

## X-Linked Recessive Inheritance

X-linked recessive disease usually occurs in males who have inherited a recessive X-linked mutation from their mother. Rarely, the disease may be seen in females who have inherited mutations in the same gene X-linked from both parents. More typically, the mother is a carrier and is unaffected, although it is not uncommon for female carriers of X-linked disorders to have mild clinical manifestations related to the disorder — for example, carriers of hemophilia may have mild bleeding problems.

### Pedigree Characteristics of X-Linked Recessive Inheritance

- A male child of a woman who is a carrier has a 50% risk of inheriting the disorder.
- A female child of a woman who is a carrier has a 50% risk of inheriting the gene mutation and thus being a carrier herself.
- An affected male - if able to reproduce - will pass on the gene mutation to all daughters, who are therefore **obligate** carriers. The affected male never passes the disease on to a son.
- The typical family history for an X-linked recessive condition is of disease in maternal uncles. A woman who has both a brother and a son affected with an X-linked disease is also an obligate carrier.

### Pitfalls in Recognizing X-Linked Recessive Inheritance and Providing Genetic Counseling

- **Small families.** Small family size and few male children may make the pattern of an X-linked recessive disorder difficult to discern.
- **New mutation.** An affected male may be the first person in the family with the condition, due to a mutation arising for the first time in sperm, egg or embryo.
- **Germline mosaicism.** A new mutation may arise in testis or ovary, resulting in a parent who can pass on the condition or the carrier state to children, without being either affected (in the case of a male parent) or a carrier (in the case of a female parent).