HUMAN GENETICS

Lecture Three

MODE OF INHERITANCE

Objectives:

By the end of this lecture, students should be able to:

- Assess Mendel's laws of inheritance
- Understand the bases of Mendelian inheritance
- Define various patterns of single gene inheritance using family pedigree and Punnett square

Father of Genetics

- Born in 1822
- Monk and teacher
- Discovered some of the basic laws of heredity
- Published his work, entitled *Experiments on Plant Hybrids* in1866 However, largely ignored
- He died in 1884 with his work still unnoticed
- His work rediscovered in 1900.

Interpreting the outcomes of Mendel's breeding experiments:

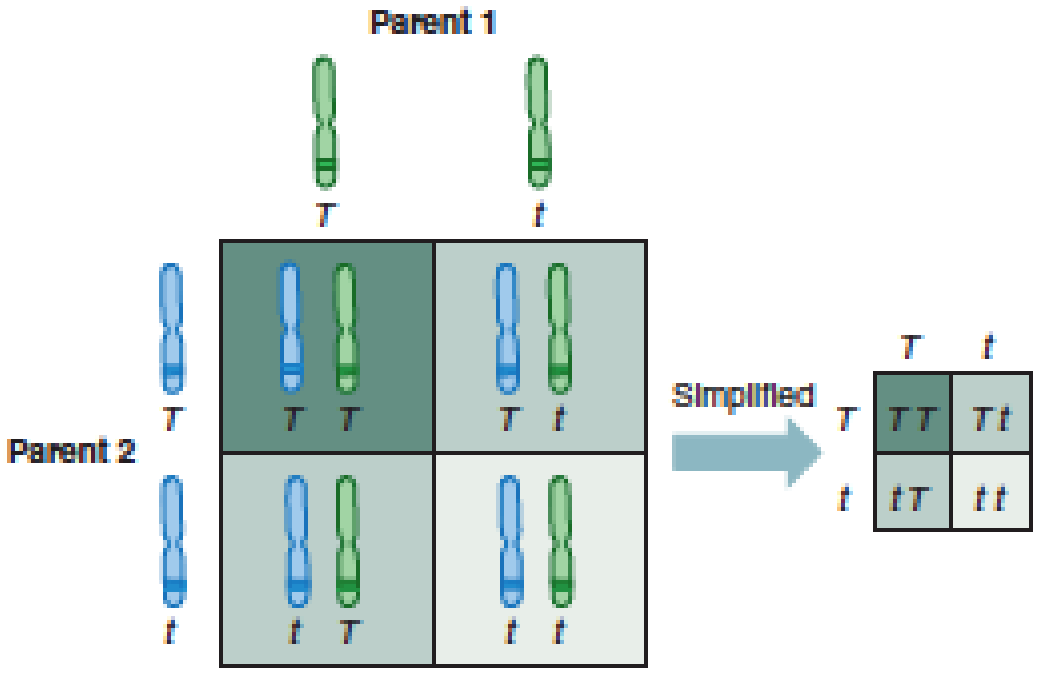
- The plant characteristics being studied were each controlled by a pair of **factors**, one of which was inherited from each parent.
- The pure-bred plants, with two identical genes, used in the initial cross would now be referred to as **homozygous**.
- The hybrid F1 plants, each of which has one gene for tallness and one for shortness, would be referred to as **heterozygous**.
- The genes responsible for these contrasting characteristics are referred to as *allelomorphs*, or **alleles** for short.

Genotypes

Genotype:	*AA*	*Bb*	*cc*
	Homozygous for the dominant allele	Heterozygous	Homozygous for the recessive allele

Punnett Square

- Each parent can only contribute one allele per gene
- These genes are found on the chromosomes of gametes of parents
- Offspring will inherit **2 alleles** to express that gene



