Human genetics

- Genes follow Mendel's law of inheritance, but differences in **gene action** can generate more complex inheritance patterns for phenotypes
- ***Single genes*** - dominance, codominance, incomplete dominance, overdominance, allelic series**,** pleiotropy, lethals
- ***Multiple genes*** - epistasis, polygenic traits
- ***Genes & the environment*** - sex-influenced traits, environment-dependent gene expression, incomplete penetrance

- Pedigree analysis
- *In humans, pedigree analysis is an important tool for studying inherited diseases*

  Pedigree analysis uses family trees and information about affected individuals to

  - figure out the genetic basis of a disease or trait from its inheritance pattern
  - predict the risk of disease in future offspring in a family (genetic counseling)

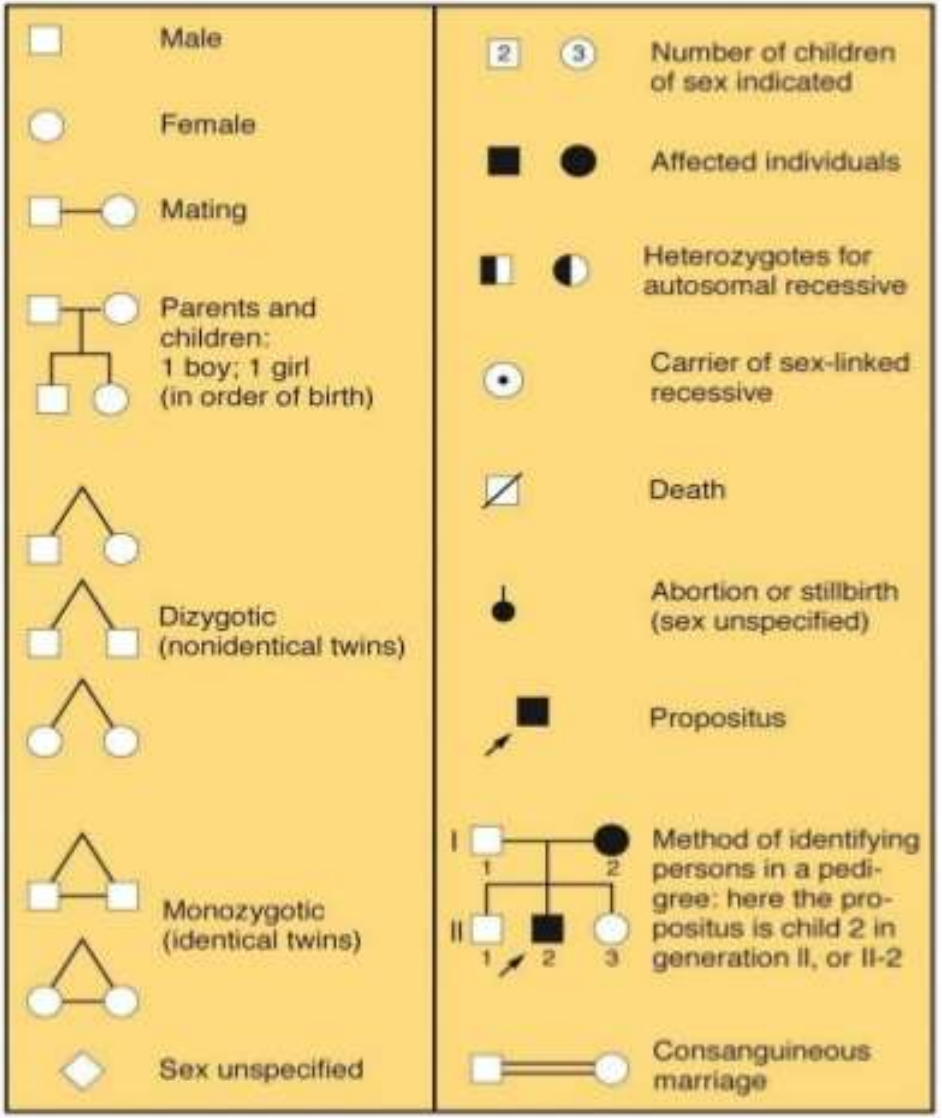
Pedigree analysis

- Analysis of inheritance in human families
- A very important tool for studying human inherited diseases
  - Allow inferences concerning genotypes in a family or population
  - Allows predictions concerning phenotypes of offspring inheriting a genetic disease (genetic counseling)
- Typically small number of offspring
  - Mendelian ratios rarely observed
  - this means the normal 3:1 dominant to recessive ratio doesn't usually occur.

