Enrichment Course in Biology

Human Genetics

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Learning Outcomes

- Describe the Mendel's laws of inheritance
- List and describe the types and properties of inheritance in humans

Heritability of mutations

- Heritable
- Germline mutation
- Not heritable
- Somatic mutation

Somatic mutations

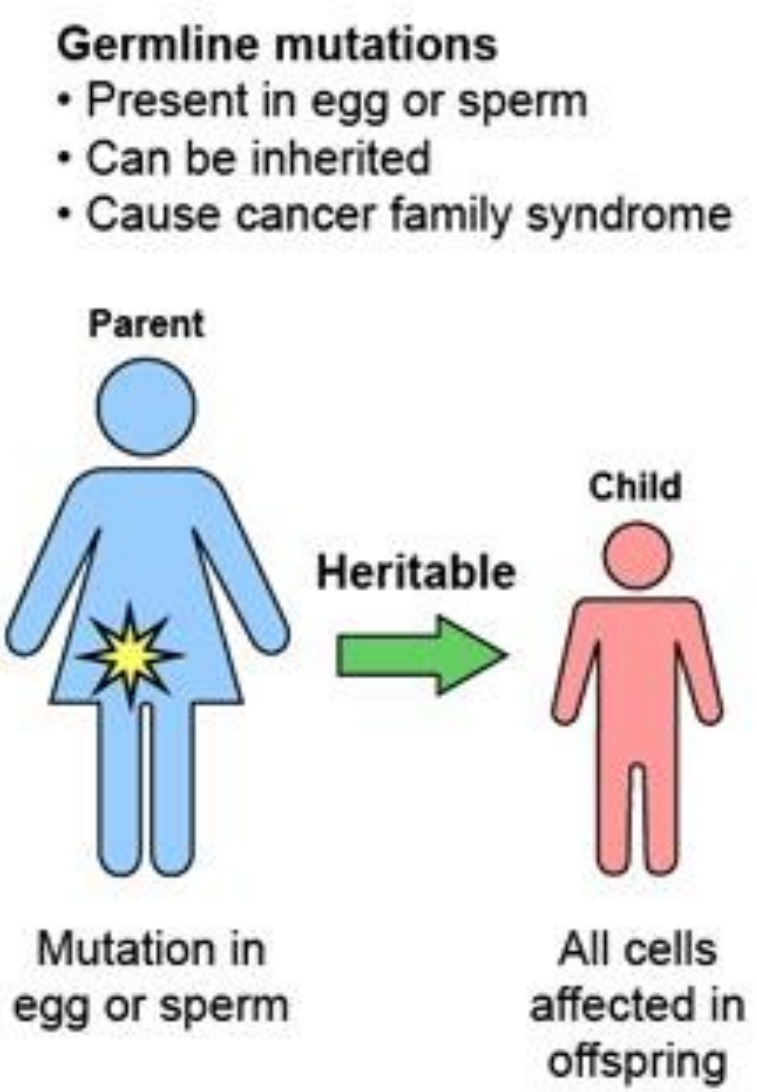
- Occur in ***nongermline*** tissues
- Cannot be inherited

- Sporadic mutation
- Occur in a single body cell
- Cannot be inherited
- Only tissues derived from mutated cell are affected

Nonheritable

Mutation in tumor only

- Occur in gametes
- Can be passed onto offspring
- Every cell in the entire organism will be affected.
- Can be due to sporadic mutation
  - Once developed, this mutation can be passed on to offspring – such inherited mutation is described as constitutional mutation

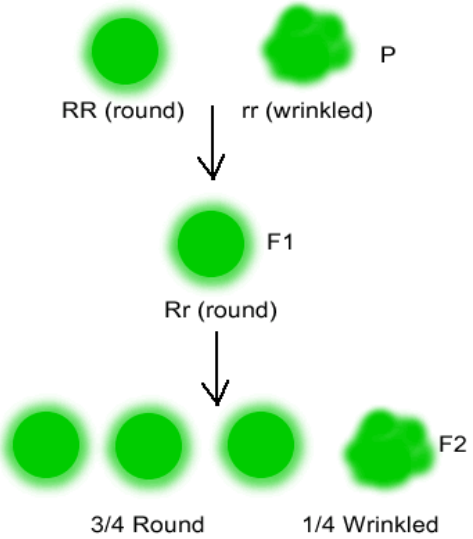


Mendel's laws of heredity

- Some traits of the sweat pea can only occur in one or the other form but no intermediate.

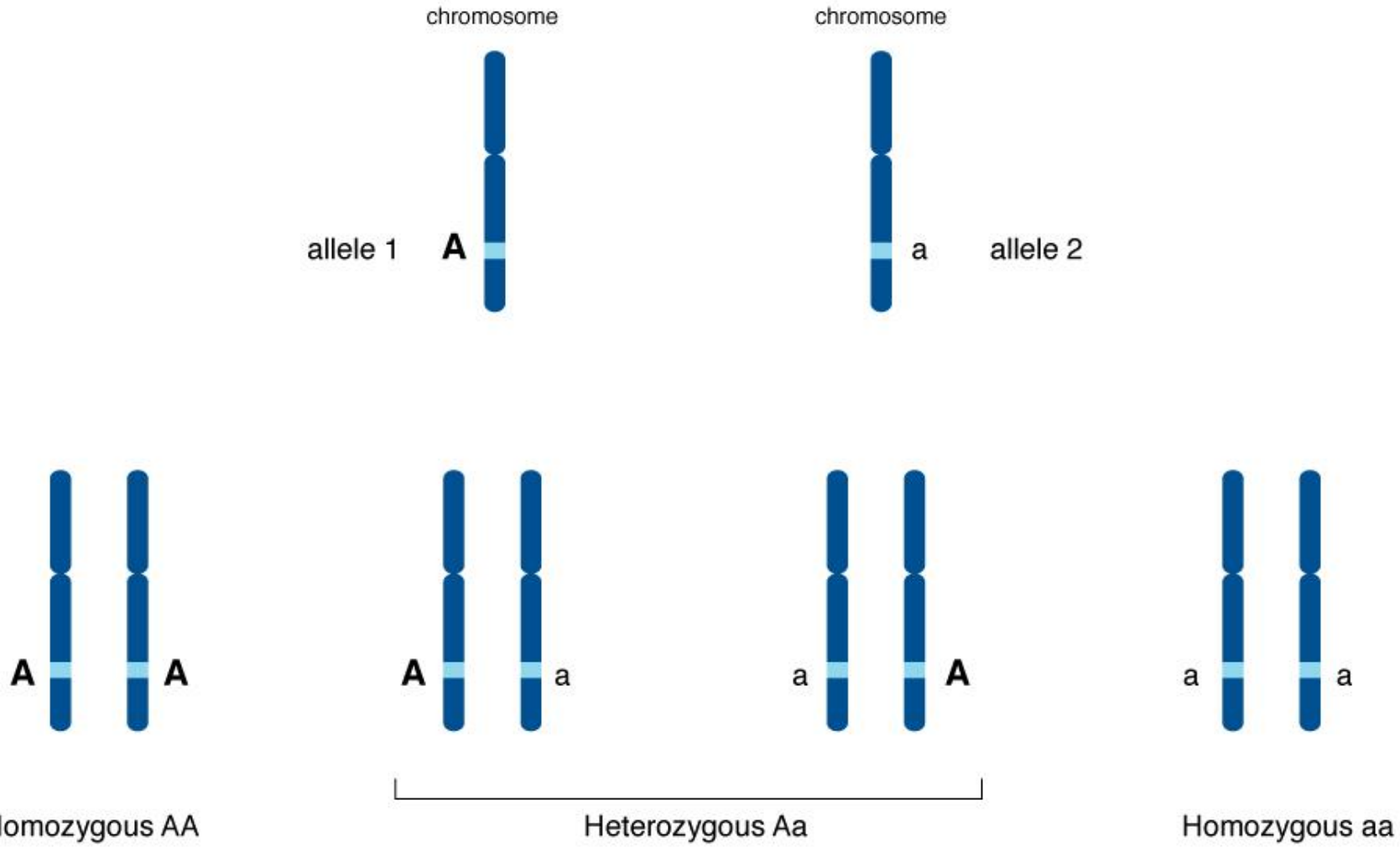
  For example:

