Pedigree Analysis

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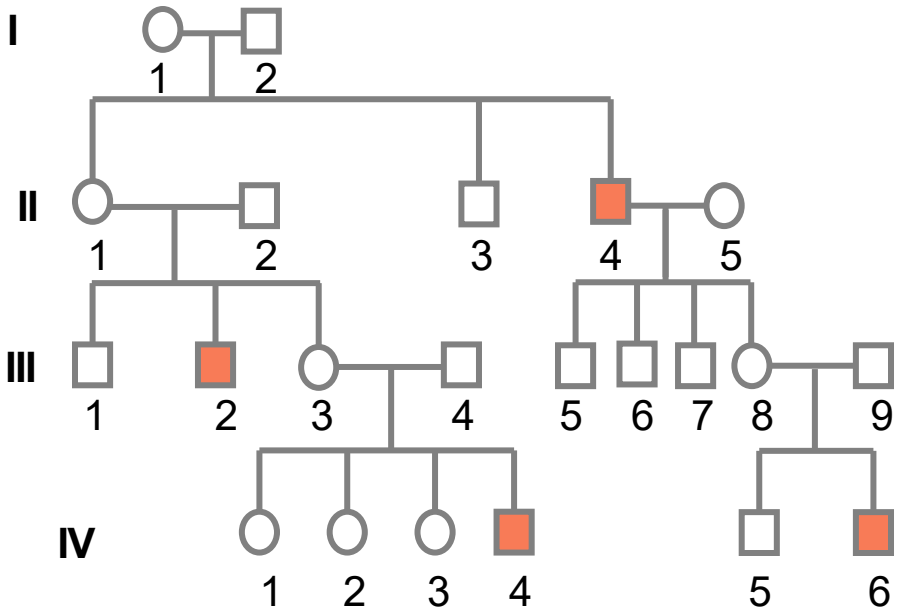
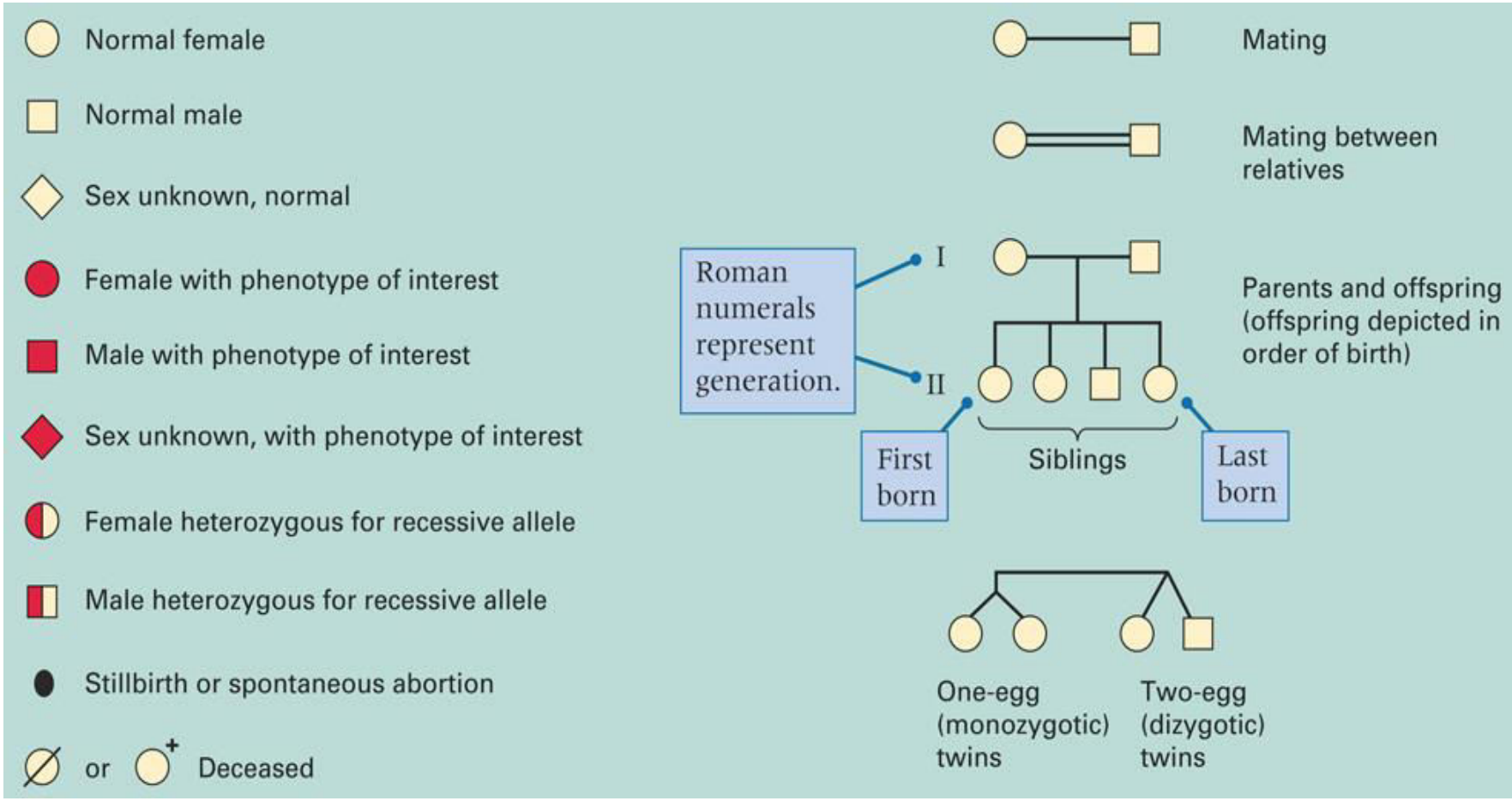
What is a Pedigree?