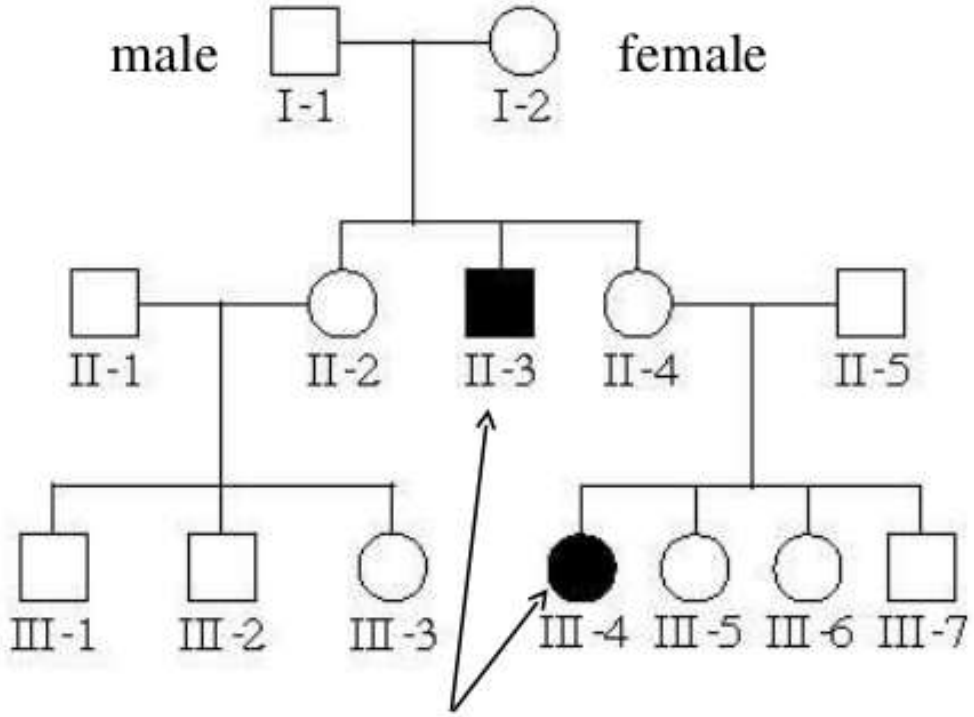
Most common symbols used in creating a pedigree

			
unaffected male	unaffected female	affected male	affected female

Other common signs and symbols used in pedigree analysis



Sample pedigree - cystic fibrosis



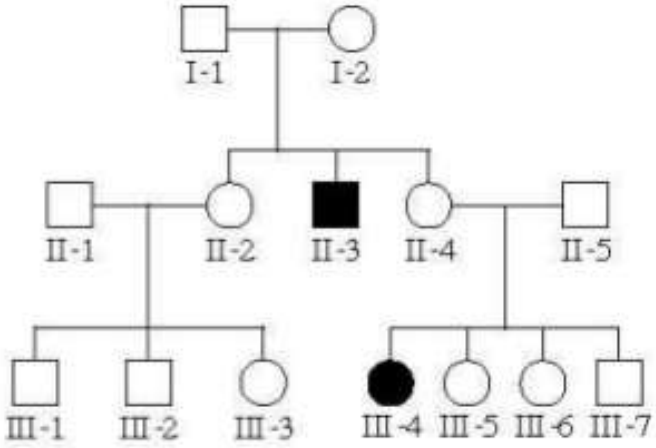
The roman numerals indicate the generation (I, II or III) and the numbers show birth order of children (1, 2, 3, 4 etc.)