  - colour of flowers –either white or purple
  - Colour of peas – either round or wrinkled



Conclusions from Mendel's experiments

- Alternative versions of genes account for variations in inherited characters (alleles)
- For each character trait (e.g. colour, height, etc in case of peas): the organism inherits 2 genes, one from each parents.
- If 2 genes differs
  - The dominant allele is fully expressed in the organism's appearance
  - The other has no noticeable effect on the organism's appearance
- The 2 genes for each character segregate during gamete production


chromosome
chromosome
allele 1
A
a
allele 2
A
A
A
a
a
A
a
a
Homozygous AA
Heterozygous Aa
Homozygous aa

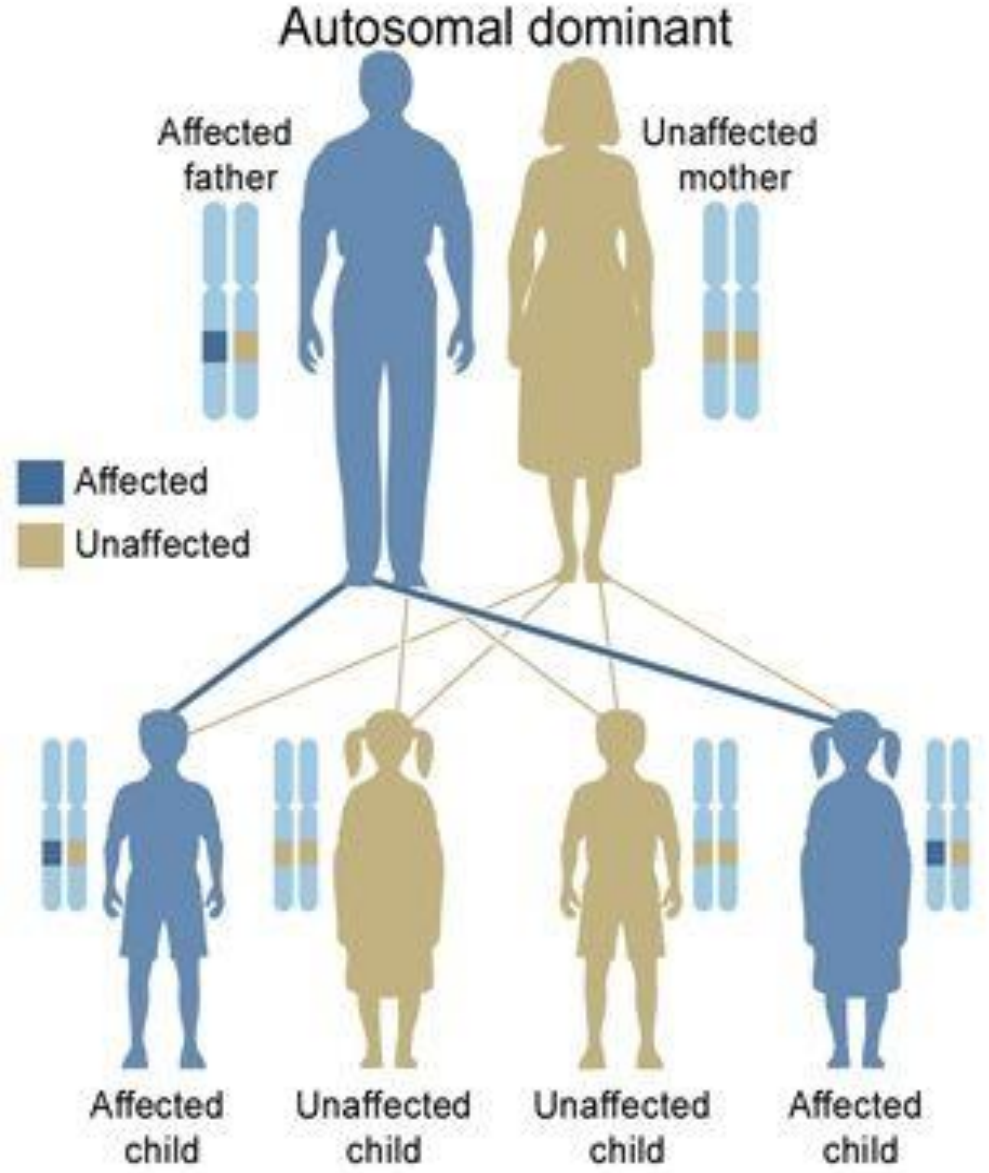
Types of inheritance

Autosome refers to chromosome 1-22
Chromosome 23 = X or Y = sex chromosome

1. Autosomal dominant
2. Autosomal recessive
3. X-linked dominant
   - Inheritance of x-linked dominant genes (on X-chromosome)
4. X-linked recessive
5. Co-dominance
   - The alleles are equally strong

Autosomal dominant

- Inheritance of autosomal dominant genes
- One allele is enough for the expression of a particular phenotype. e.g.
  - Detached Ear-lobe,
  - Huntington's disease
  - Von Willebrand disease