Law of Dominance or Uniformity

COMPLETE DOMINANCE - one allele is dominant to another allele

RECALL MENDEL'S 1st EXPERIMENT

CROSS: Pure bred purple female x White male

P1 generation = **PP** x **pp**

Female gametes

Male gametes

	P	P
p	Pp	Pp
p	Pp	Pp

F1 generation

Genotype ratio = 1Pp

Phenotype ratio = 1 purple

LAW OF SEGREGATION

RECALL MENDEL'S 2nd EXPERIMENT

CROSS: Two F1 generation offspring with each other

P1 generation = Pp x Pp

Male gametes

Female gametes

	P	p
P	PP	Pp
p	Pp	pp

F1 generation

Genotype ratio = 1PP:2Pp:1pp

Phenotype ratio = 3 purple:1 white

LAW OF INDEPENDENT ASSORTMENT

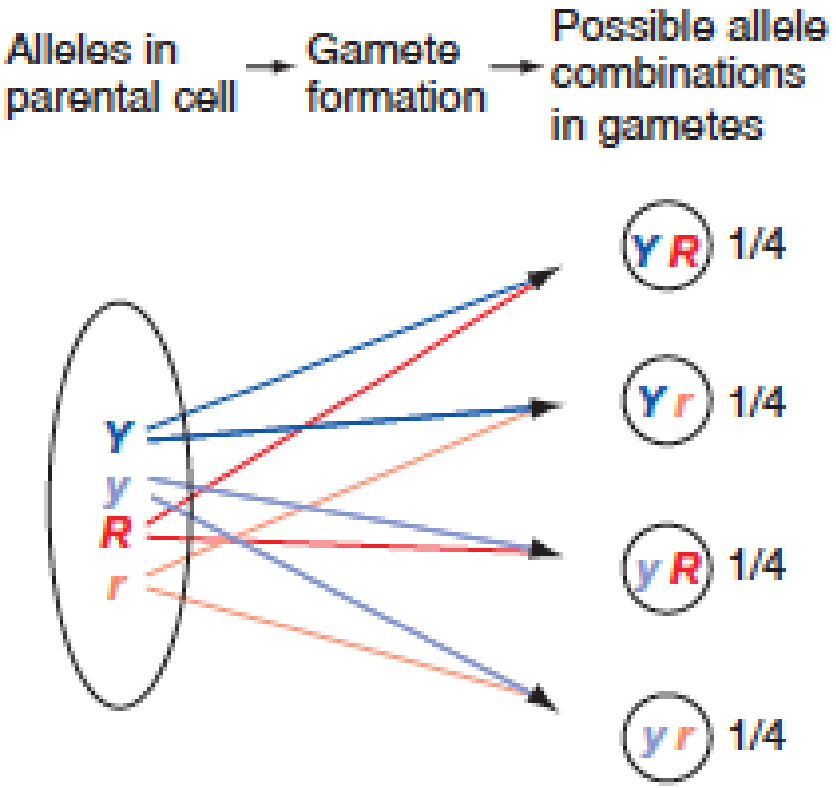
DEFINITION

During gamete formation, different pairs of alleles segregate independently of each other.

INTERPRETATION

In a dihybrid cross, each pair of alleles assorts independently during gamete formation. In the gametes, Y is equally likely to be found with R or r (that is, Y R = Y r); the same is true for y (that is, y R = y r).

As a result, all four possible types of gametes (Y R , Y r , y R , and y r) are produced in equal frequency among a large population.