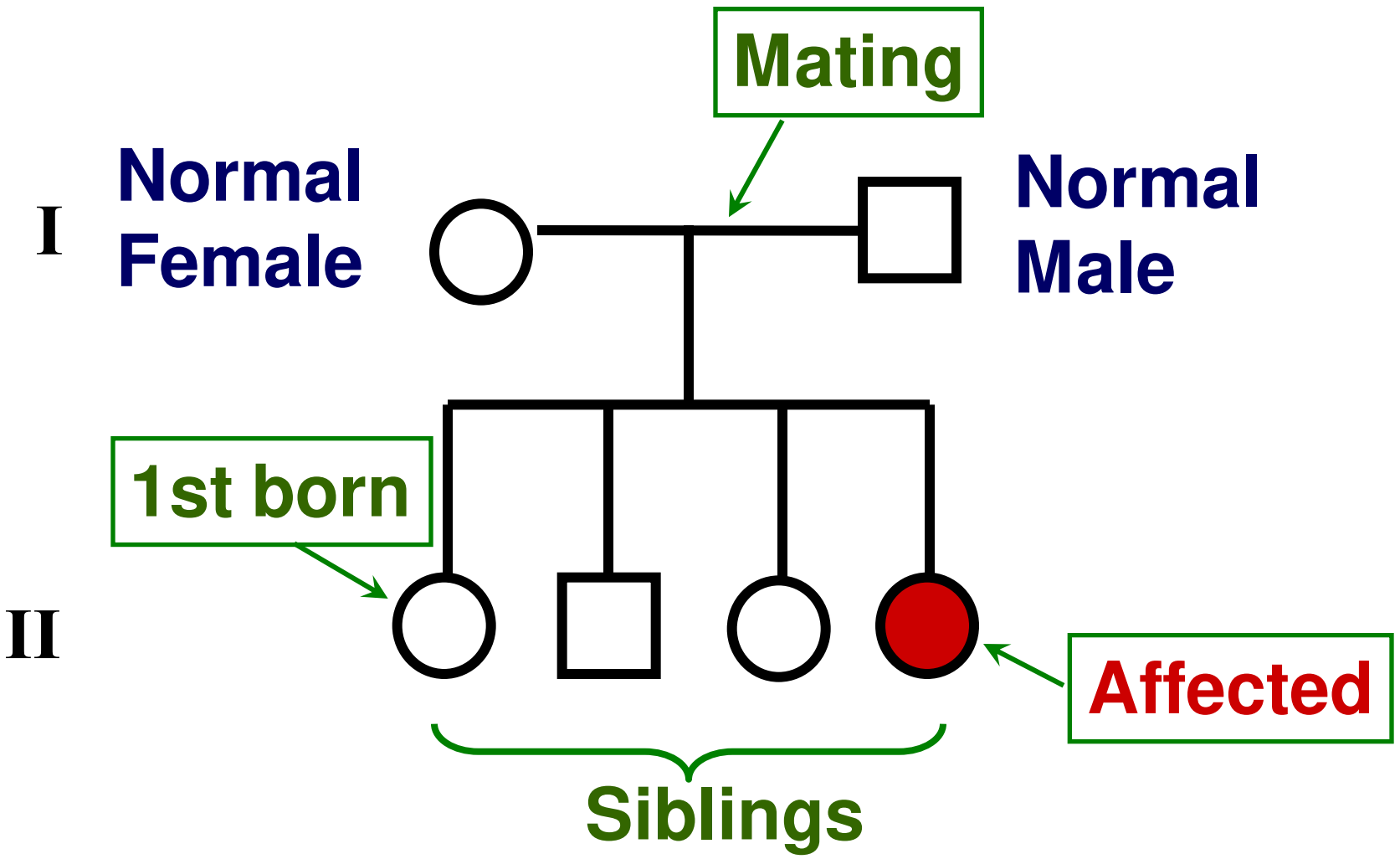
- A pedigree is a pictorial representation of a family history.
- It is an important tool for studying inherited diseases and other traits.
- Pedigree analysis uses family trees and information about affected individuals .