Categories of inheritance

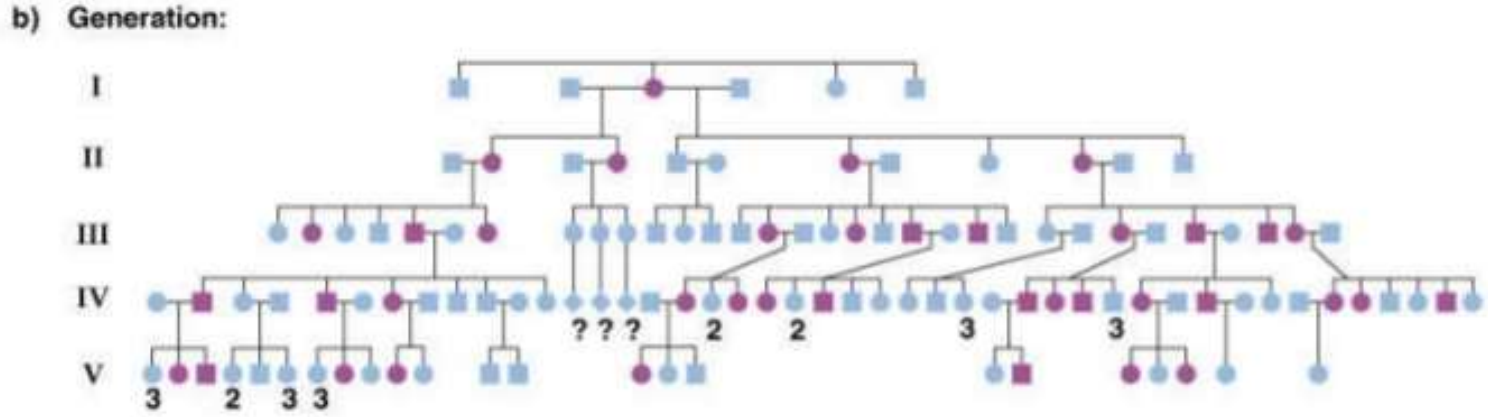
- Autosomal means inherited on chromosome 1-22 while sex-linked means inherited on either X or Y chromosome.
- Autosomal recessive
  - e.g., PKU, Tay-Sachs, albinism
- Autosomal dominant
  - e.g., Huntington's Disease
- X-linked recessive (meaning this allele is found on only the X chromosome: can be in males or females)
  - e.g., color-blindness, hemophilia
- X-linked dominant (meaning this allele is found on X chromosomes; can be in males or females)
  - e.g., hypophosphatemia
- Y-linked (meaning the allele is found on the Y chromosome and can only be in males)

Autosomal recessive traits

- Trait is rare in the pedigree
- Trait often skips generations (hidden in heterozygous carriers)
- Trait affects males and females equally
- Possible diseases include: Cystic fibrosis, Sickle cell anemia, Phenylketonuria (PKU), Tay-Sachs disease



Autosomal dominant pedigrees



- Trait is common in the pedigree
- Trait is found in every generation
- Affected individuals transmit the trait to about 1/2 of their children (regardless of sex)

