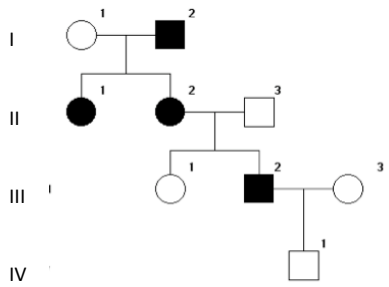
Pedigree Analysis

A pedigree chart displays a family tree, and shows the members of the family who are affected by a genetic trait.

This chart shows four generations of a family with four individuals who are affected by a form of colorblindness.

- Circles represent females and squares represent males.
- Each individual is represented by:
  - a Roman Numeral, which stands for the generation in the family,
  - a Digit, which stands for the individual within the generation.

  (For instance, The female at the upper left is individual **I-1**.)
- A darkened circle or square represents an individual affected by the trait.



- The "founding parents" in this family are the female I-1 and the male I-2 in the first generation at the top.

- A male and female directly connected by a horizontal line have mated and have children. These three pairs have mated in this tree:

  I-1 & I-2, II-2 & II-3, III-2 & III-3

- Vertical lines connect parents to their children. For instance the females , II-1 and II-2 are daughters of I-1 and II-2
- The "founding family" consists of the two founding parents and their children, II-1 and II-2.

In this pedigree, the unaffected founding mother, I-1, and affected founding father, I-2, are parents to two affected daughters, II-1 and II-2.

The affected founding daughter II-2 and the unaffected male II-3 who "marries into the family" have two offspring, an unaffected daughter III-1 and affected son, III-2.

Finally, this affected male III-2 and the unaffected female III-3 who "marries in" have an unaffected son, IV-1.

Pedigrees are interesting because they can be used to do some detective work and are often used to study the genetics of inherited diseases. For example, pedigrees can be analyzed to determine the **mode of transmission** for a genetic disease:

(1) **Dominance** - whether the disease alleles are **dominant** or **recessive;**
(2) **Linkage** - whether the disease alleles are **X-linked** (on the X chromsome) or **autosomal**

- **Some Definitions**

Autosomal chromosomes - The 22 chromosome pairs other than the XX (female) or XY (male) sex chromosomes.

Hemizygous - Males are "hemizygous" for X-linked genes – males only have one X chromosome and one allele of any X-linked gene.

Allele - A version of a gene. Humans have 2 alleles of all their autosomal genes; females have 2 alleles of X-linked genes; males have one allele of X-linked genes (and one allele of Y-linked genes).

Pedigree analysis is an example of abductive reasoning. In pedigree analysis you need to look for any clues that will allow you to decide if the trait is dominant or recessive and whether it is linked to an autosomal chromosome, or to the X chroomsome.

On the following page(s) we'll discuss the reasoning that goes into solving pedigree analysis puzzles.

General Assumptions

In the problems that follow, you'll be reasoning about the mode of transmission of genetic traits that are **controlled by one gene, with two alleles, a dominant allele and a recessive allele**.

We also make three simplifying assumptions:

1. **Complete Penetrance**. An individual in the pedigree will be affected (express the phenotype associated with a trait) when the individual carries at least one dominant allele of a dominant trait, or two recessive alleles of a recessive a trait.
2. **Rare-in-Population.** In each problem, the trait in question is rare in the general population. **Assume for the purposes of these problems that individuals who marry into the pedigree in the second and third generations are not carriers**. This does not apply to the founding parents – either or both of the individuals at the top of the pedigree could be carriers.
3. **Not-Y-Linked**. The causative genes in these problems may be autosomal or X-Linked, but are not Y-linked.

5 Key Clues

There are five things to remember in reasoning about pedigrees.

(1) An unaffected individual cannot have any alleles of a dominant trait.
(because a single allele of a dominant trait causes an individual to be affected).

(2) Individuals marrying into the family are assumed to have no disease alleles
- they will never be affected and can never be carriers of a recessive trait.
(because the trait is rare in the population)

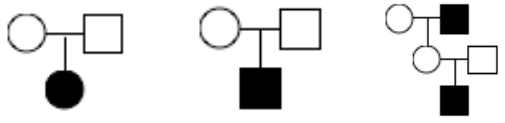
(3) An unaffected individual can be a carrier (have one allele) of a recessive trait.
(because two alleles of a recessive trait are required for an individual to be affected)

(4) When a trait is X-linked, a single recessive allele is sufficient for a male to be affected.
(because the male is hemizygous – he only has one allele of an X-linked trait)

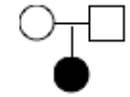
(5) A father transmits his allele of X-linked genes to his daughters, but not his sons.
A mother transmits an allele of X-linked genes to both her daughters and her sons.

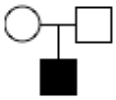
Key Patterns in Pedigree Analysis

Patterns that Indicate a RECESSIVE Trait

	• **The disease must be RECESSIVE if any affected individual has 2 unaffected parents.** Since this is a genetic disease at least one parent must have an allele for the disease. If neither parent is affected, the trait <u>cannot be dominant</u>. (See Clue 1 above).

Patterns that Indicate a RECESSIVE Trait (cont)





• **AUTOSOMAL RECESSIVE**: If any affected **founding daughter** has 2 unaffected parents the disease must be autosomal recessive.

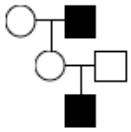
An affected individual must inherit a recessive allele from both parents, so both parents must have an allele.

If the father had a recessive X-linked allele, he would have to be affected (since he only has one X-linked allele).

• **RECESSIVE:** If an affected **founding son** has 2 unaffected parents, we cannot determine if the recessive disease is autosomal or x-linked.

If the trait is autosomal, both parents can be unaffected carriers of the disease.

If the trait is x-linked, the son must have inherited his allele from his mother only, and his father can be unaffected.



• **X-LINKED RECESSIVE**: When an affected **non-founding son** has 2 unaffected parents the disease must be X-linked recessive**.**

The father, who is marrying in, does not have any disease alleles, since he is marrying into the family;

so the affected son inherits an allele only from his unaffected mother.

A male cannot be affected by a single autosomal recessive allele, but <u>can</u> be affected by a single X-linked recessive allele.

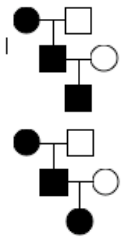
Patterns that Indicate a DOMINANT Trait

• **The disease must be DOMINANT if every affected child of NON-FOUNDING parents has an affected parent.**

The unaffected mother, who is marrying in, does not carry an allele for the disease;

so the affected child inherits an allele only from the affected father.

No child could be affected by a single autosomal recessive allele, or X-linked recessive allele, so the trait is dominant.



• When an affected **son** of **non-founding parents** has an affected father the disease must be **AUTOSOMAL DOMINANT.**

A father does not transmit X-linked alleles to a son, so the disease cannot be X-linked dominant.

• When an affected **daughter** of **non-founding parents** has an affected father, we cannot determine whether the **DOMINANT** disease is autosomal or x-linked.

The affected father can transmit either an autosomal dominant allele, or an X-linked dominant allele to his daughter.