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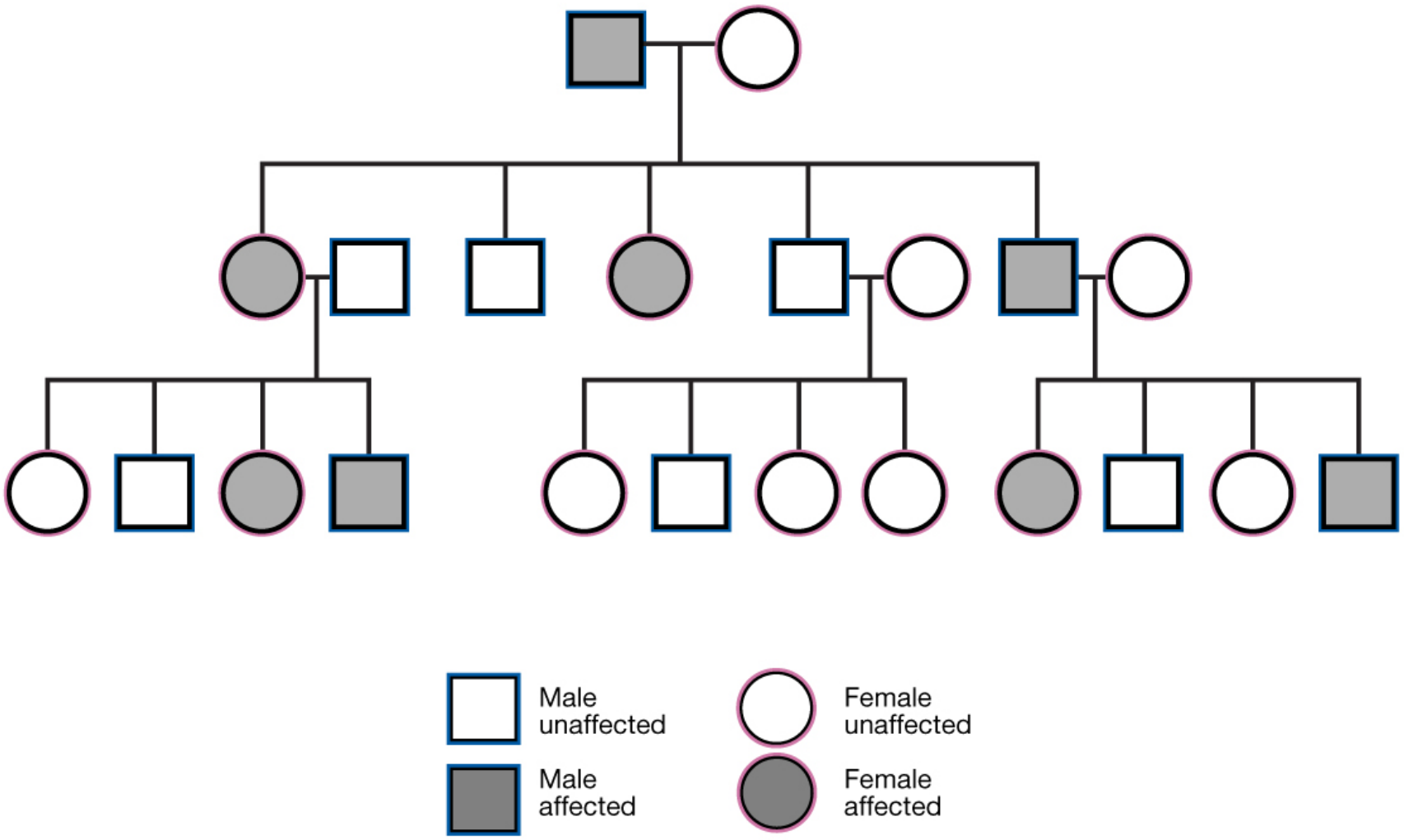
Punnett table		
Let A = affected a = unaffected		
Mother	Father	
	A	a
a	Aa	aa
a	Aa	aa
Chance for offspring to be affected is 2/4, ie 50%.		