THE CHROMOSOME THEORY OF INHERITANCE AND SEX CHROMOSOMES

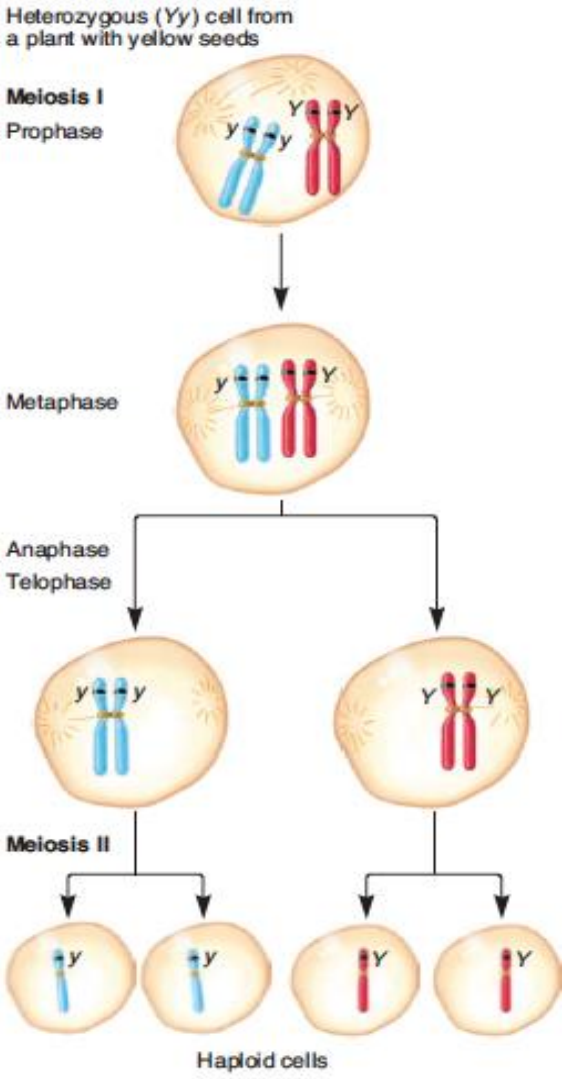
How chromosomal transmission is related to the patterns of inheritance observed by Mendel?

Mendel's law of segregation can be explained by the segregation of homologs during meiosis

The two copies of a gene are contained on homologous chromosomes.

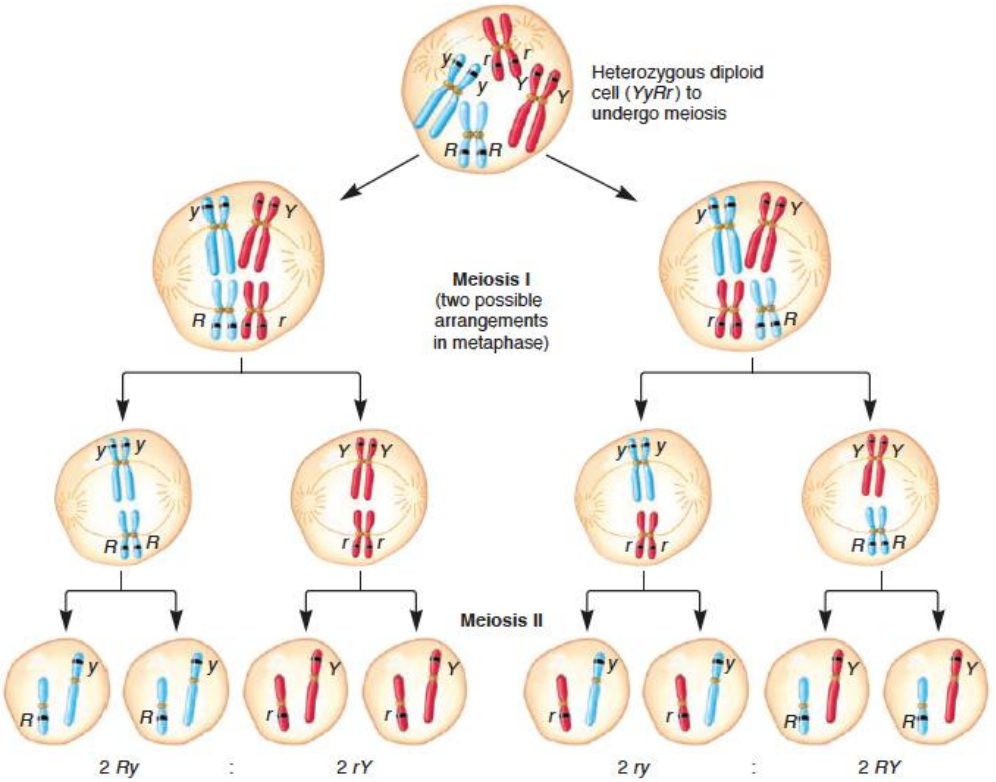
In this example using pea seed color, the two alleles are Y (yellow) and y (green).

During meiosis, the homologous chromosomes segregate from each other, leading to segregation of the two alleles into separate gametes.

