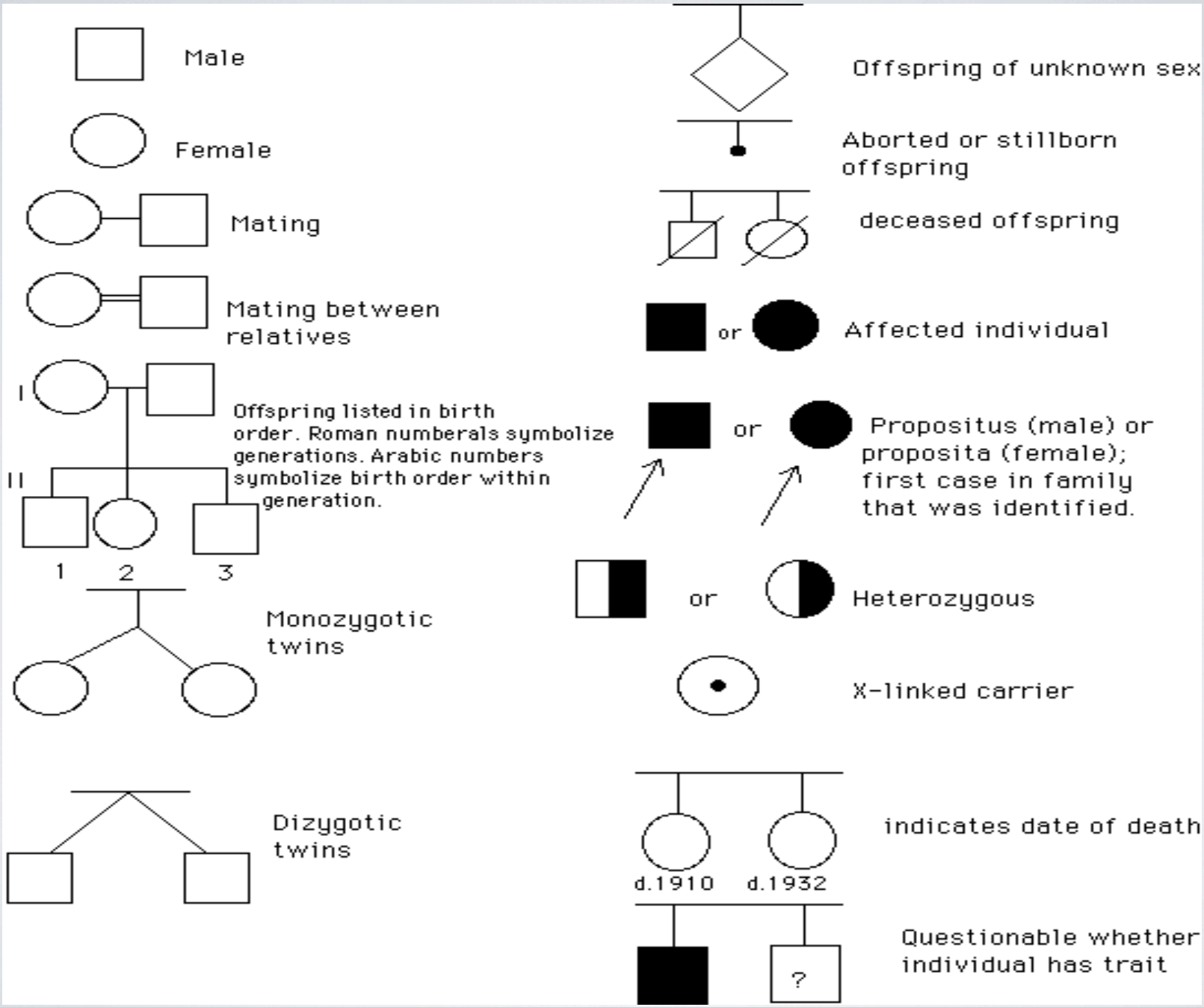
IMPORTANCE DEFINITION

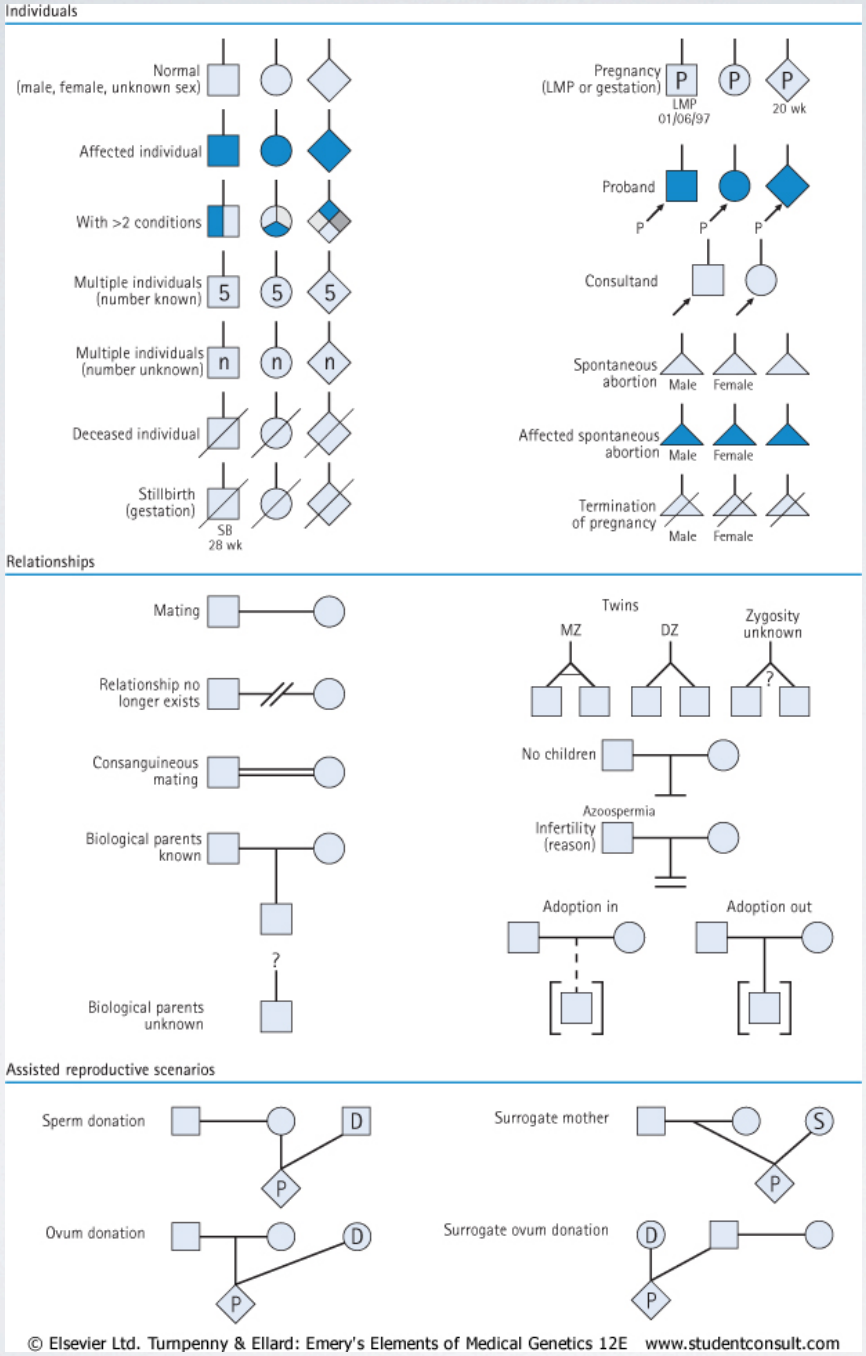
- A pedigree is a chart of the genetic history of family over several generations.



Standard symbols for pedigrees.




Male
Female
Mating
Mating between relatives
I
II
1
2
3
Offspring listed in birth order. Roman numberals symbolize generations. Arabic numbers symbolize birth order within generation.
Monozygotic twins
Dizygotic twins
Offspring of unknown sex
Aborted or stillborn offspring
deceased offspring
or
Affected individual
or
Propositus (male) or proposita (female); first case in family that was identified.
or
Heterozygous
X-linked carrier
d.1910
d.1932
indicates date of death
?
Questionable whether individual has trait