Autosomal dominant



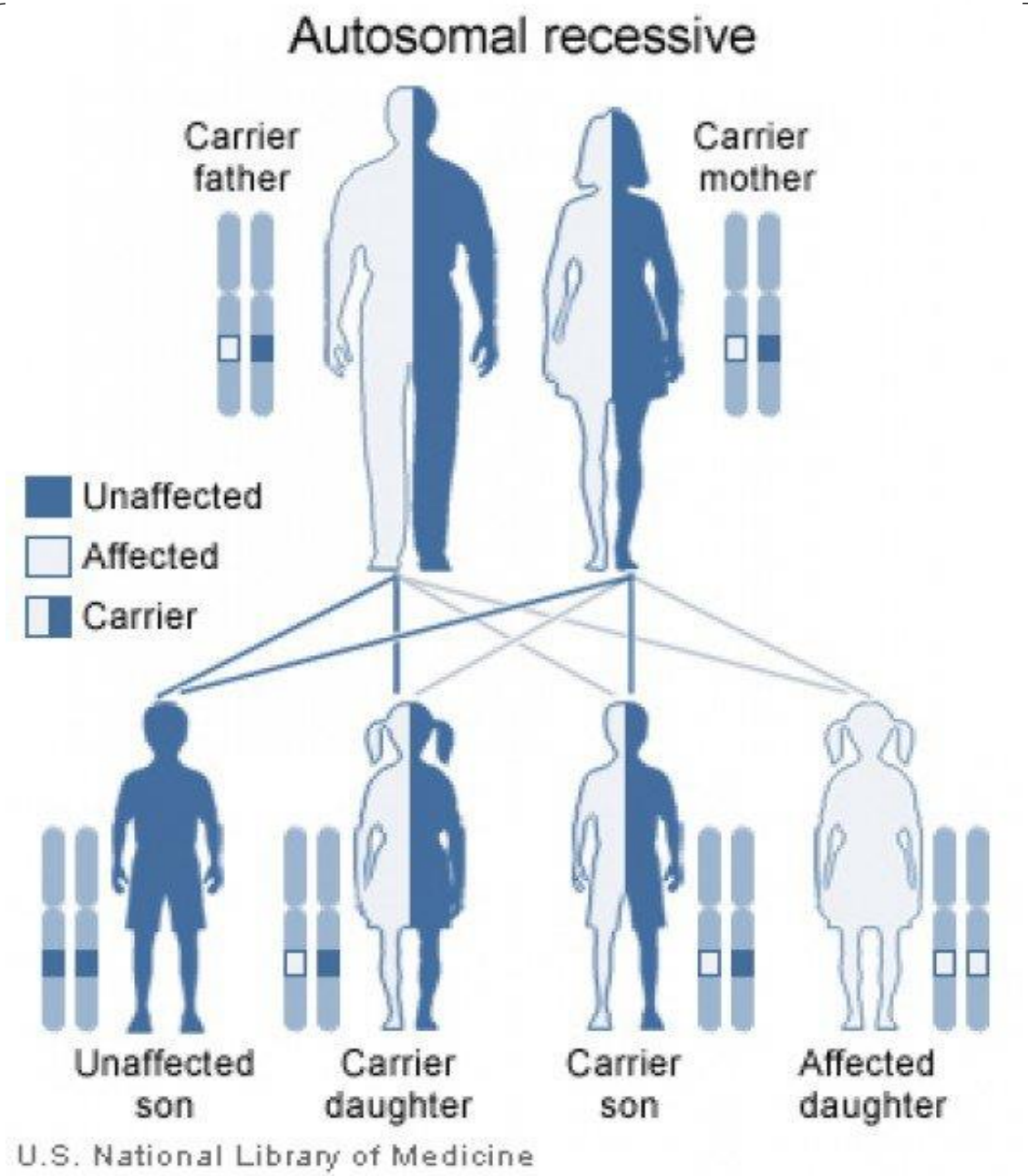
Autosomal recessive

- Two alleles are required for the expression of a particular phenotype. e.g.
  - Albinism
  - Cystic fibrosis
  - Sickle cell disease

Properties of autosomal recessive inheritance

Recessive = need to have 2 recessive alleles to exhibit a particular phenotype

- Parents are unaffected (they are carriers of the recessive genes)



Punnett table		
Let A = unaffected a = affected		
Mother	Father	
	A	a
A	AA	Aa
a	Aa	aa
Chance for offspring to be affected is 1/4, ie 25%.		

Properties of autosomal recessive inheritance

If A = dominant allele (dark skin colour);
a = recessive allele (no colouration)

Mother \ Father	A	a
A	AA	Aa
a	Aa	aa

25% homozygous dominant (AA)
50% carrier (Aa) } Normal dark skin
25% homozygous recessive (aa) → albino

Properties of autosomal recessive inheritance

1. Parents are unaffected (they are carriers of the recessive genes)

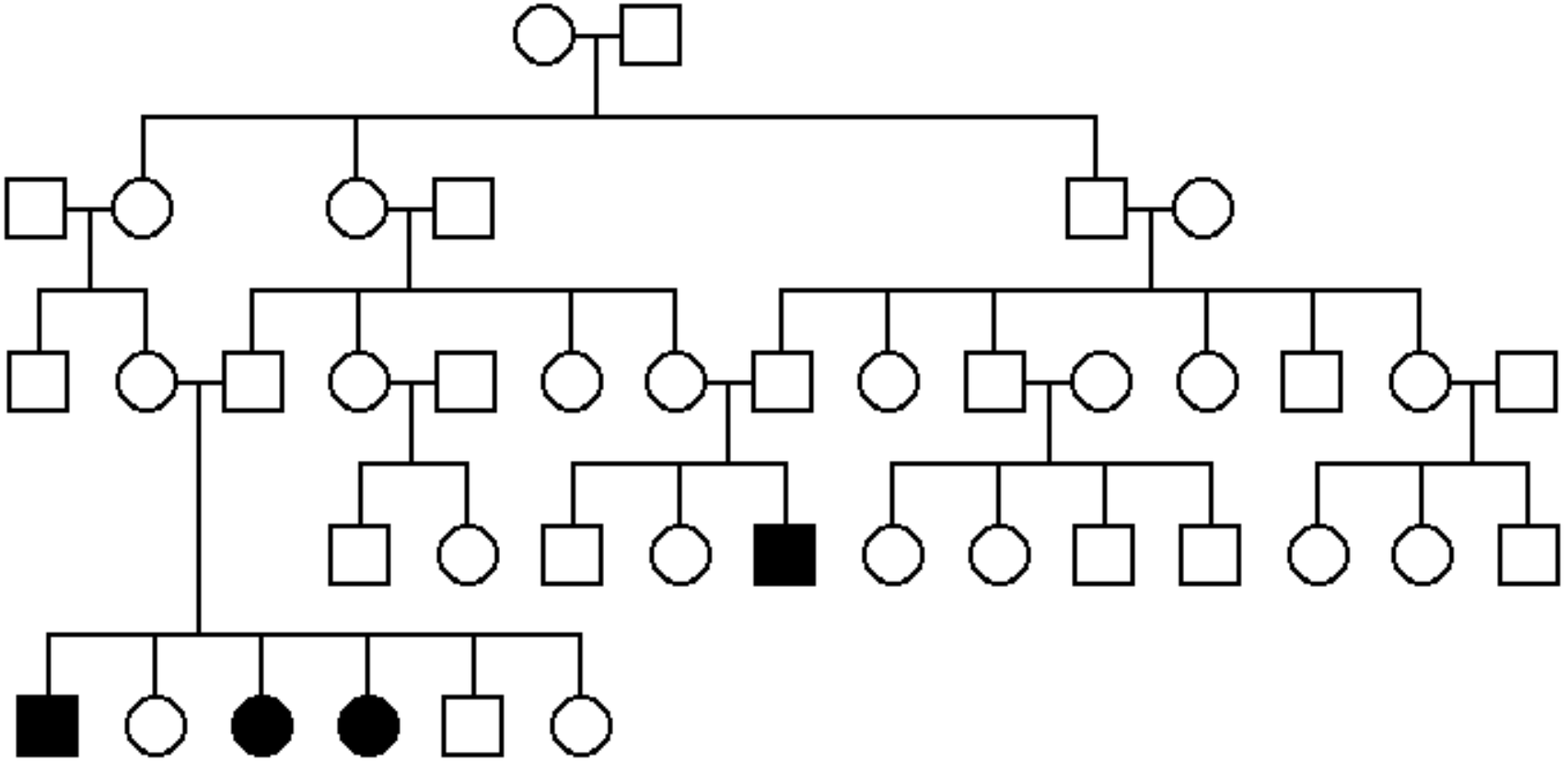
2. An affected individual will have approx. 25% of siblings being affected