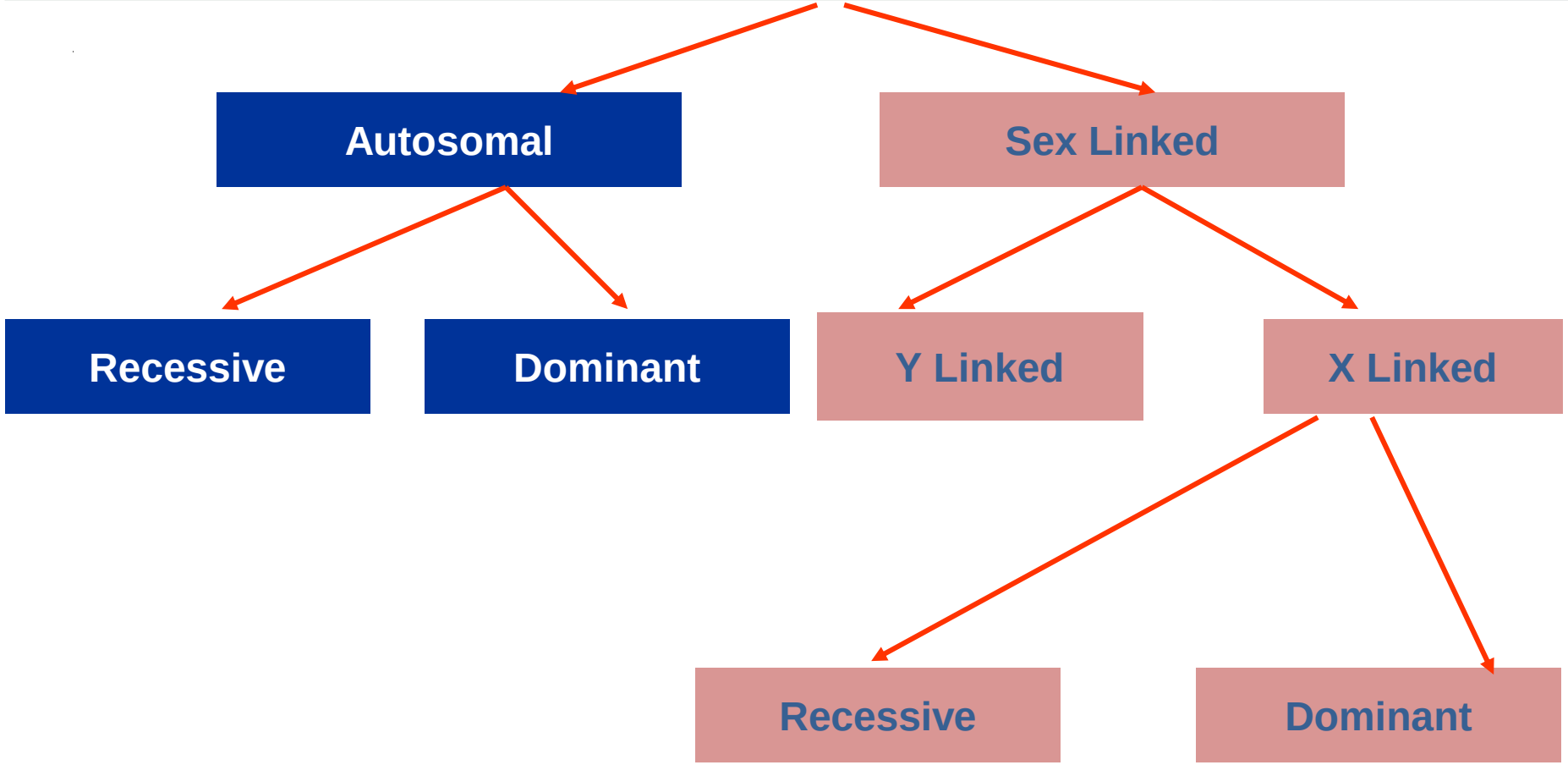


Mendel's law of independent assortment can be explained by the random alignment of bivalents during metaphase of meiosis I