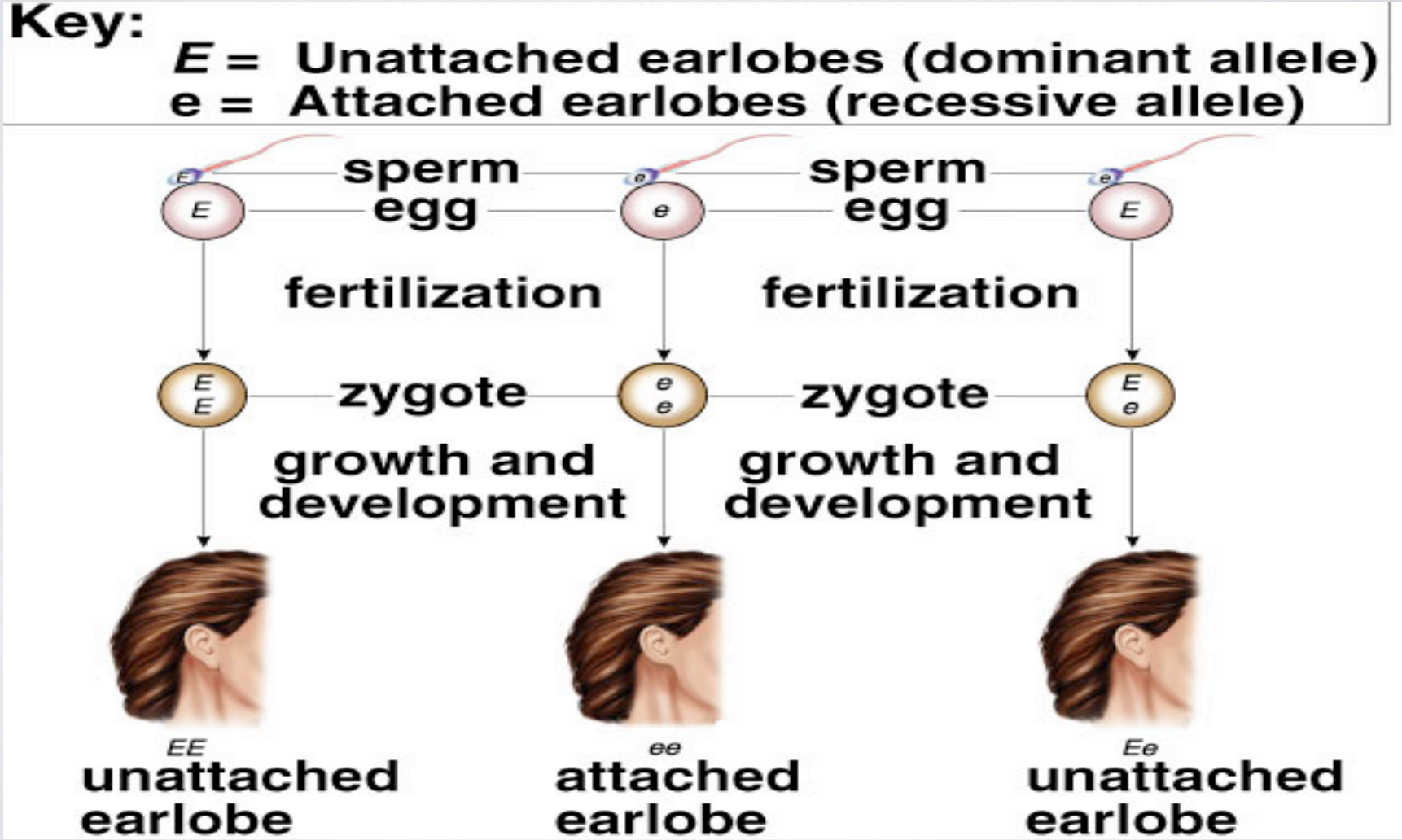


IMPORTANCE DEFINITION

- **Locus:** The position of a gene on a chromosome.
- **Allele:** one of several alternative form of a gene at a given gene locus.
- **Genotype:** refers to an individual's genes.
- **Phenotype:** refers to an individual's physical appearance.
- **Heterozygous:** having two different alleles at a given gene locus.
- **Homozygous:** having identical alleles at a given gene locus.

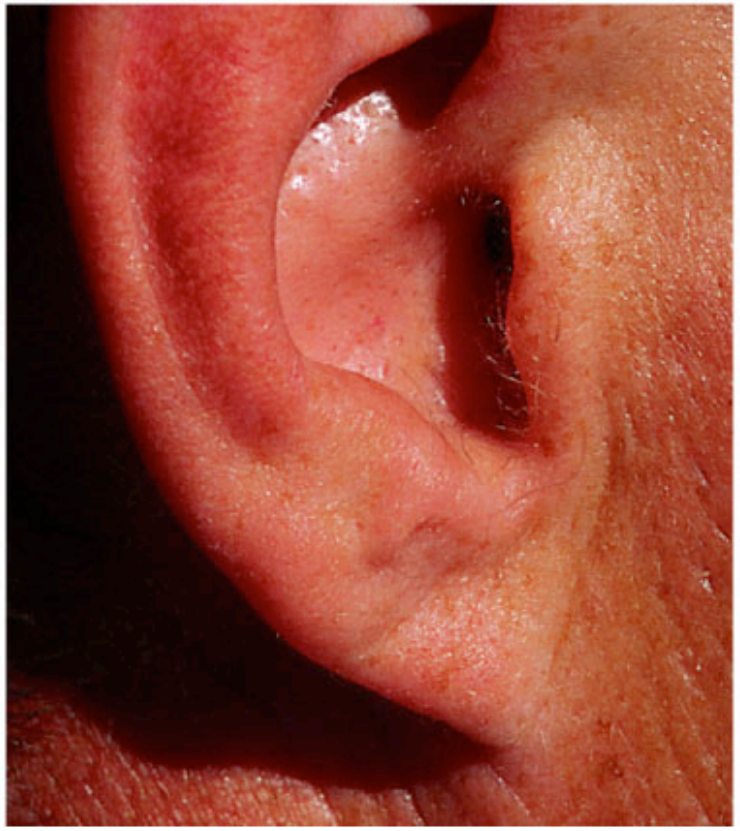
Genotype

- the gene types a person inherited

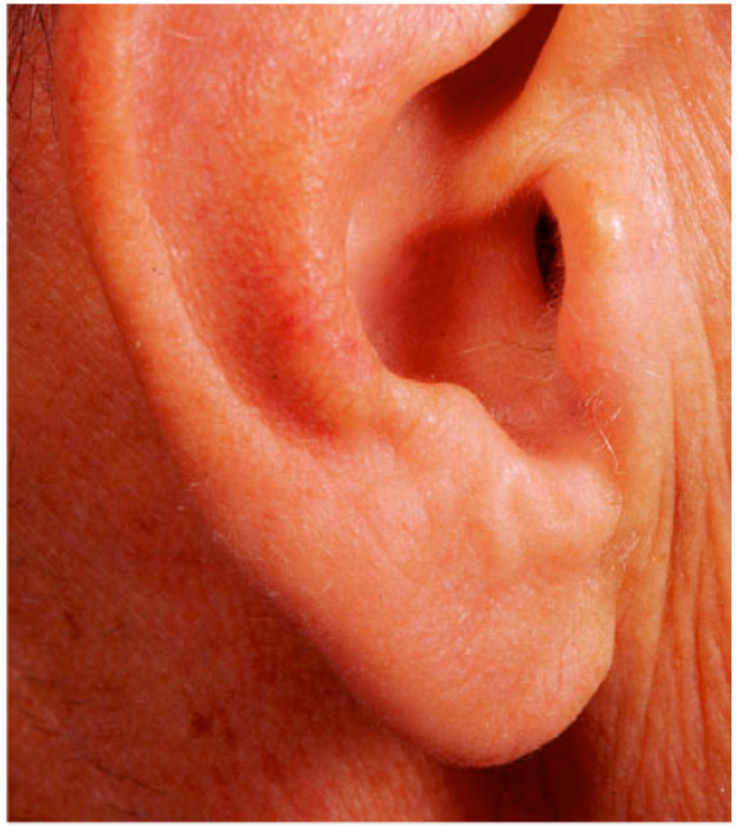


Phenotype

- the physical (& behavioral) characteristics an individual displays



d. Attached earlobes: *ee*

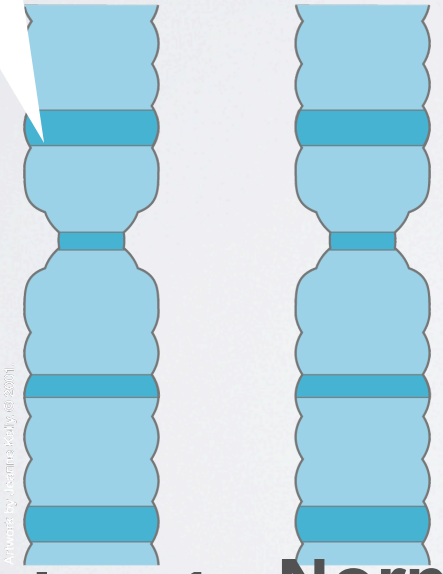


c. Unattached earlobes: *EE* or *Ee*

Alleles

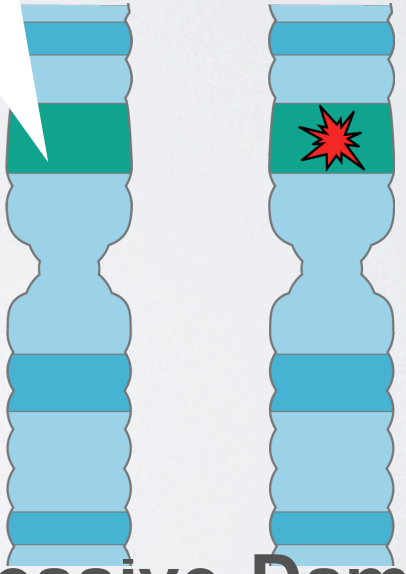
Quiet! I'll speak for both of us!

I'll have to be in charge now!



Dominant Allele

Normal Allele



Recessive Allele

Damaged Allele

MENDELIAN DISORDERS

- Austrian botanist Gregor Mendel (1822-84)
- More than 11,000 Mendelian (monogenic) disorders have been revealed
- OMIM (Online Mendelian Inheritance in Man) database

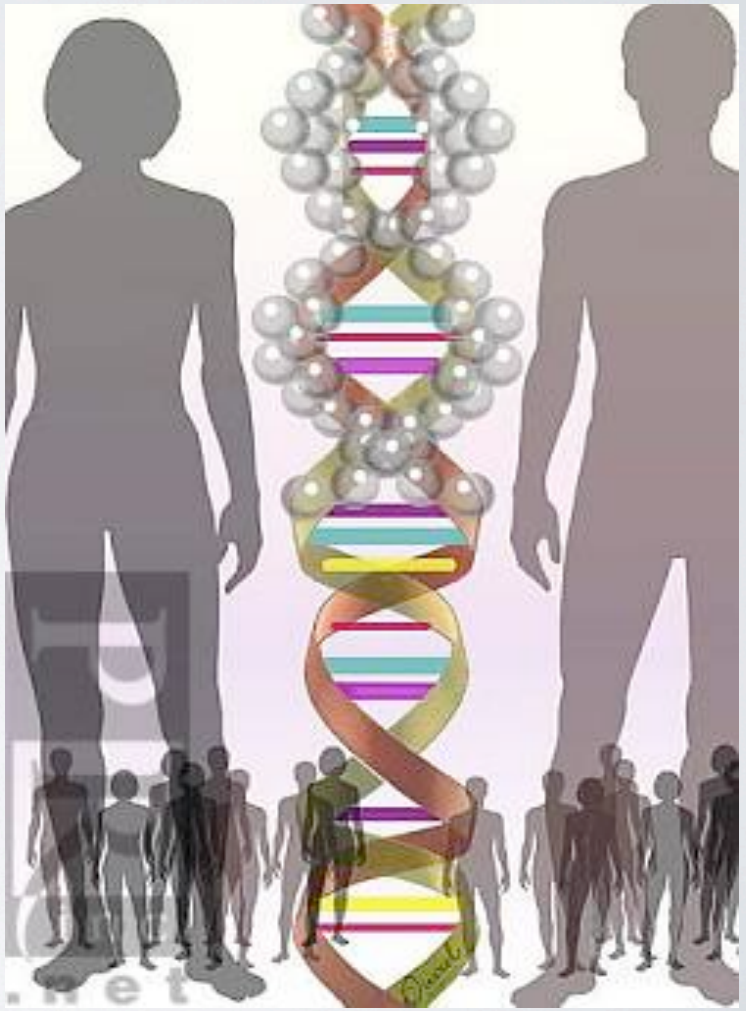
MENDELIAN INHERITANCE

Autosomal inheritance:

- Dominant.
- Recessive.