   - Ie. chance of having another affected child is 25%

3. Often resulted from consanguineous mating (between close relatives)

   - The number of recessive allele (esp. disease) in the whole gene pool is rare

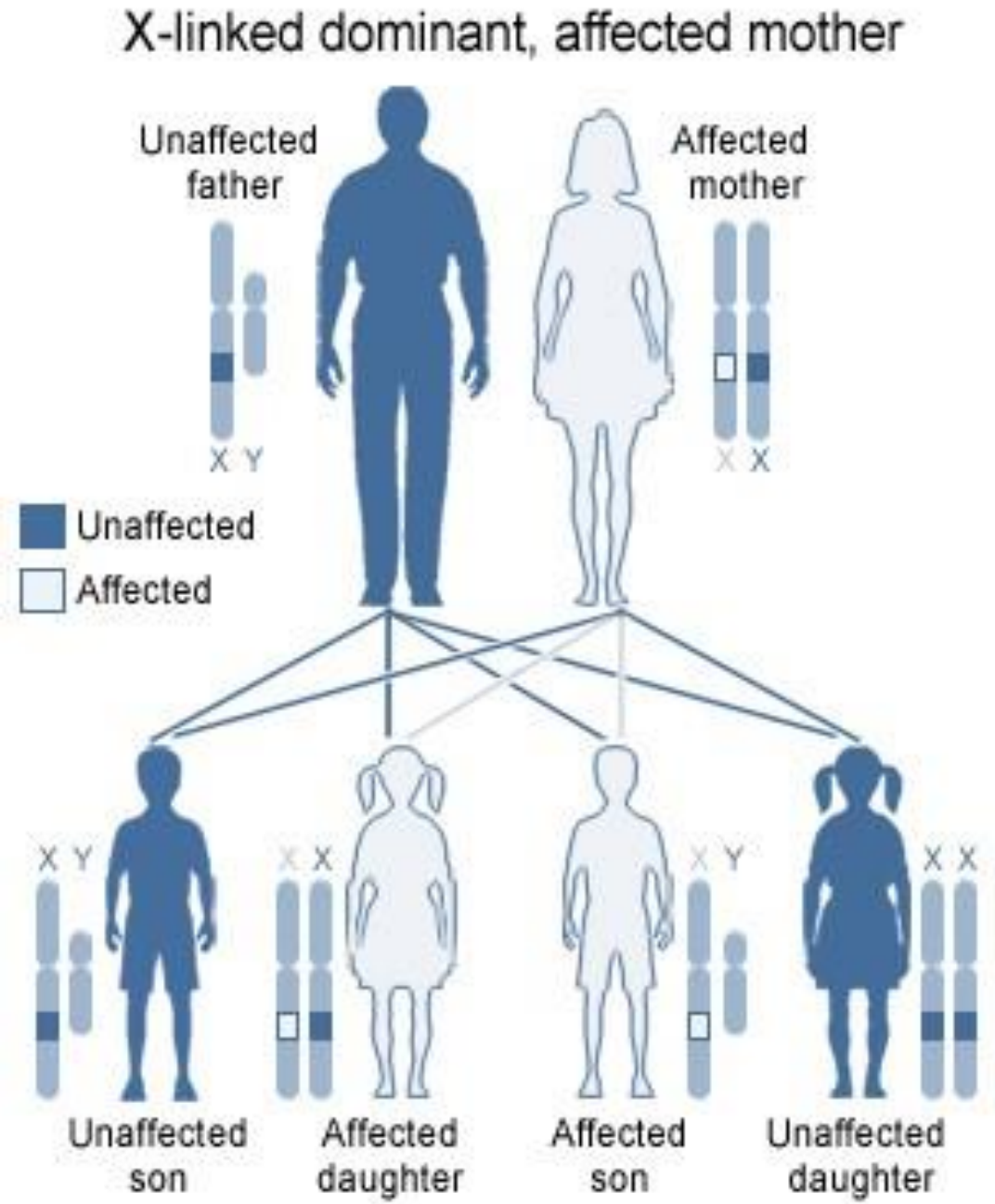
Pedigree of autosomal recessive disease



Properties of X-linked dominant inheritance

- X-linked means the allele is on chromosome X

1. Trait is never passed from father to son


X-linked dominant, affected mother
Unaffected father
Affected mother
X Y
X X
Unaffected
Affected
X Y
X X
X Y
X X
Unaffected son
Affected daughter
Affected son
Unaffected daughter
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Properties of X-linked dominant inheritance