Huntington's disease: an example of AD disorder

- Half the people in the Venezuelan village of Barranquitas are affected

- A large-scale pedigree analysis was conducted including 10,000 people

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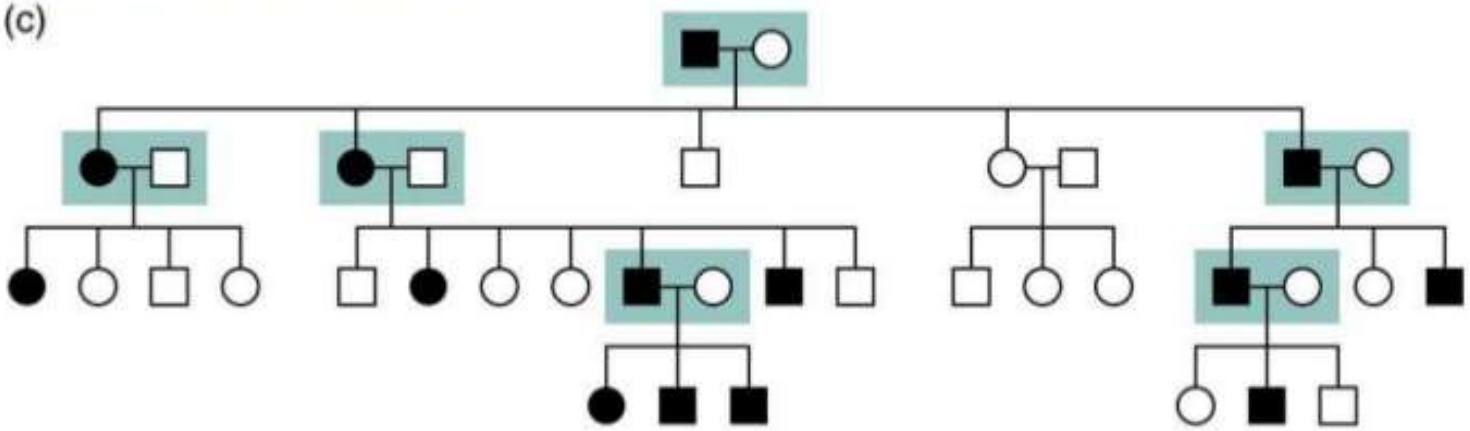
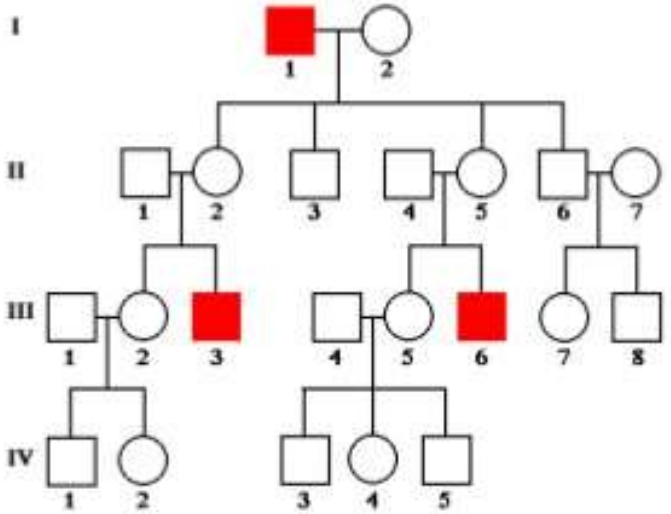