Most common signs and symbols used in pedigree analysis



A Typical Pedigree



Basic patterns of inheritance

- Autosomal, recessive
- Autosomal, dominant
- X-linked, recessive
- X-linked, dominant (very rare)
- Y-linked

Autosomal vs. sex-linked traits

- Autosomal traits are caused by genes on autosomes (chromosome #1- #22)
  - e.g., we speak of autosomal recessive or autosomal dominant traits or diseases.
- Sex-linked traits are caused by genes on the sex chromosome (X or Y)
  - e.g., we speak of X-linked recessive or X-linked dominant traits or diseases.

Recessive inheritance

- If **d** is the disease allele and **D** is normal, then only dd genotypes are affected
- Typically ***not*** seen in every generation
- Affected offspring *can* be born to unaffected parents

Dominant inheritance

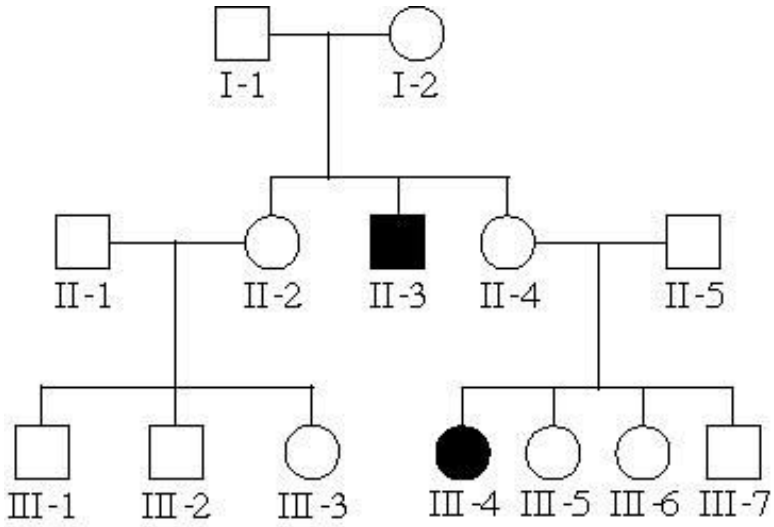
- If **D** is the disease allele and d is normal, then only **dd** genotypes are disease free*
- Dominant trait/disease found in every generation*
- Affected offspring *never*** born to unaffected parents