2. If an affected male mates with a normal female
   - All daughters are affected
   - All sons are normal

Properties of X-linked dominant inheritance

3. If an affected female mates with a normal male
   - ➢ 50% children are affected (no sex difference)

If X^A = dominant x-linked allele

X = normal

Father

Mother		X^A	Y
	X	XX^A	XY
	X	XX^A	XY

All females are affected

All males are unaffected

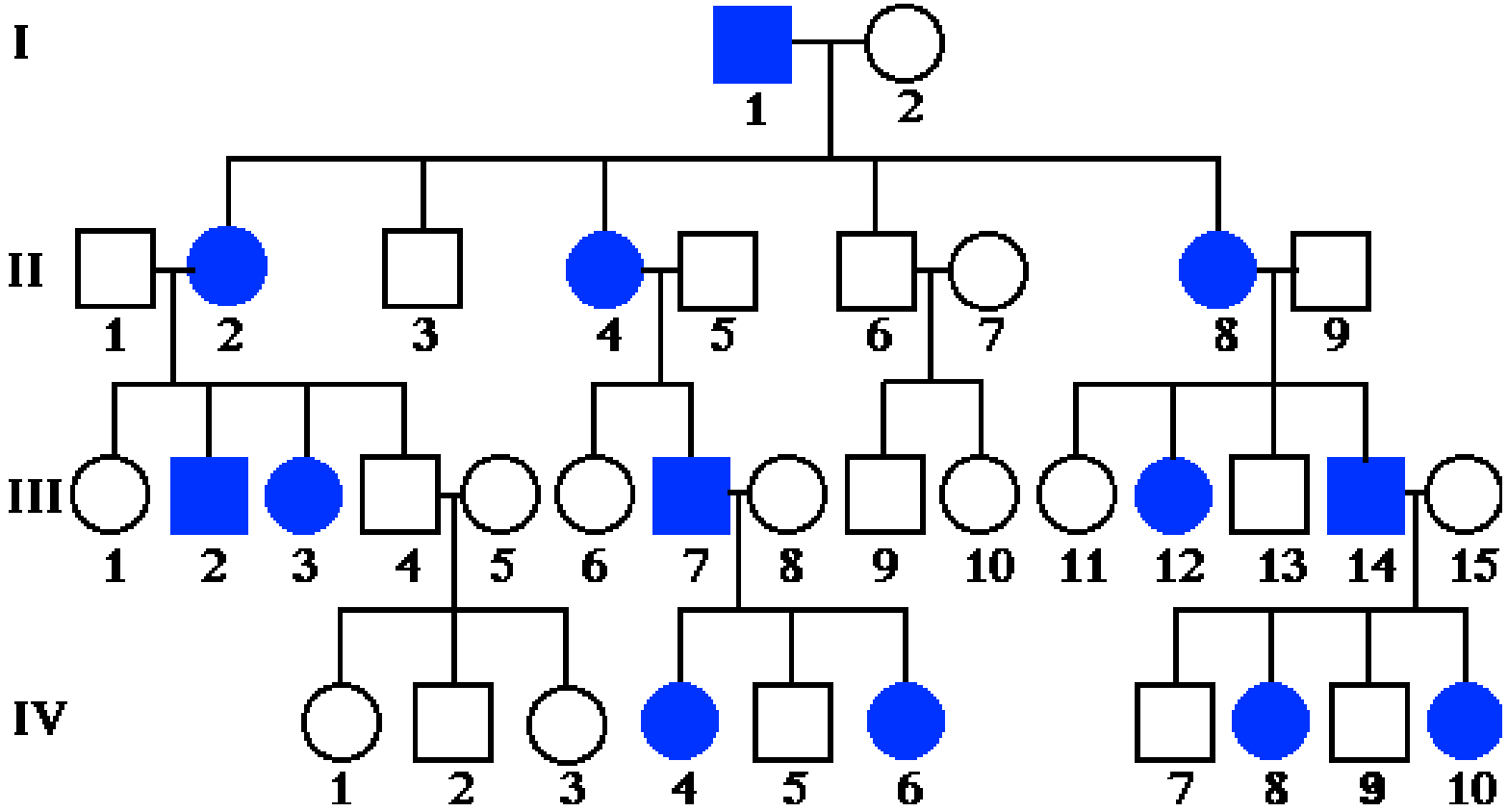
Father

Mother		X	Y
	X	XX	XY
	X^A	XX^A	X^AY

50% females are affected

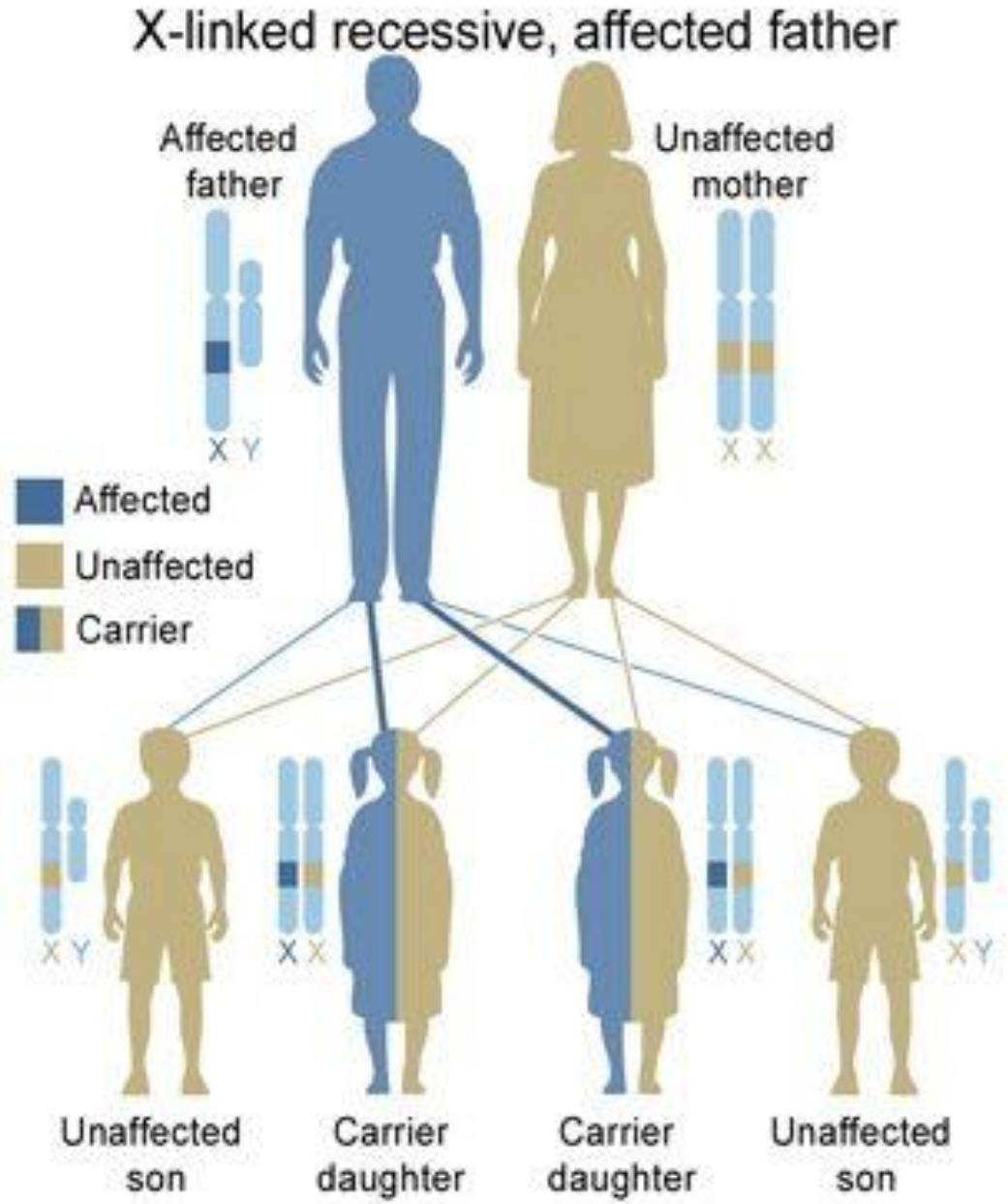
50% males are affected

A pedigree of X-linked dominant inheritance



Properties of X-linked recessive inheritance

- Common examples:
  - G6PD deficiency
  - Red-green colour blindness
- Rare examples:
  - Haemophilia
  - Duchenne muscular dystrophy


X-linked recessive, affected father
Affected father
Unaffected mother
X Y
X X
Affected
Unaffected
Carrier
X Y
X X
X X
X Y
Unaffected son
Carrier daughter
Carrier daughter
Unaffected son
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Properties of X-linked recessive inheritance

1. Males are more likely affected
2. Trait never pass from father to son.
3. Trait can pass from an affected grandfather to half of his grandsons through his carrier daughters, i.e. it skips a generation.