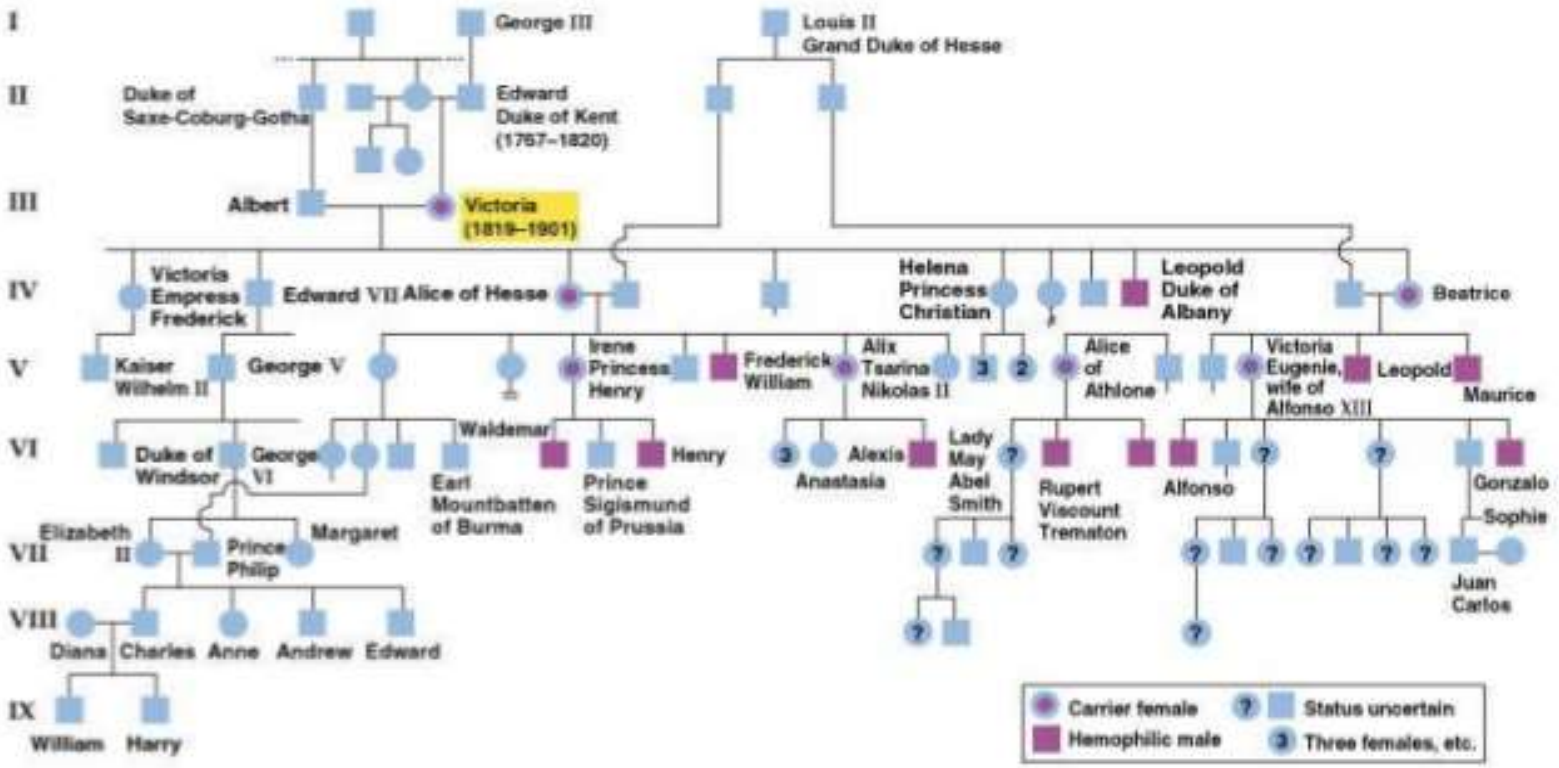
X-linked recessive pedigrees

- Trait is rare in pedigree
- Trait skips generations
- Affected fathers DO NOT pass to their sons
- Males are more often affected than females
- Females are carriers (passed from mom to son)



X-linked recessive traits

ex. Hemophilia in European royalty



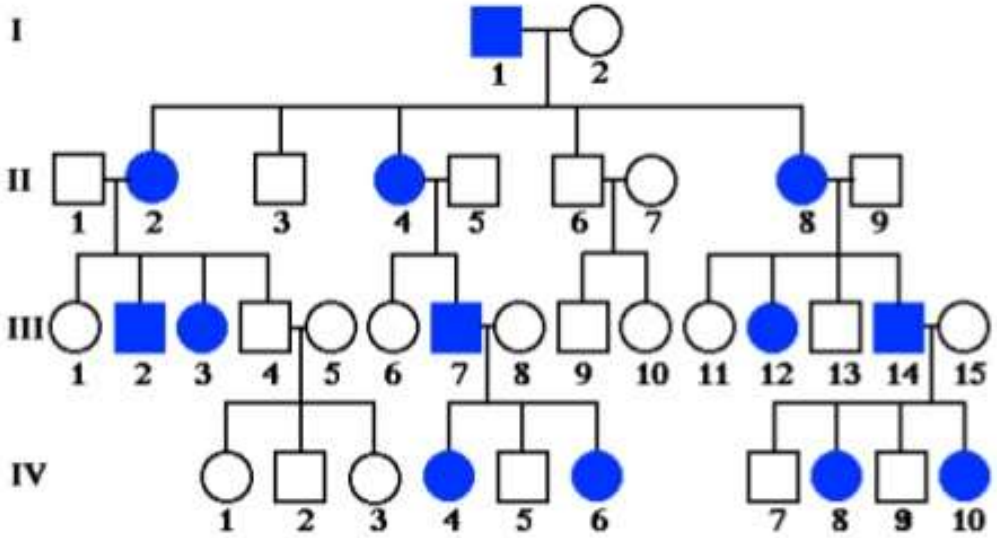
X-linked recessive traits

ex. Glucose-6-Phosphate Dehydrogenase deficiency

- hemolytic disorder causes jaundice in infants and (often fatal) sensitivity to fava beans in adults

- the most common enzyme disorder worldwide, especially in those of Mediterranean ancestry
- may give the individual resistance to malaria

X-linked dominant pedigrees



- Trait is common in pedigree
- Affected fathers pass to ALL of their daughters
- Males and females are equally likely to be affected