Sex-linked inheritance:

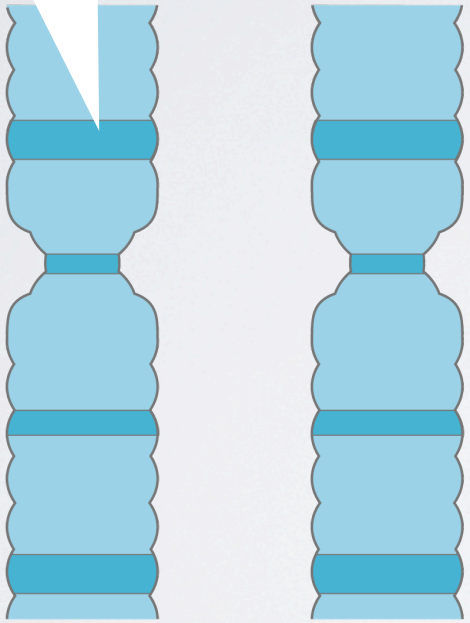
- Dominant.
- Recessive.

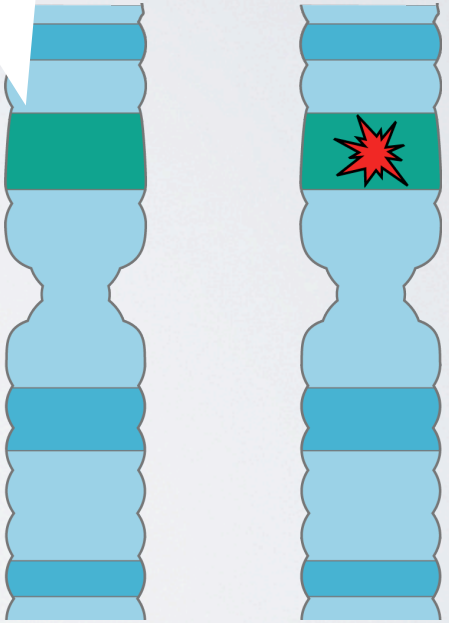


Autosomal Inheritance

Quiet! I'll speak for both of us!

I'll have to be in charge now!





Dominant Allele

Normal Allele

Recessive Allele

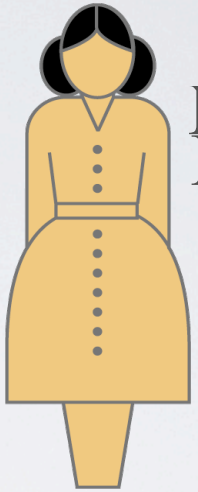
Damaged Allele

AUTOSOMAL DOMINANT INHERITANCE

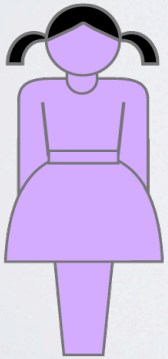
- Both male and female are affected
- The disease is observe in multiple generations
- Transmission of the disease can be from both sexes
- Mutation in only one allele is enough to express the disease
- Vertical transmission
- The offspring have 50% chance to have the disease

AUTOSOMAL DOMINANT DISORDER

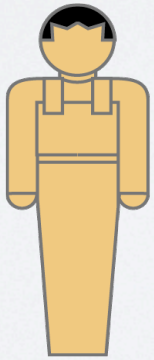
Affected Father



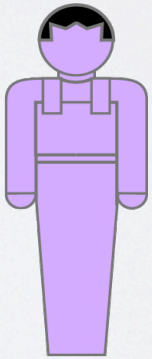
Normal Mother



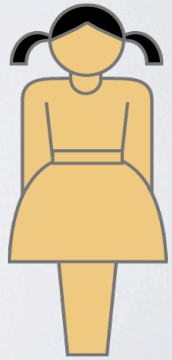
Affected Daughter



Normal Son



Affected Son



Normal Daughter

- Punnett`s square showing possible gamete combinations for an autosomal dominant allele

	w	w
W	W w	W w
w	w w	w w

AUTOSOMAL DOMINANT DISORDERS

- **Huntington disease**
- Autosomal dominant
- Gene in chromosome 4p
- Adult onset of the disease
- Choreic movement disorder
- Mood disturbance
- Progressive loss of mental activity

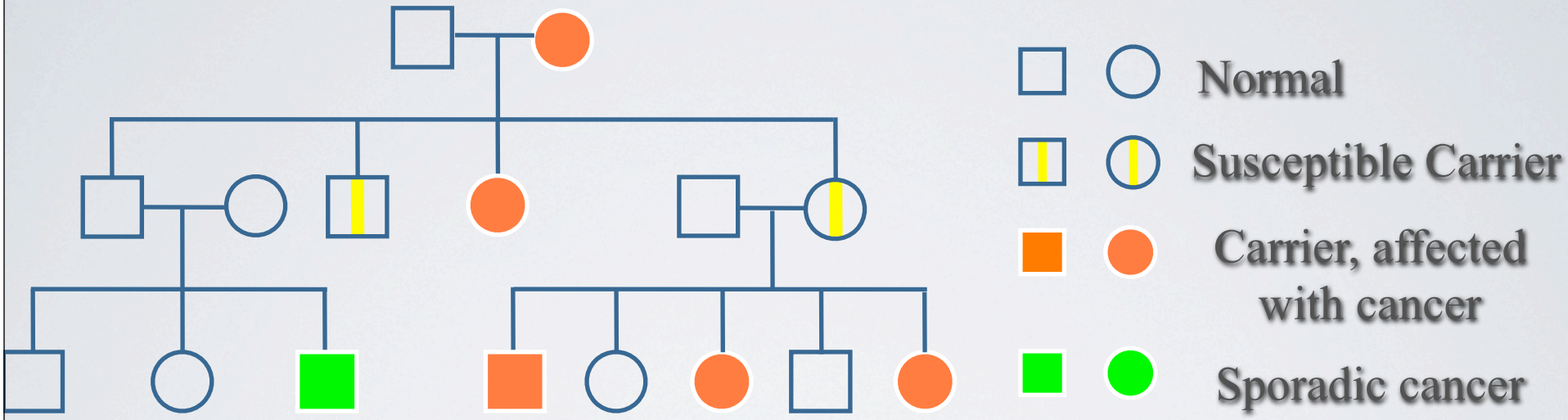
AUTOSOMAL DOMINANT DISORDER

- **Marfan Syndrome**
- Autosomal dominant
- Gene in chromosome 15q (Fibrillin)
- Connective tissue disorder with characteristic skeletal, dermatological, cardiac, aortic, ocular and dural malformations.

AUTOSOMAL DOMINANT DISORDER

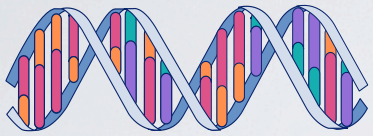
Achondroplasia is autosomal dominant genetic disorder that is a common cause of **dwarfism**

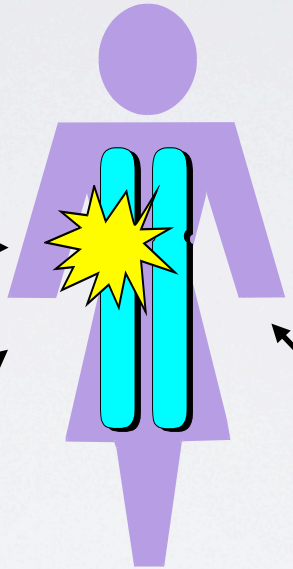
Most Cancer Susceptibility Genes Are Dominant With Incomplete Penetrance



- Penetrance is often incomplete
- May appear to "skip" generations
- Individuals inherit altered cancer susceptibility gene, not cancer

Factors Affecting Penetrance





Modifier genes

Carcinogens

Response to DNA damage

Hormonal/ reproductive factors

Not everyone with an altered gene develops cancer

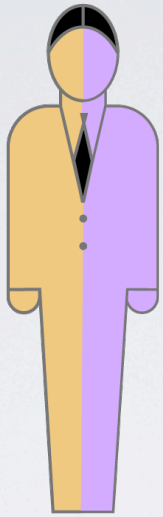
AUTOSOMAL DOMINANT DISORDERS

- Variable expressivity: some individuals show more aggressive form of the disease while other showed a milder form of the disease.
- Reduced penetrance: is term used to indicate that the disease some time to presenting no abnormal clinical feature
- New mutation
- Codominance: the presence of two alleles in heterozygous state (e.g. AB blood group)

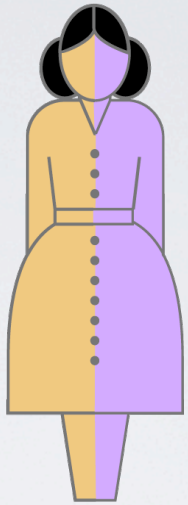
AUTOSOMAL RECESSIVE INHERITANCE

- Both male and female are affected
- The disease is observe in only single generation
- Both gene alleles (Heterozygous) need to be affected in order to express the disease