Properties of X-linked recessive inheritance

If X^A = dominant x-linked allele

X = normal

Affected grandfather

Grandmather

	X^A	Y
X	XX^A	XY
X	XX^A	XY

All females are carriers

All males are unaffected

Normal Father

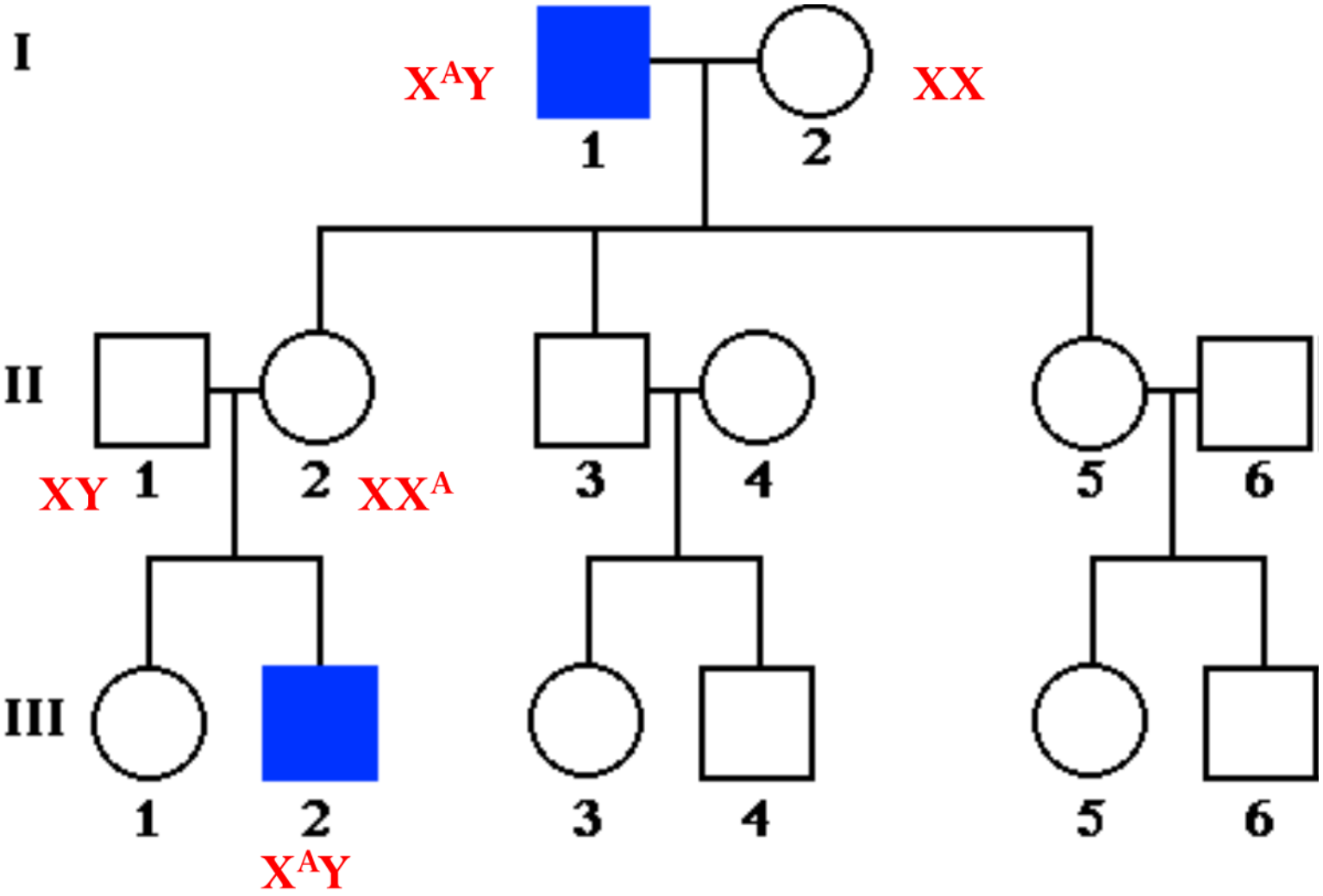
Carrier Mother

	X	Y
X	XX	XY
X^A	XX^A	X^AY

50% affected grandsons

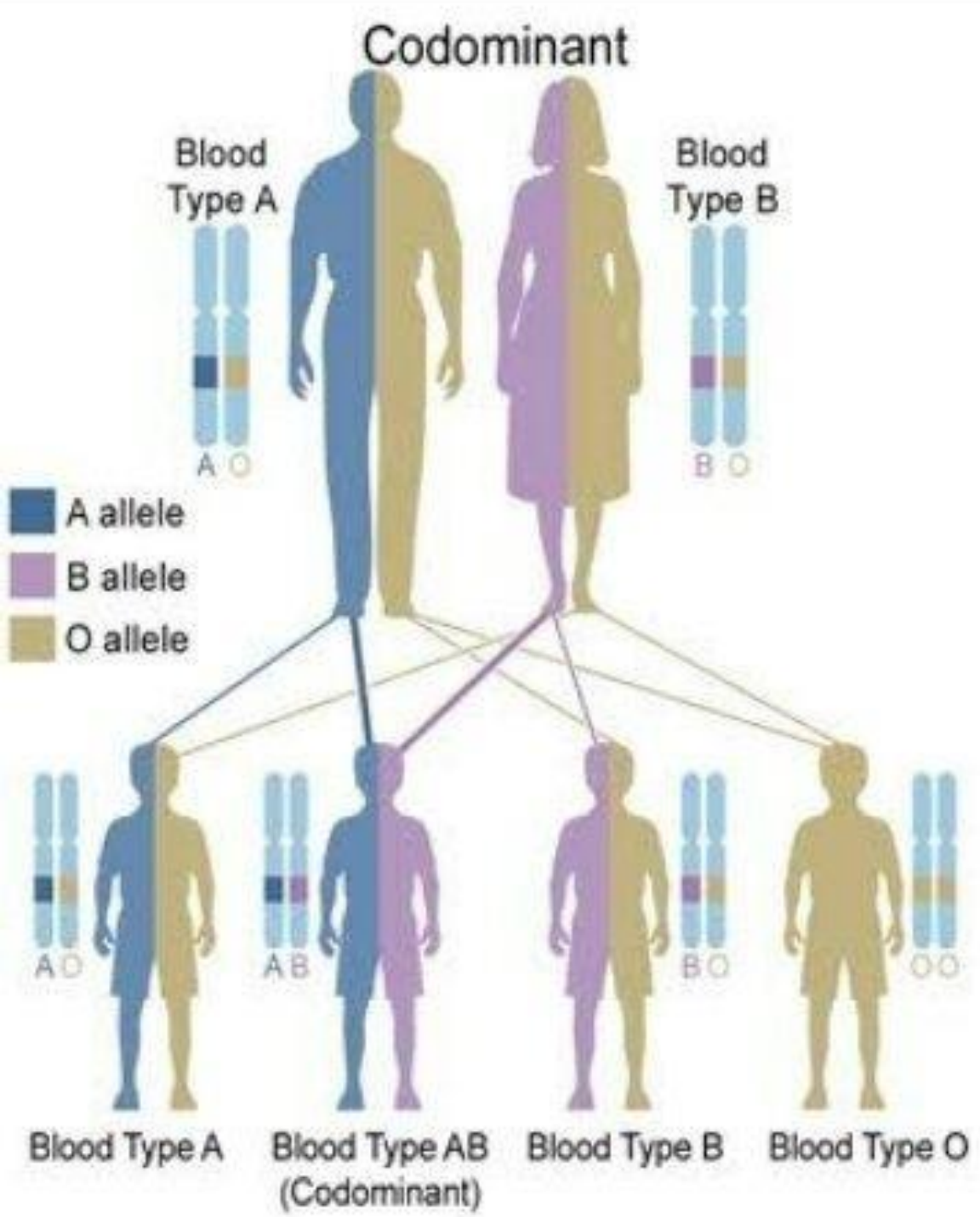
50% carrier granddaughters

A pedigree of X-linked recessive inheritance



Co-dominance

- Equally strong alleles and the characteristics defined each allele are shown equally
- 3 alleles control ABO blood grouping
  - A: an enzyme that make antigen A (dominant)
  - B: an enzyme that make antogen B (dominant)
  - O: an non-functional enzyme → no antigen (recessive)