X-linked dominant diseases

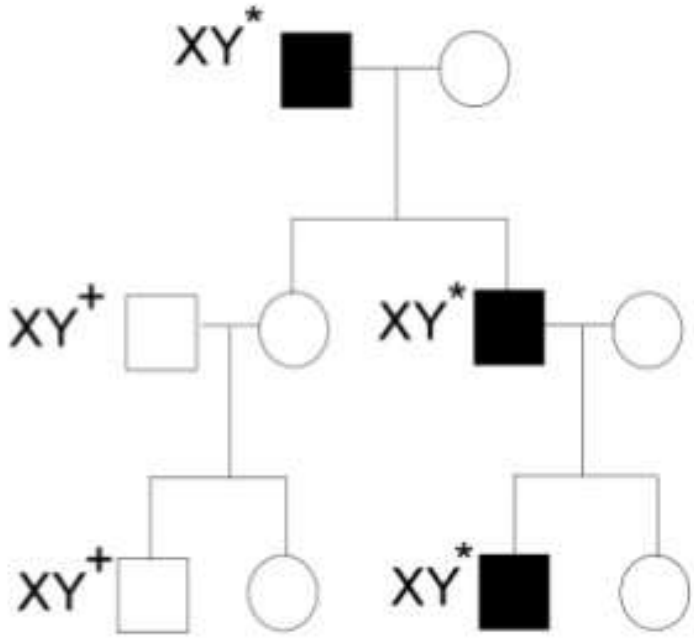
- X-linked dominant diseases are extremely unusual
- Often, they are lethal (before birth) in males and only seen in females

    ex. incontinentia pigmenti (skin lesions)

    ex. X-linked rickets (bone lesions)

Y-Linked Inheritance

- Traits on the Y chromosome are only found in males, never in females.
- The father's traits are passed to all sons.
- Dominance is irrelevant: there is only 1 copy of each Y-linked gene (hemizygous).



Mitochondrial Genes

- Mitochondria are only inherited from the mother.
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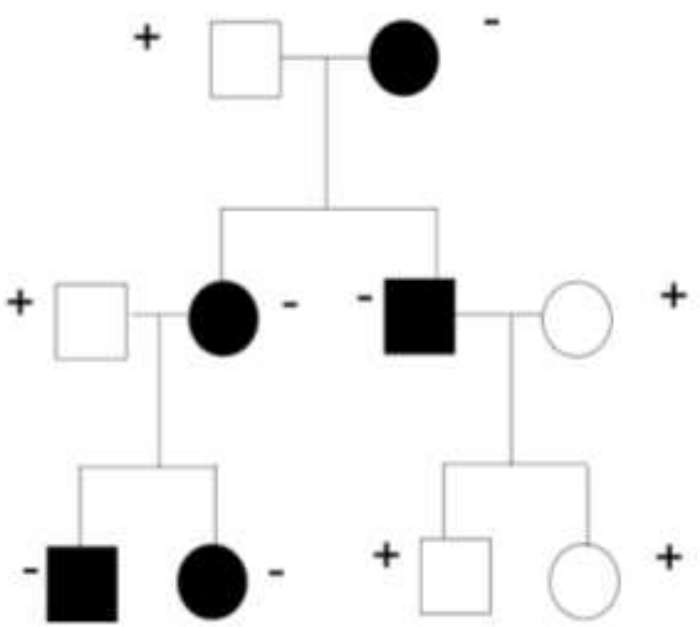
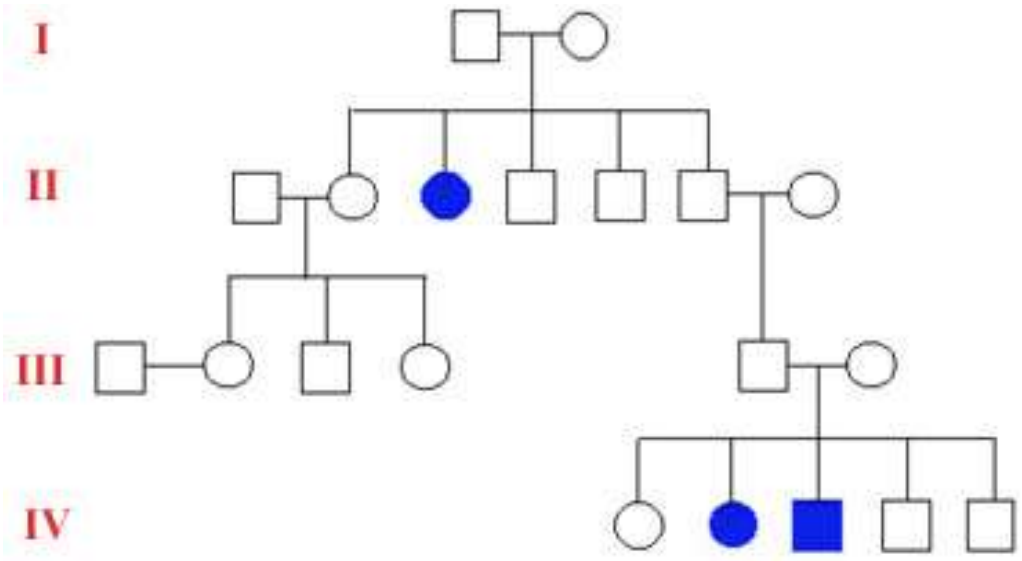
- If a female has a mitochondrial trait, all of her offspring inherit it.
- If a male has a mitochondrial trait, none of his offspring inherit it.