*Assuming 100% penetrance

**Assuming no new mutation

Autosomal recessive

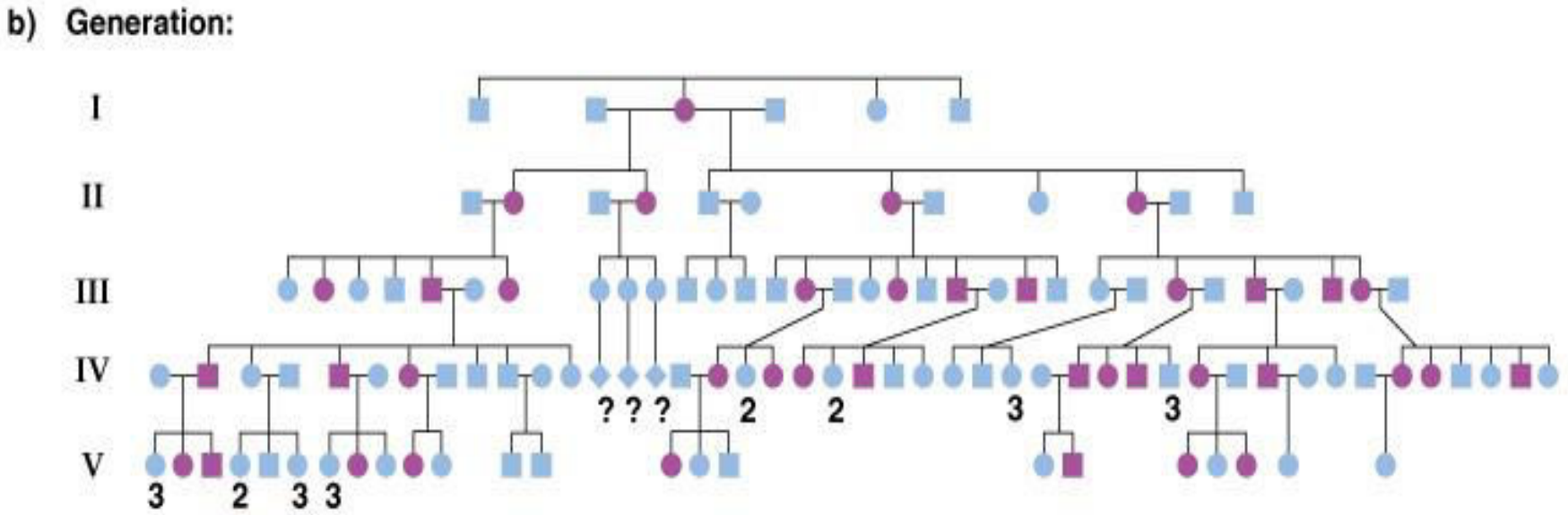
- Trait is rare in pedigree
- Trait often skips generations (hidden in heterozygous carriers)
- Trait affects males and females equally



Autosomal recessive diseases in humans

- Most common ones
  - Cystic fibrosis
  - Sickle cell anemia
  - Phenylketonuria (PKU)
  - Tay-Sachs disease

Autosomal dominant



- Trait is common in the pedigree.
- Trait is found in every generation.
- Appears in both sexes in equal frequency.
- Affected individuals transmit the trait to ~1/2 of their children (regardless of sex).