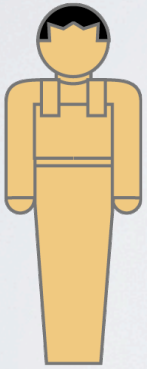
Autosomal Recessive Inheritance



Carrier Father

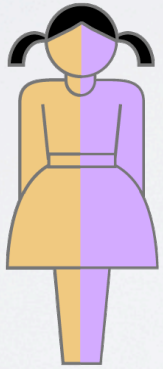


Carrier Mother

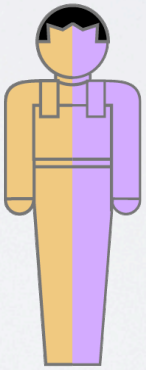


Normal Son

25% normal

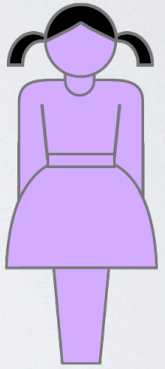


Carrier Daughter



Carrier Son

50% chance carrier

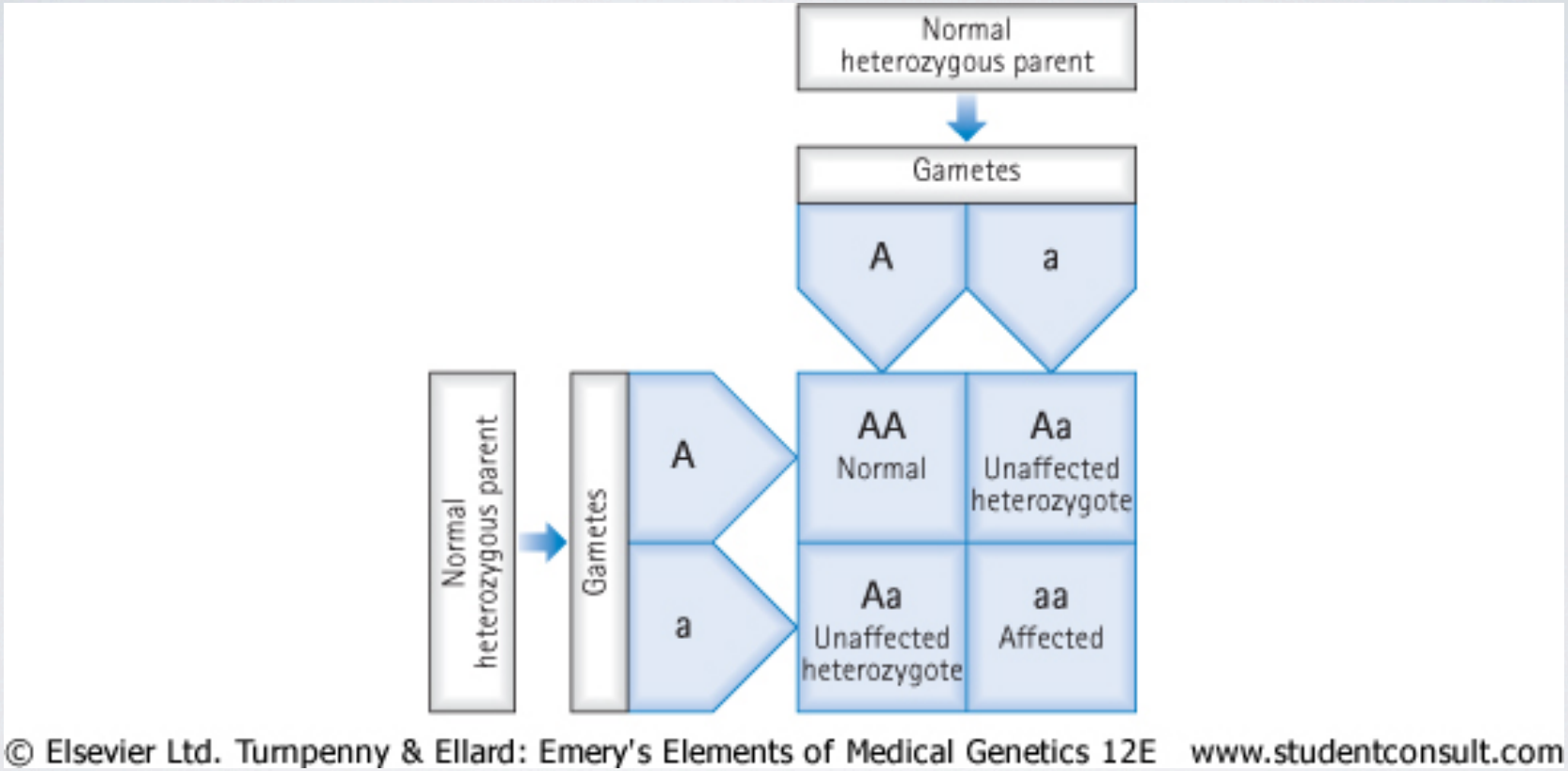


Affected Daughter

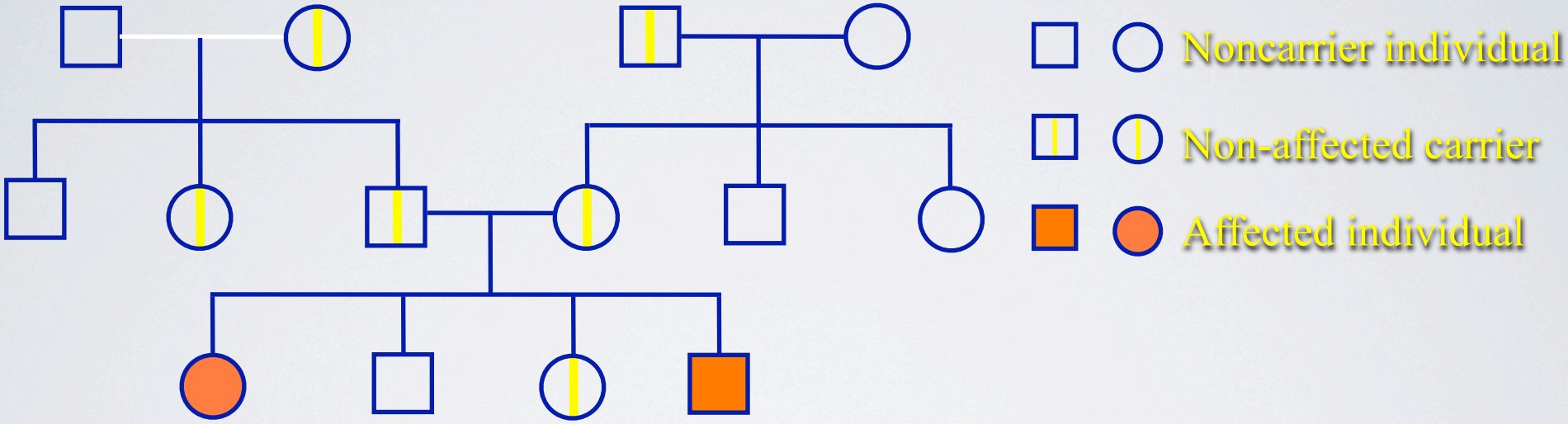
25% affected

- Punnet`s square showing possible gamete combinations for an autosomal recessive allele

	a	A
A	Aa	AA
a	aa	aA

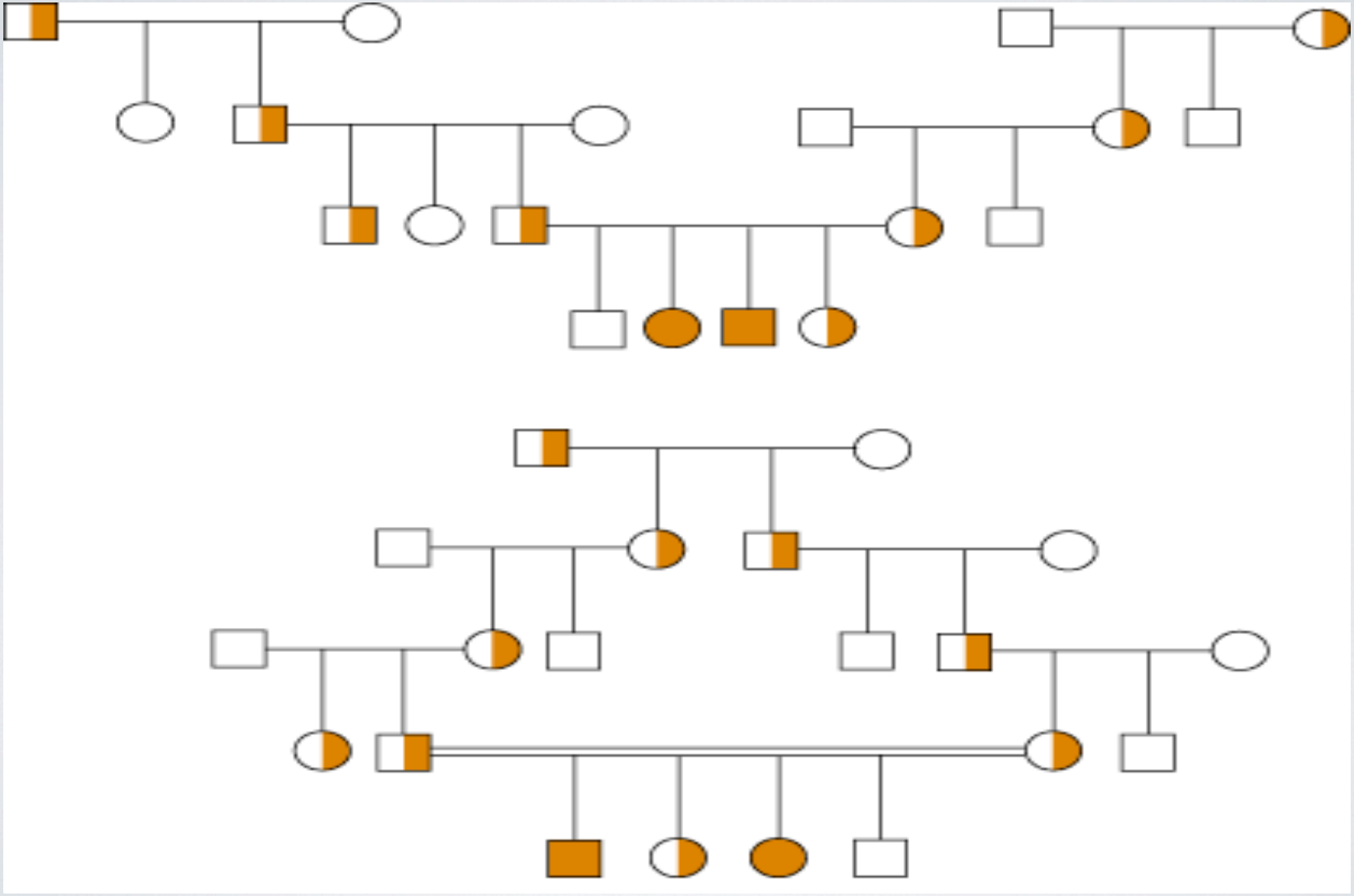


Autosomal Recessive Inheritance



- Two germline mutations (one from each parent) to develop disease
- Equally transmitted by men and women