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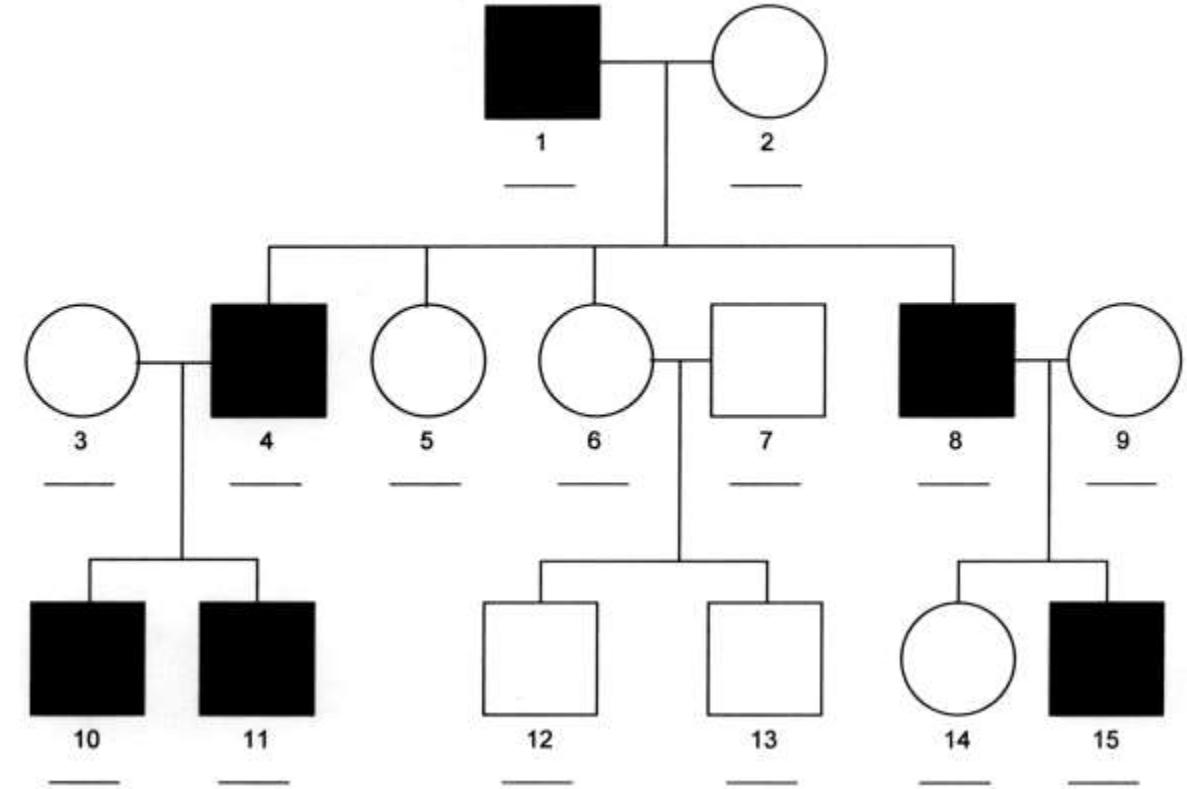
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