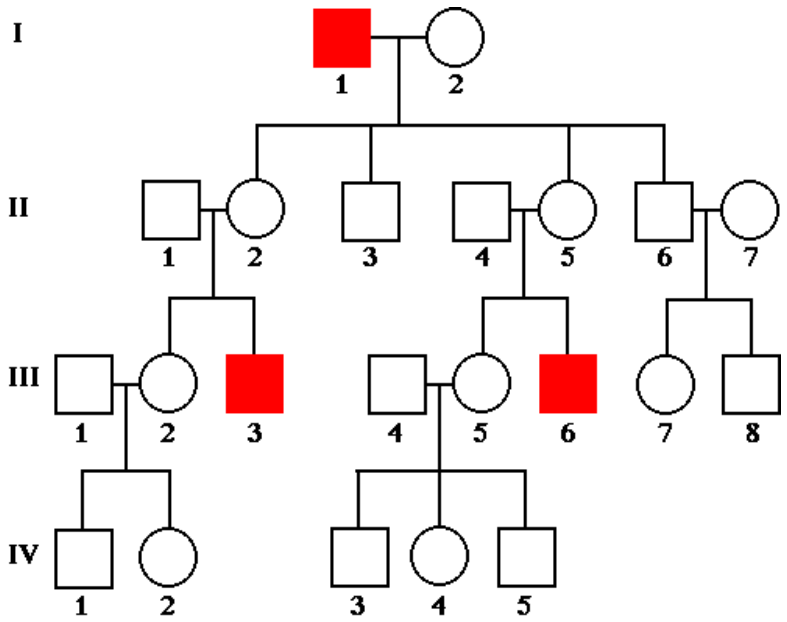
Autosomal Dominant disease in humans

- ACHONDROPLASIA
(a sketelal disorder causing dwarfism)

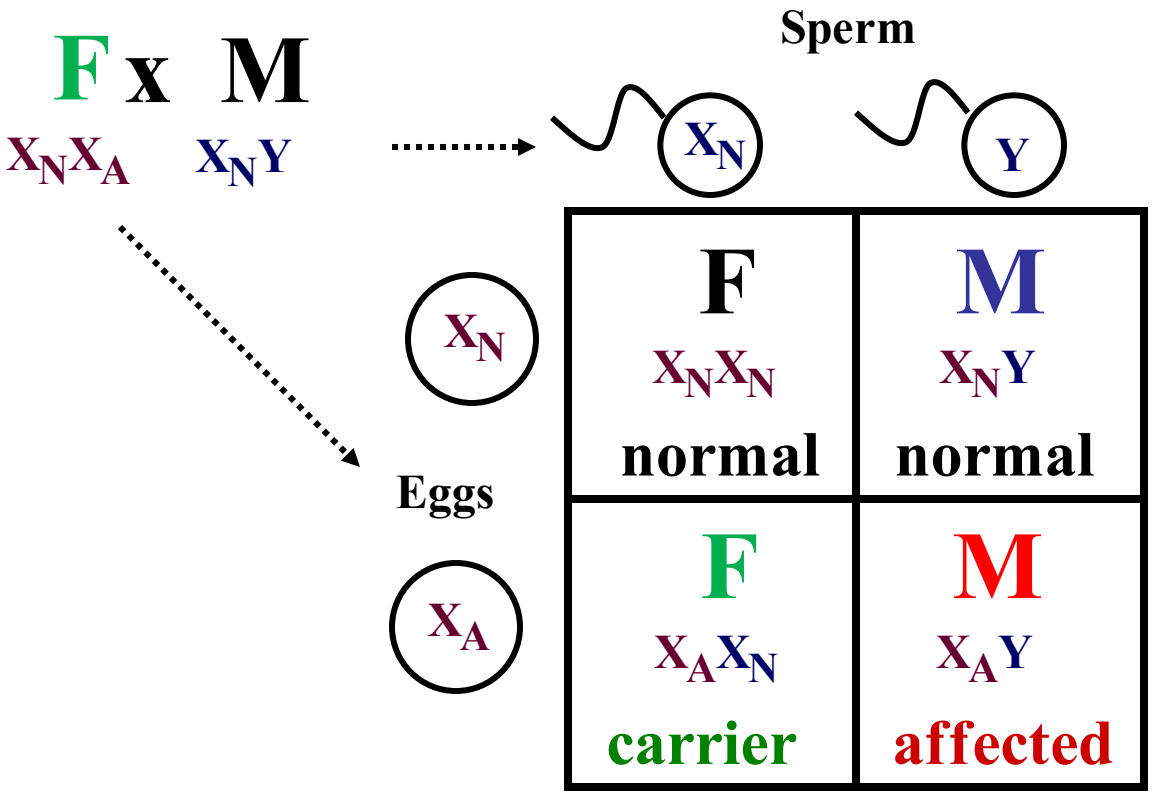
- **Huntington's disease**

X-linked recessive

- Trait is rare in pedigree.
- Trait skips generations.
- Affected sons are usually born to unaffected but carrier mothers.
- Affected fathers DO NOT pass trait to their sons.
- Males are more often affected than females.