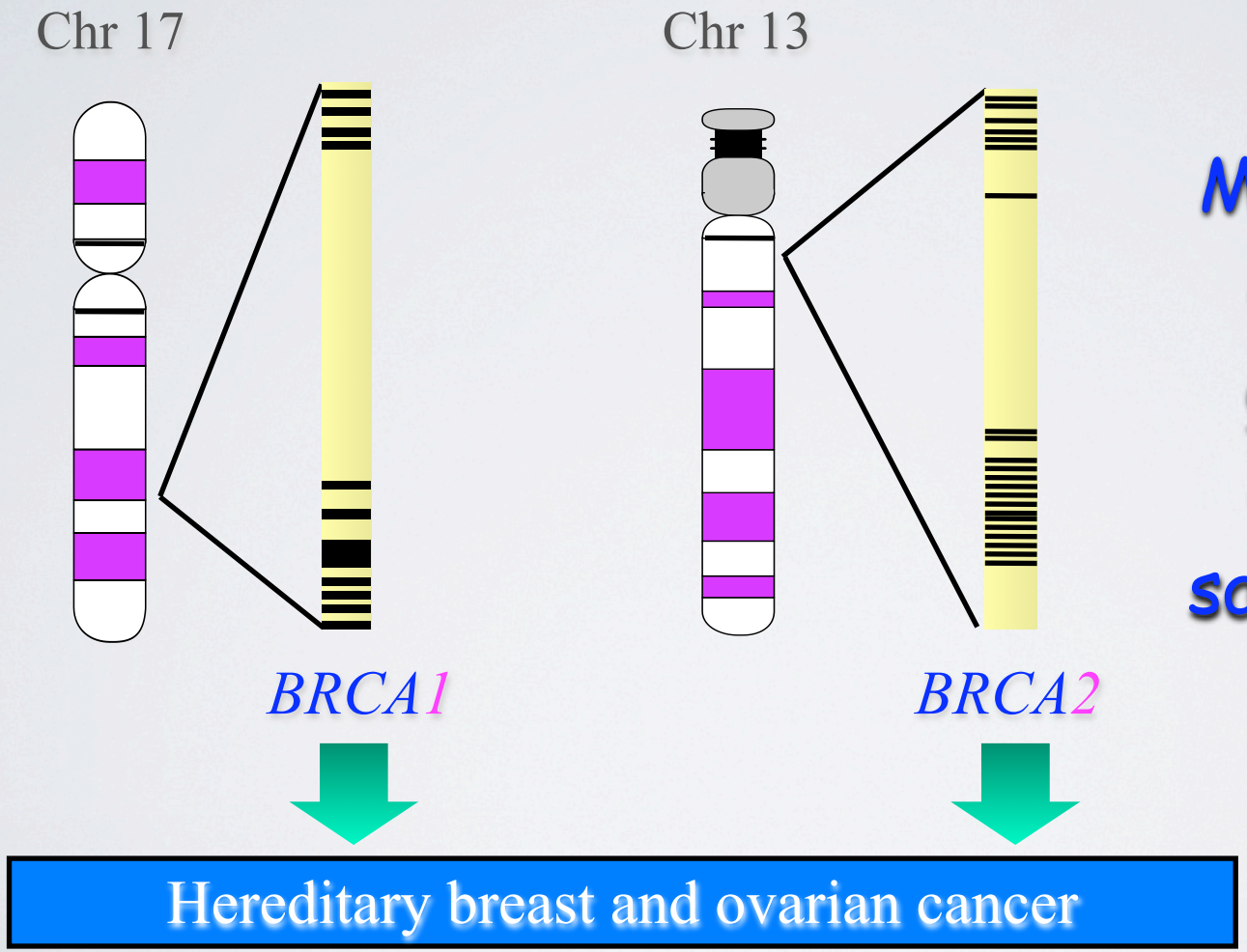
Families with individuals expressing autosomal recessive phenotypes.



AUTOSOMAL RECESSIVE INHERITANCE

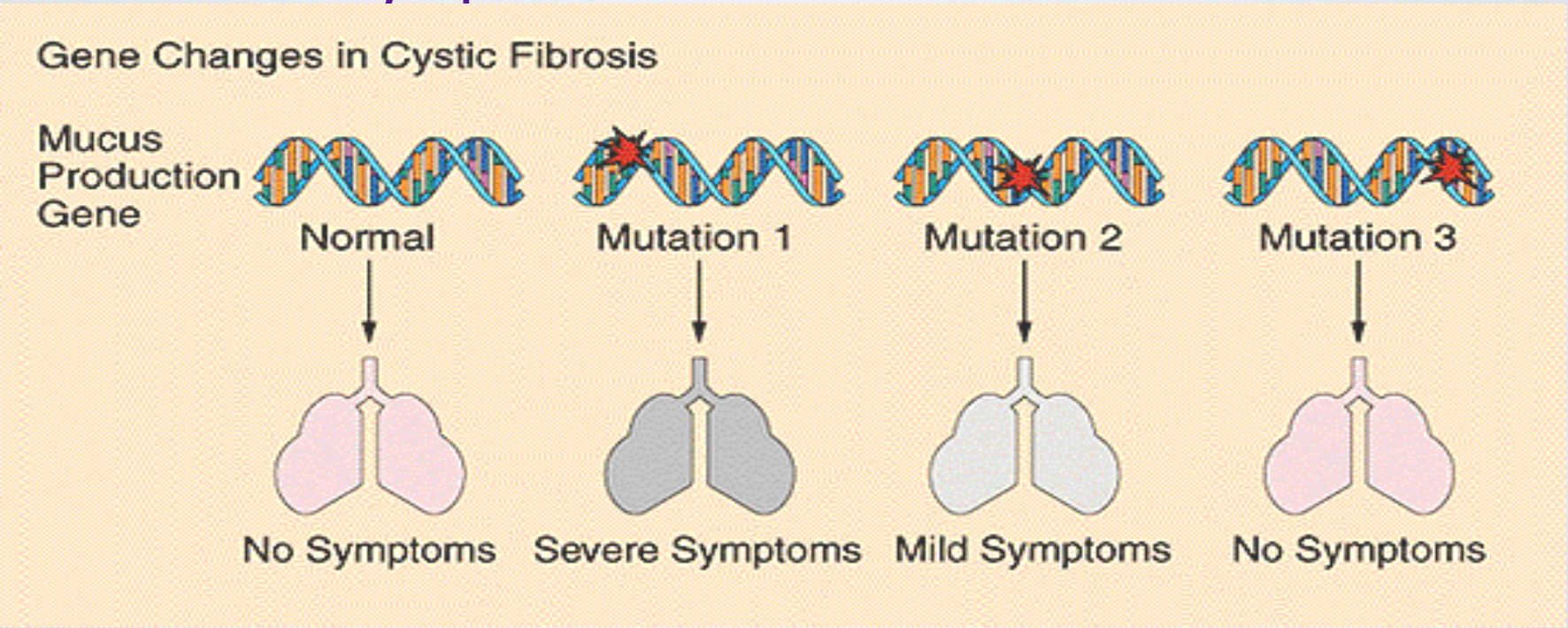
- Consanguinity
- Pseudodominance is an autosomal recessive condition appears in subsequent generations and so therefore appears to follow an autosomal dominant pattern.
- Locus heterogeneity: A single disorder, trait, or pattern of traits caused by mutations in genes at different chromosomal loci.

Genetic Heterogeneity

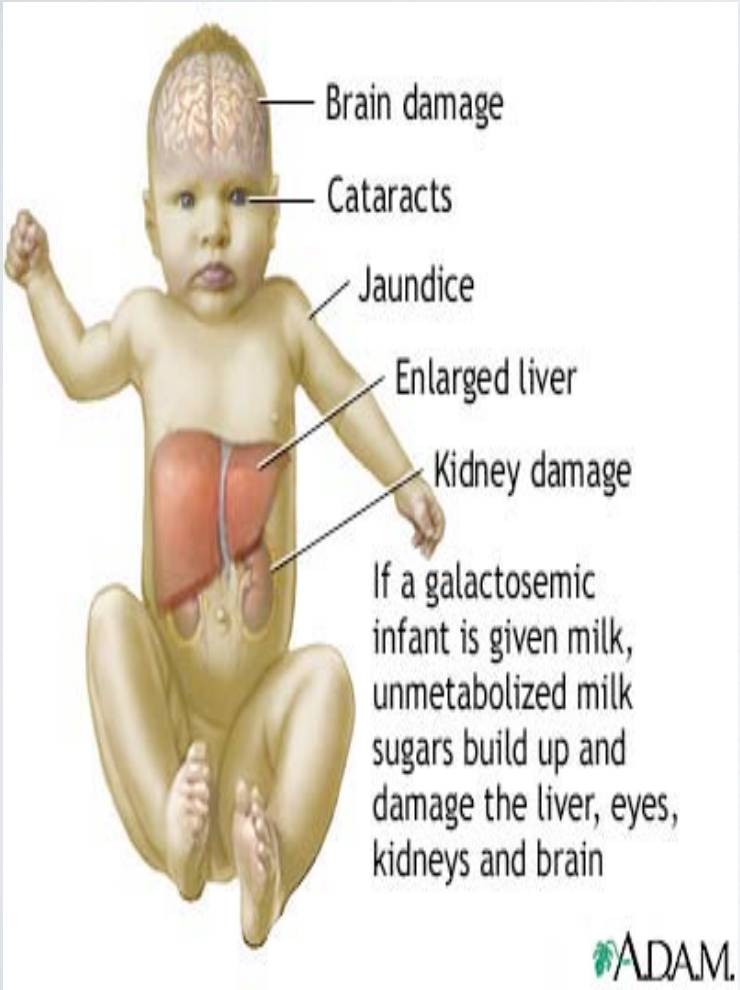


Mutations in different genes can cause the same disease

- Different mutations in the same gene can produce a wide range of effects. In cystic fibrosis, for instance, the gene that controls mucus production can have more than 300 different mutations; some cause severe symptoms; some, mild symptoms; and some, no symptoms at all.