Codominant
Blood Type A
Blood Type B
A O
B O
A allele
B allele
O allele
A O
A B
B O
O O
Blood Type A
Blood Type AB (Codominant)
Blood Type B
Blood Type O

Co-dominance

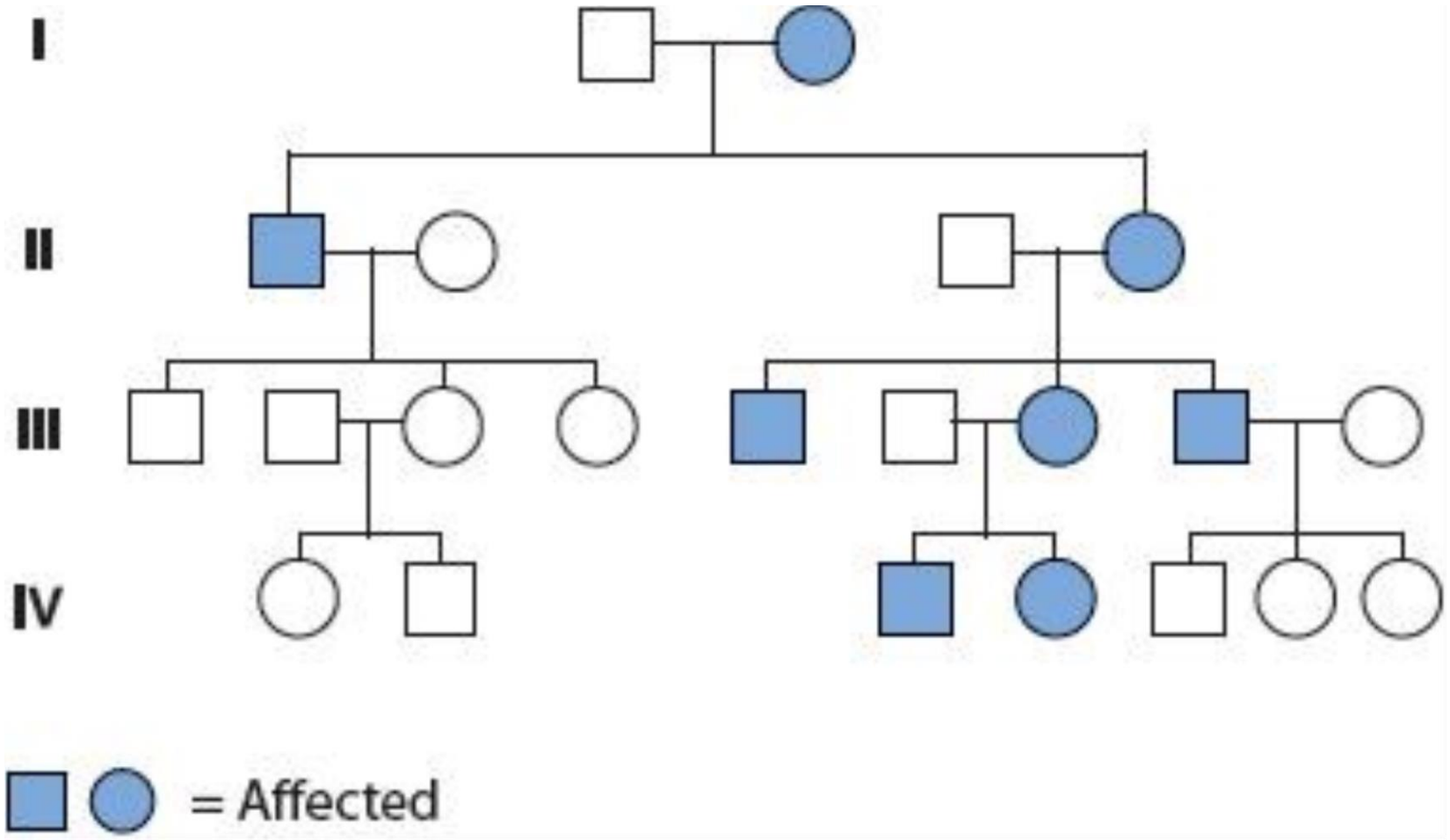
Blood group (phenotype)	Antigen(s) on RBC	Genotype (combination of alleles)
A	A	AA, AO
B	B	BB, BO
AB	A and B	AB
O	None	OO

Non-Mendelian inheritance - exemplified by mtDNA heritability

Characteristics of Mitochondrial Inheritance

- During fertilization only the head of the sperm, without mitochondria, penetrates the egg, hence the human zygote receives almost all of its mitochondria from the oocyte.
- Mitochondrial inheritance is, thus, purely **maternal.**
- Unlike the nuclear genome, mtDNA does not have a controlled segregation mechanism. mtDNA is replicated independently of the cell cycle, and the individual copies are randomly distributed to the daughter cells during mitosis.

Typical Pedigree with Mitochondrial Inheritance of a Disorder.



Mitochondrial Inheritance of Mutation

- A mitochondrial DNA mutation can result in
  - absence of enzymes involved in the respiratory chain, or enzymes that are impaired and do not work properly.
- This leads to a reduction in the supply of ATP
- Mutation may affect the normal body's functions.

Vocabulary

- Gamete
- Zygote
- Allele
- Loci
- Phenotype
- Genotype
- Homozygote
- Heterozygote
- Hybrid
- Dominant
- Recessive
- Mendelian inheritance
- Chromosome
- Consanguineous mating
- Pedigree chart
- Autosomal dominant
- Autosomal recessive
- X-linked dominant
- X-linked recessive
- Co-dominance
- Mitochondrial inheritance

Suggested reading

- Martini, F. H., Nath, J. L., & Bartholomew, E.F. (2012). Fundamentals of anatomy and physiology. (9th Ed.). San Francisco : Pearson/Benjamin Cummings (Chapter 29-, p1102-1108)

- http://anthro.palomar.edu/mendel/mendel_1.htm

- http://www.uic.edu/classes/bms/bms655/lesson9.html

- http://www.genome.gov/Glossary/index.cfm?id=1