Female carrier mates with normal male



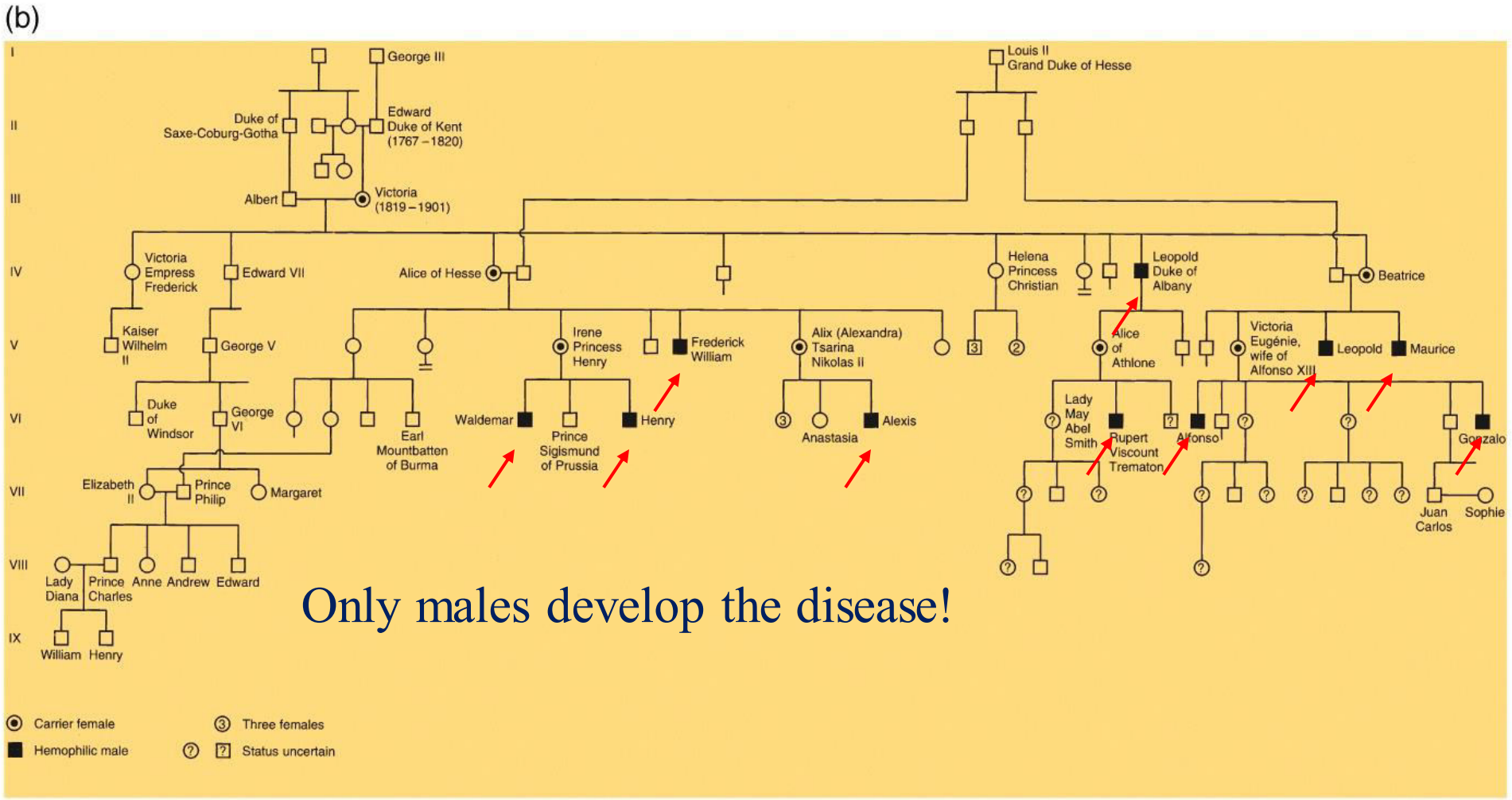
X-linked recessive disease

- Half* her daughters will be carriers
- Half* her sons will be affected

X-linked recessive diseases

- Hemophilia in European royalty
- Duchenne Muscular Dystrophy
- Glucose-6-Phosphate Dehydrogenase deficiency