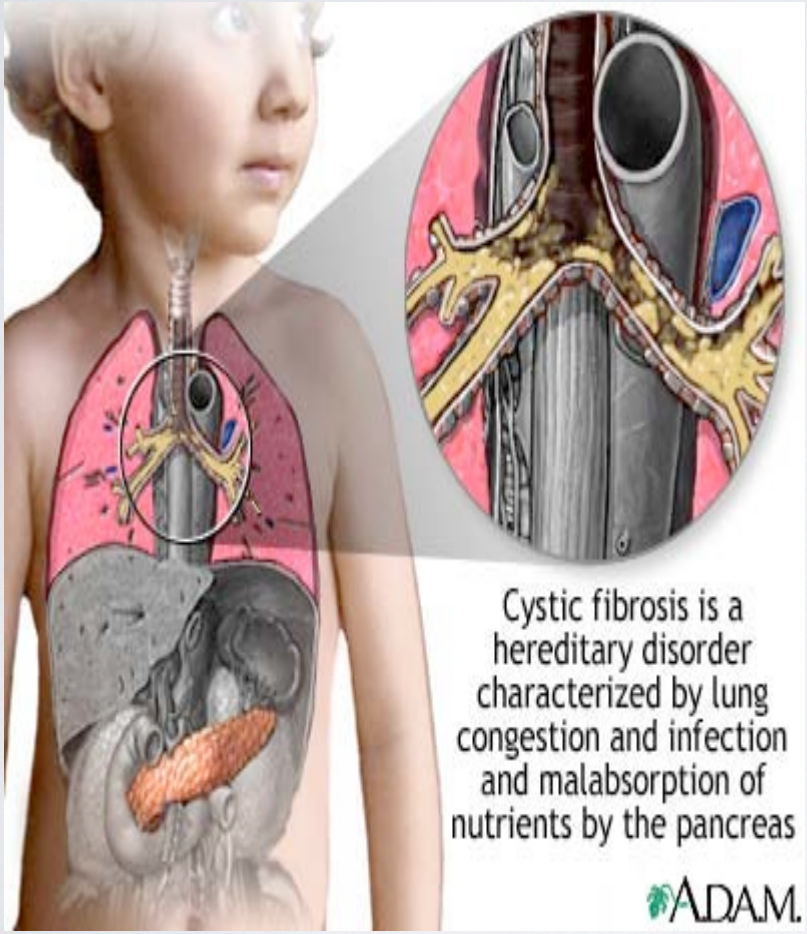


Autosomal Recessive disorder



- **Galactosemia**
- An infant is unable to metabolize galactose
- Damage of the liver, central nervous system and various other body systems
- An infant may develop jaundice, vomiting, lethargy, irritability and convulsions

Autosomal Recessive disorder



- **Cystic fibrosis (CF)**
- Gene localized at chromosome 7q
- Affected children have chronic respiratory infection, and malabsorpition

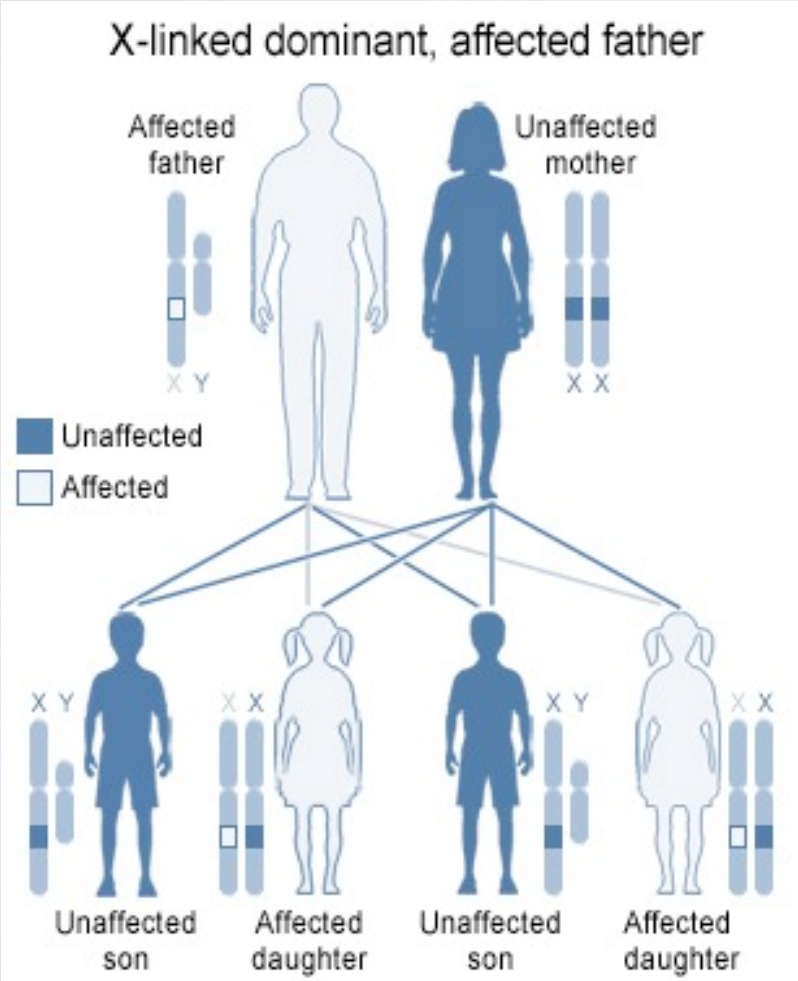
SEX-LINKED INHERITANCE

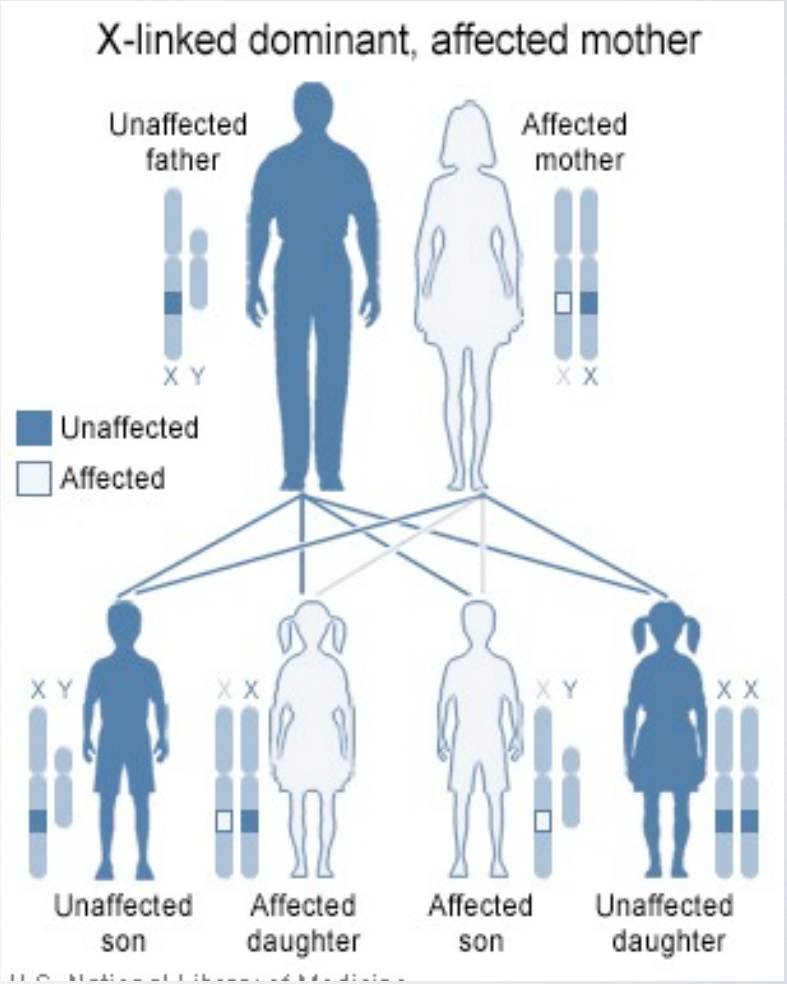
- X-linked dominant
- X-linked recessive
- Y-linked

X-LINKED DOMINANT INHERITANCE

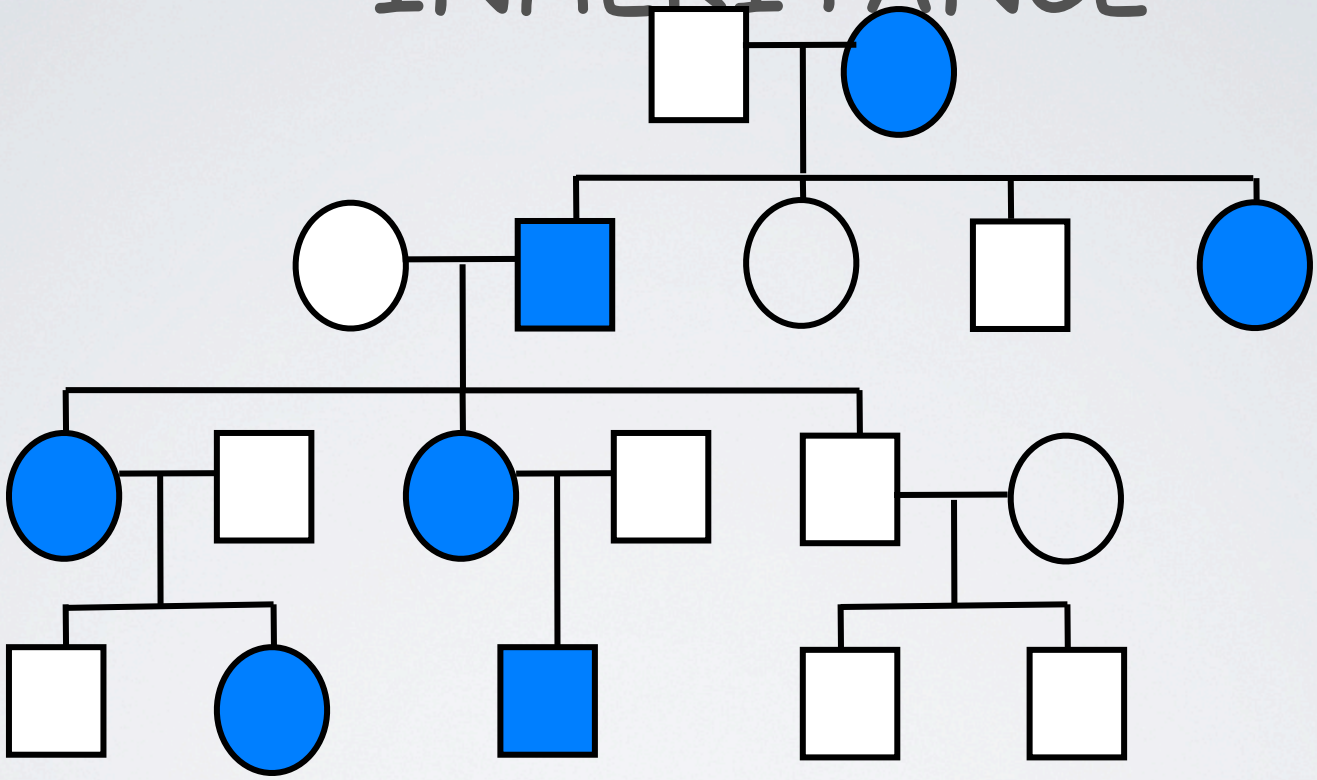
- Mutations only in X chromosome
- Both males and females are affected
- Affected males transmit the disease to their daughters (male to female only)
- Affected females transmit the disease to daughters and sons