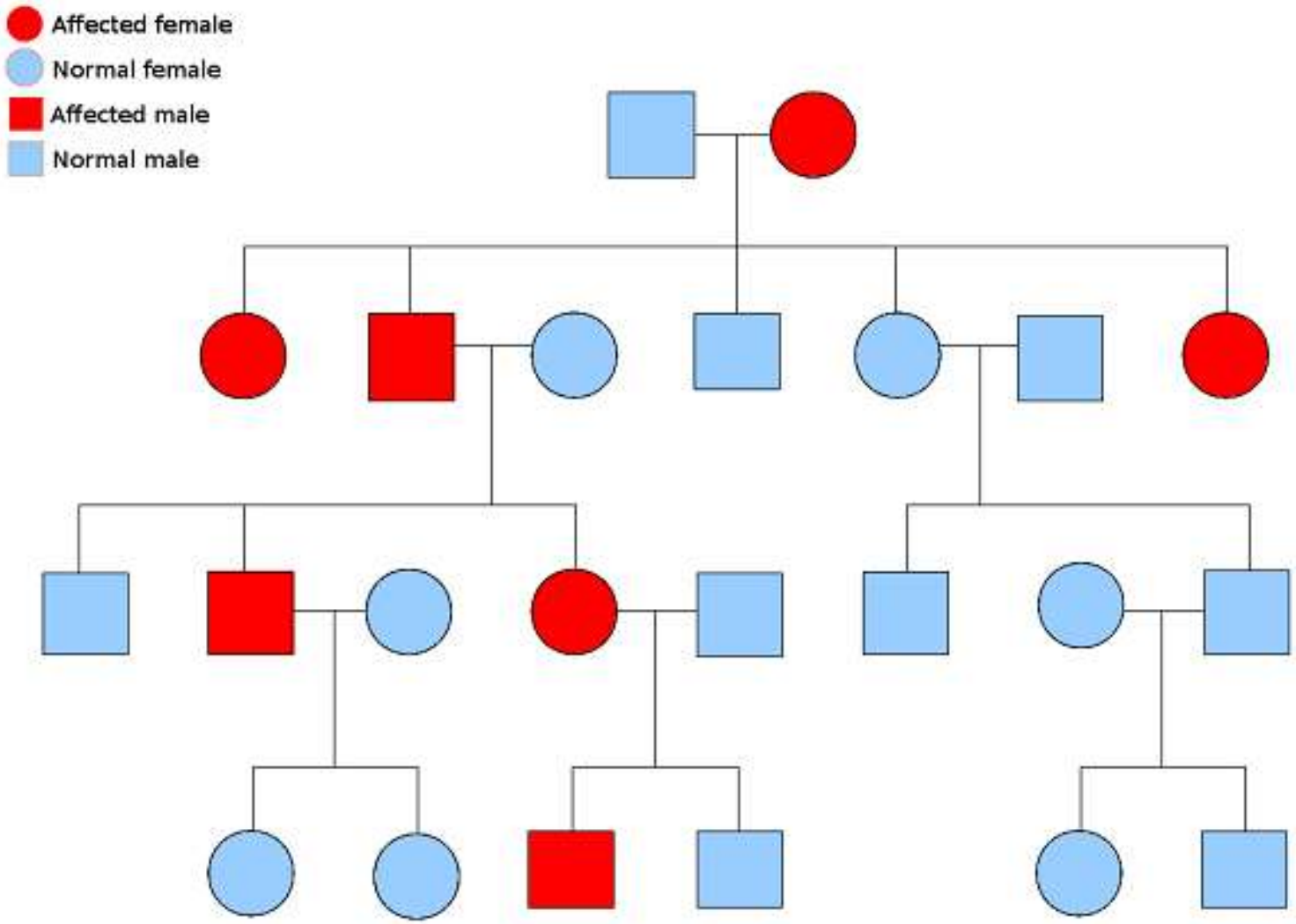
Affected female
Normal female
Affected male
Normal male