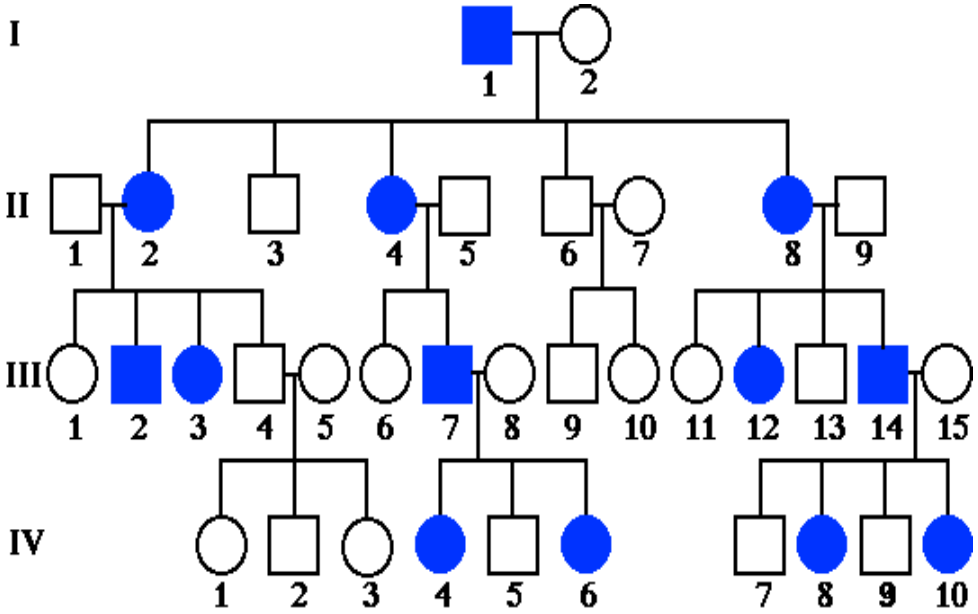
Partial pedigree analysis of haemophilia in royal families of Europe



Only males develop the disease!