X-LINKED DOMINANT INHERITANCE





X-LINKED DOMINANT INHERITANCE

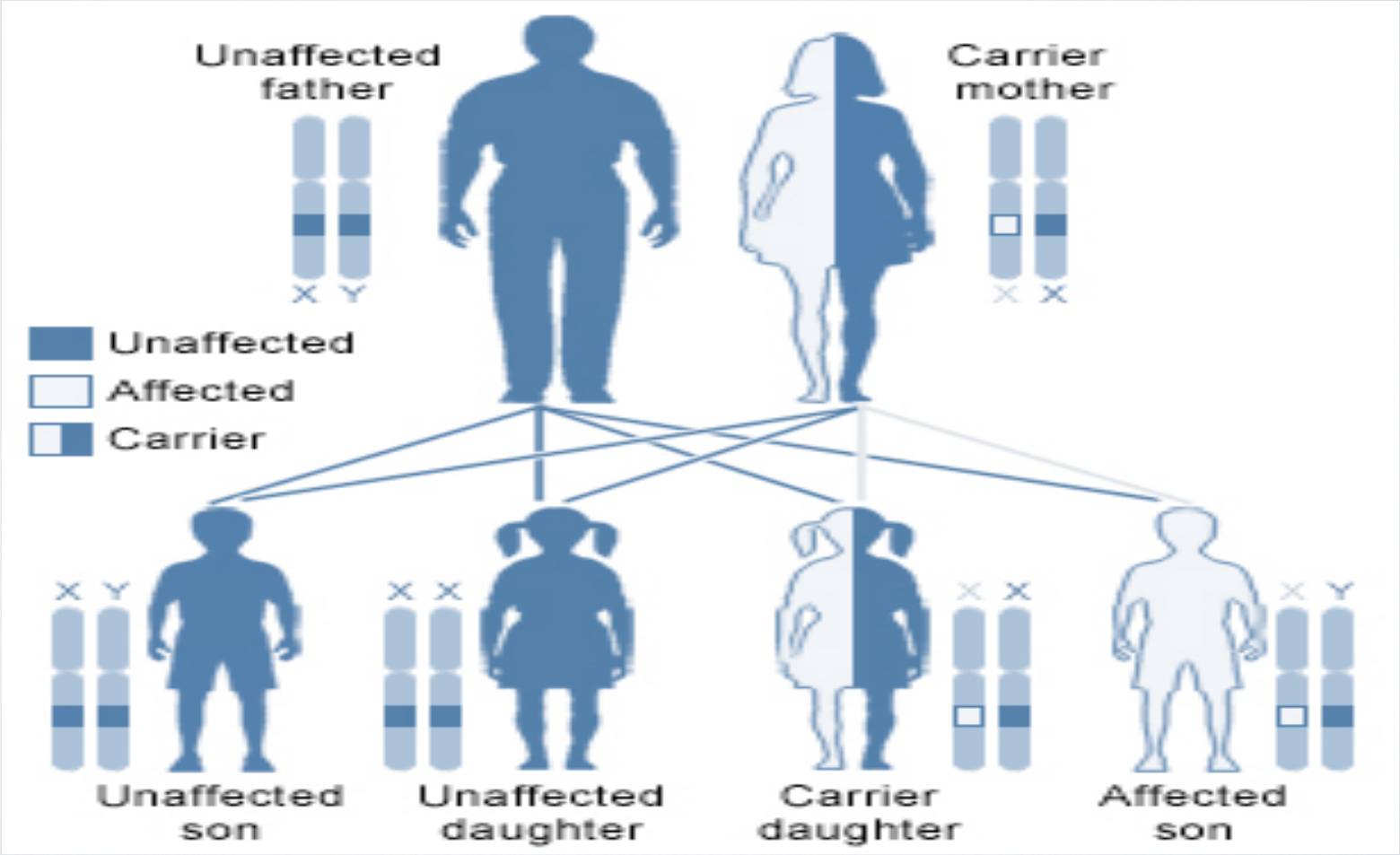


– More females than males
- All daughters of affected males are affected, but no sons
- A child of an affected female has 50% risk of disease

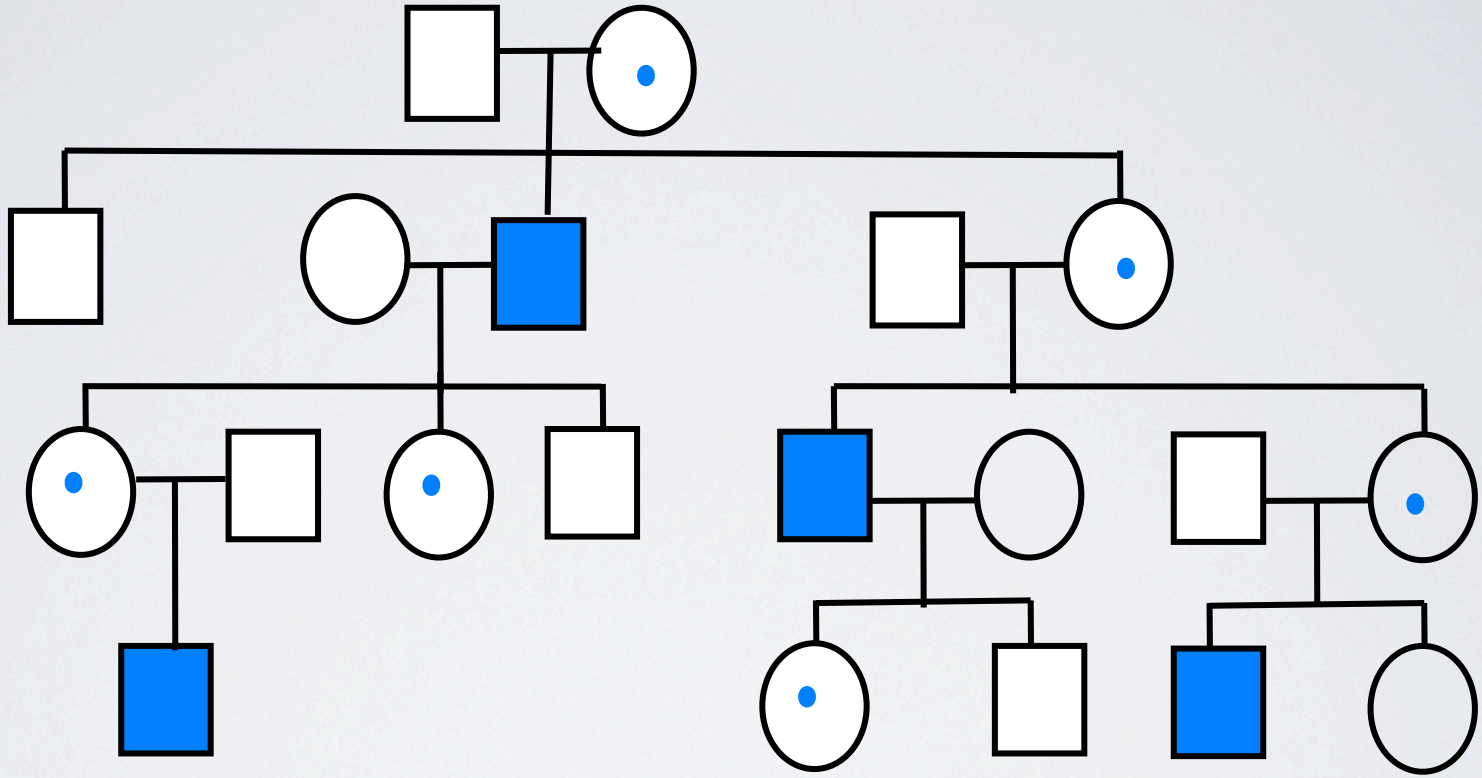
X-LINKED RECESSIVE INHERITANCE

- Mutations only in X chromosome
- Only males are affected
- Transmission through unaffected females to male
- No male to male transmission