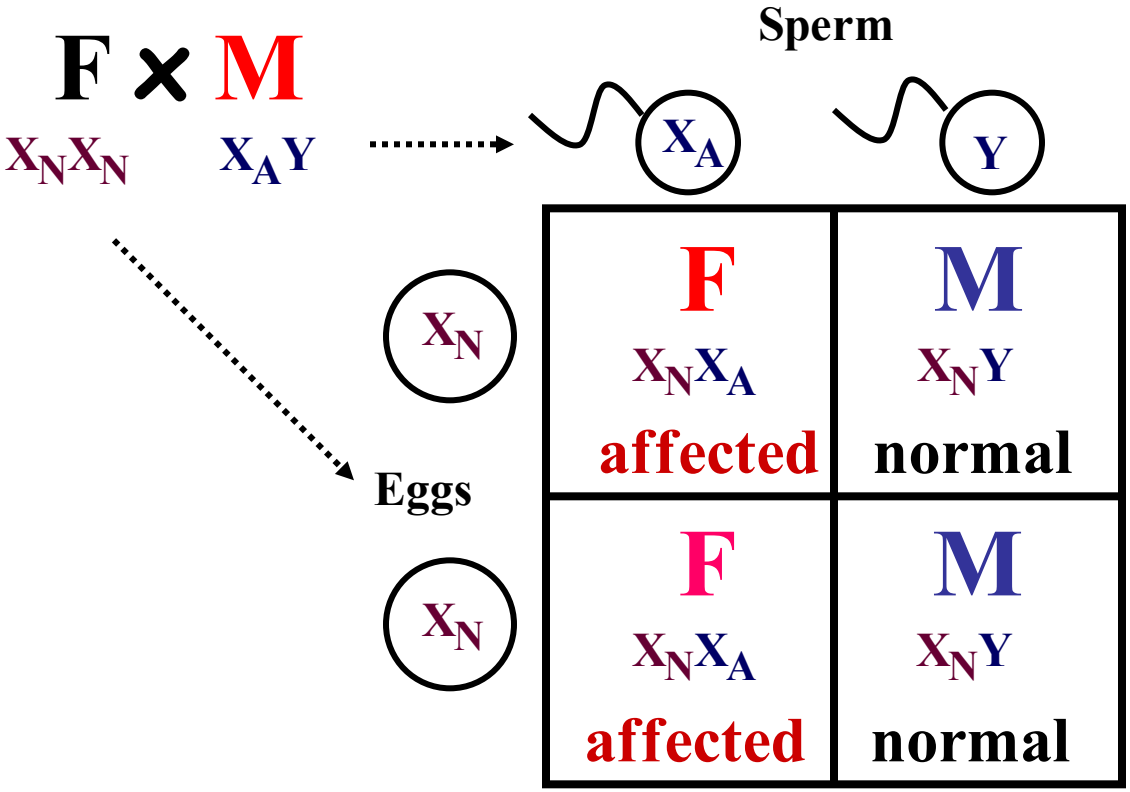
X-linked dominant

- Trait is found in every generation
- Affected sons must have an affected mother
- Affected mother if heterogygous will pass the trait to ½ of the sons and ½ of their daughters
- Affected fathers pass trait to ALL of their daughters
- Males and females are equally likely to be affected



X-linked dominant disease

Affected males mates with normal females



- All his daughters will be affected
- None of his sons will 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

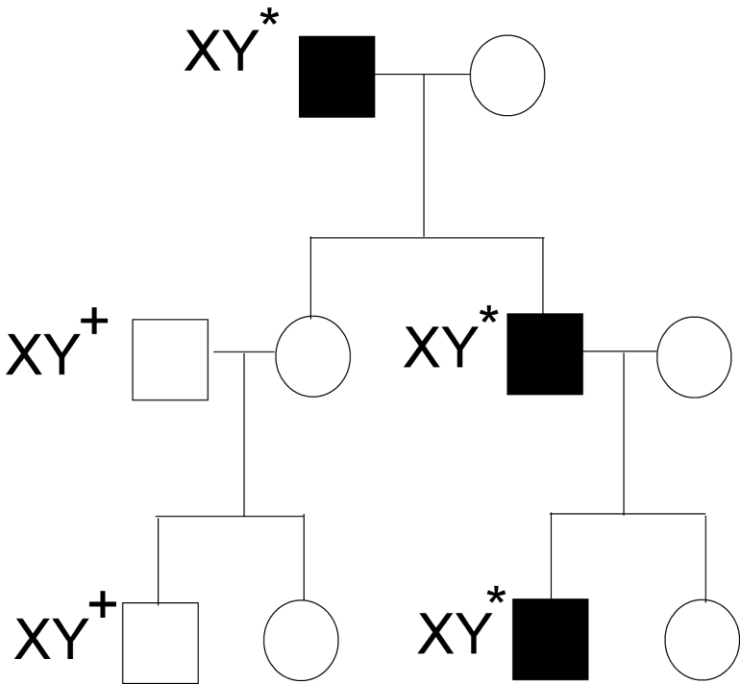
  eg. Incontinentia pigmenti (skin lesions)

  eg. X-linked rickets (bone lesions)

  eg. Hypophosphatemia

Y-Linked Inheritance

- Traits are found in every generation
- 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).



Goals of Pedigree Analysis

- Determine the mode of inheritance: dominant, recessive, partial dominance, sex-linked, autosomal, mitochondrial, maternal effect.

- Predict the risk of disease in future offspring in a family (genetic counseling).

Thank you