X-LINKED RECESSIVE INHERITANCE

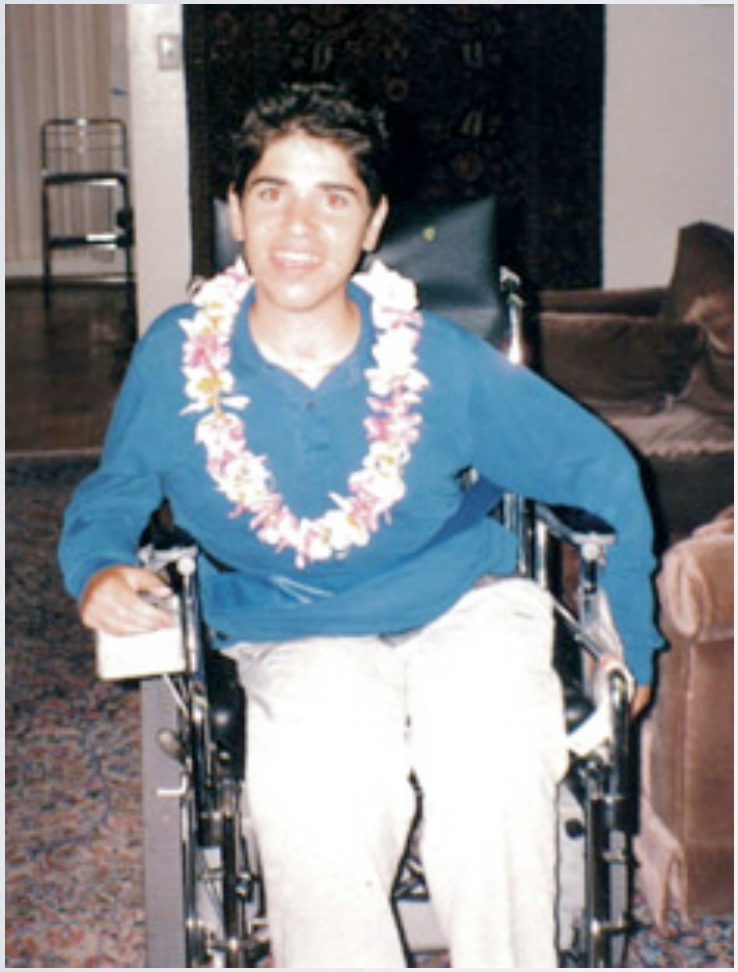


X-LINKED RECESSIVE INHERITANCE



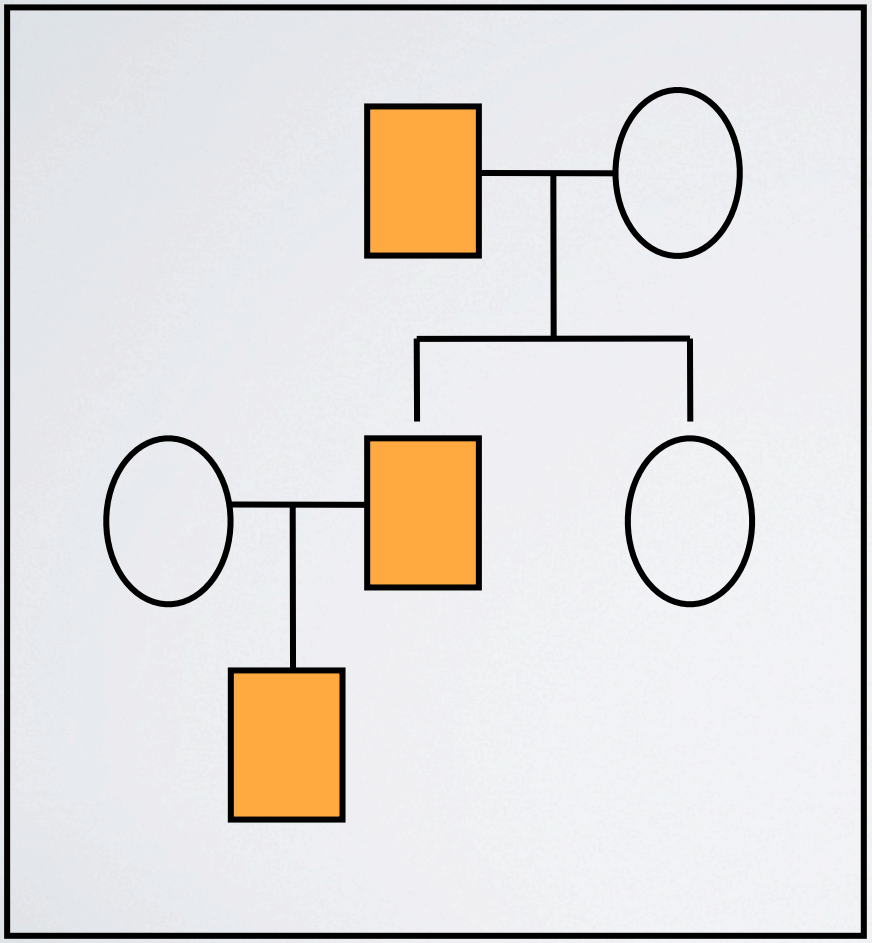
- Affects almost exclusively men
- Affected men born from carrier mother, with 50% risk of disease
- No male to male transmission

X-LINKED RECESSIVE DISORDER



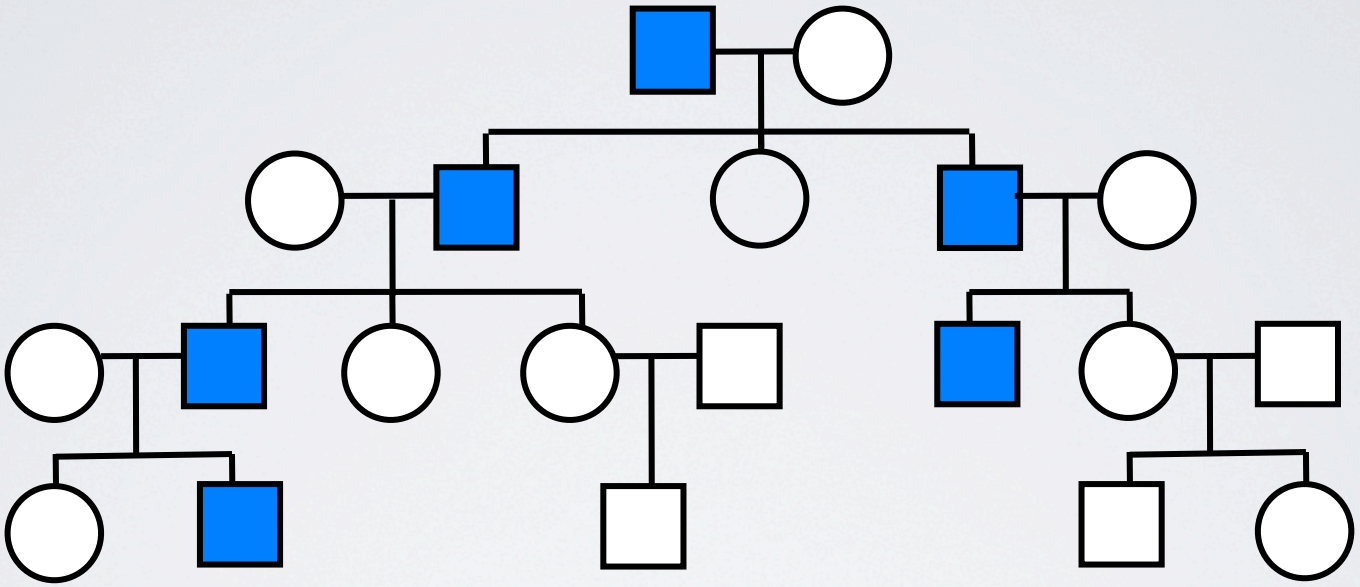
- Duchenne muscular dystrophy (DMD)
- Affected gene on chromosome Xp21
- Progressive weakness and muscle wasting

Y-LINKED INHERITANCE



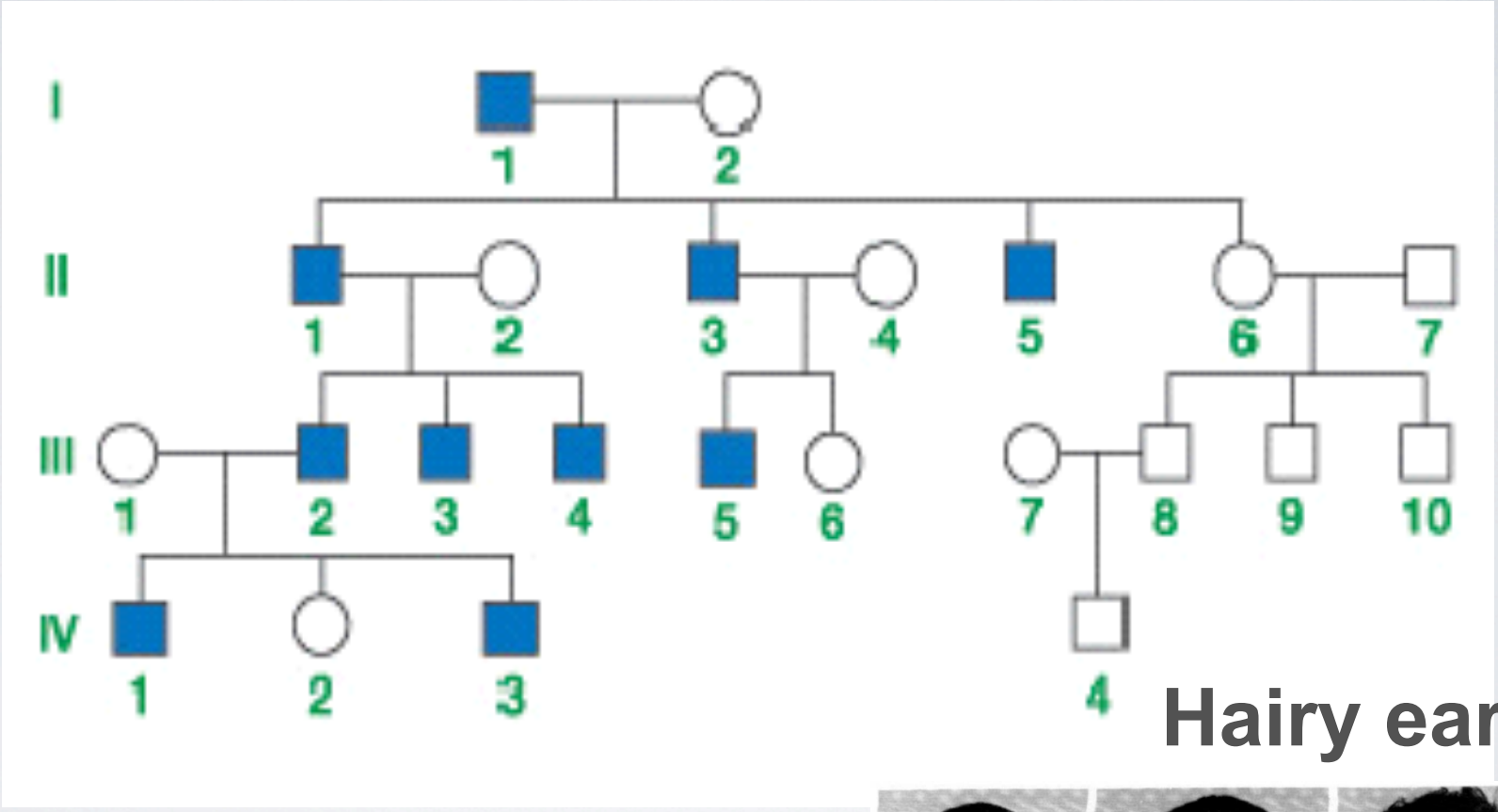
- Only males are affected
- Male infertility

Y-LINKED INHERITANCE (Y)

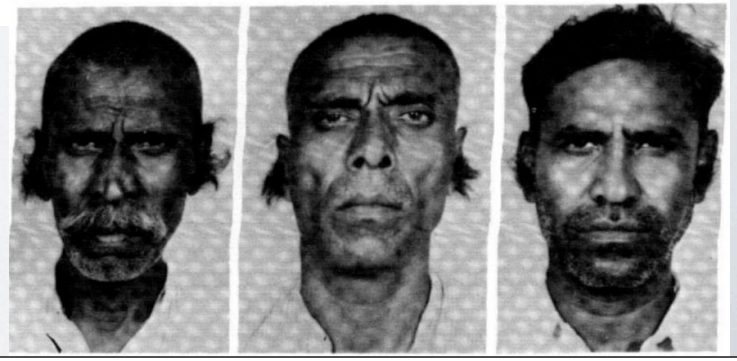


- Affects only males
- Affected males always have affected fathers
- All sons of an affected male are affected

Y-linked gene (feature)



Hairy ears



Only males are affected

MITOCHONDRIAL INHERITANCE