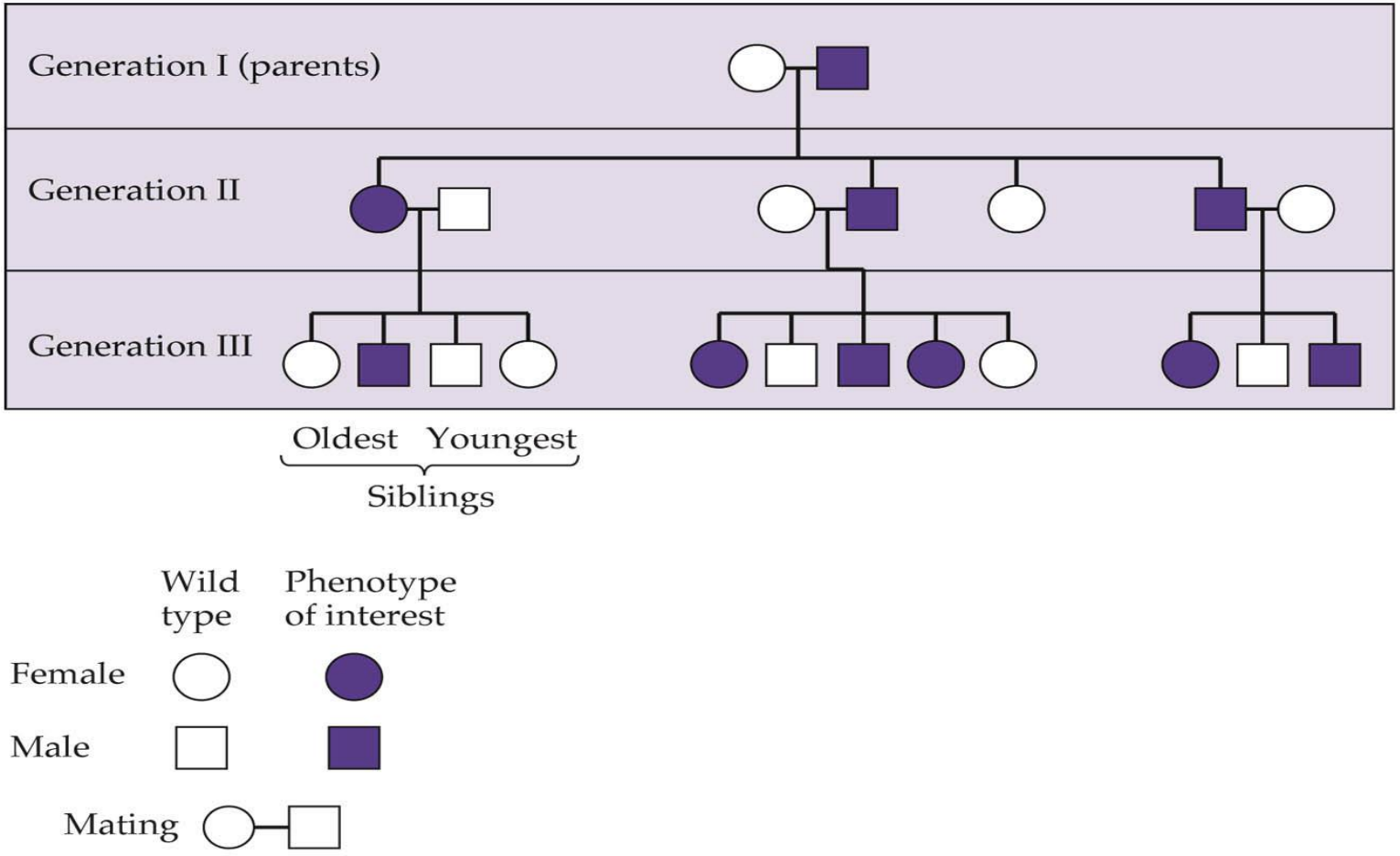
- This figure shows the assortment of two genes located on two different chromosomes, using pea seed color and shape as an example (YyRr).
- During metaphase of meiosis I, different possible arrangements of the homologs within bivalents can lead to different combinations of the alleles in the resulting gametes.
- For example, on the left, the dominant R allele has sorted with the recessive y allele; on the right, the dominant R allele has sorted with the dominant Y allele.



MODES OF INHERITANCE FOR SINGLE GENE DISORDERS



A Pedigree Analysis

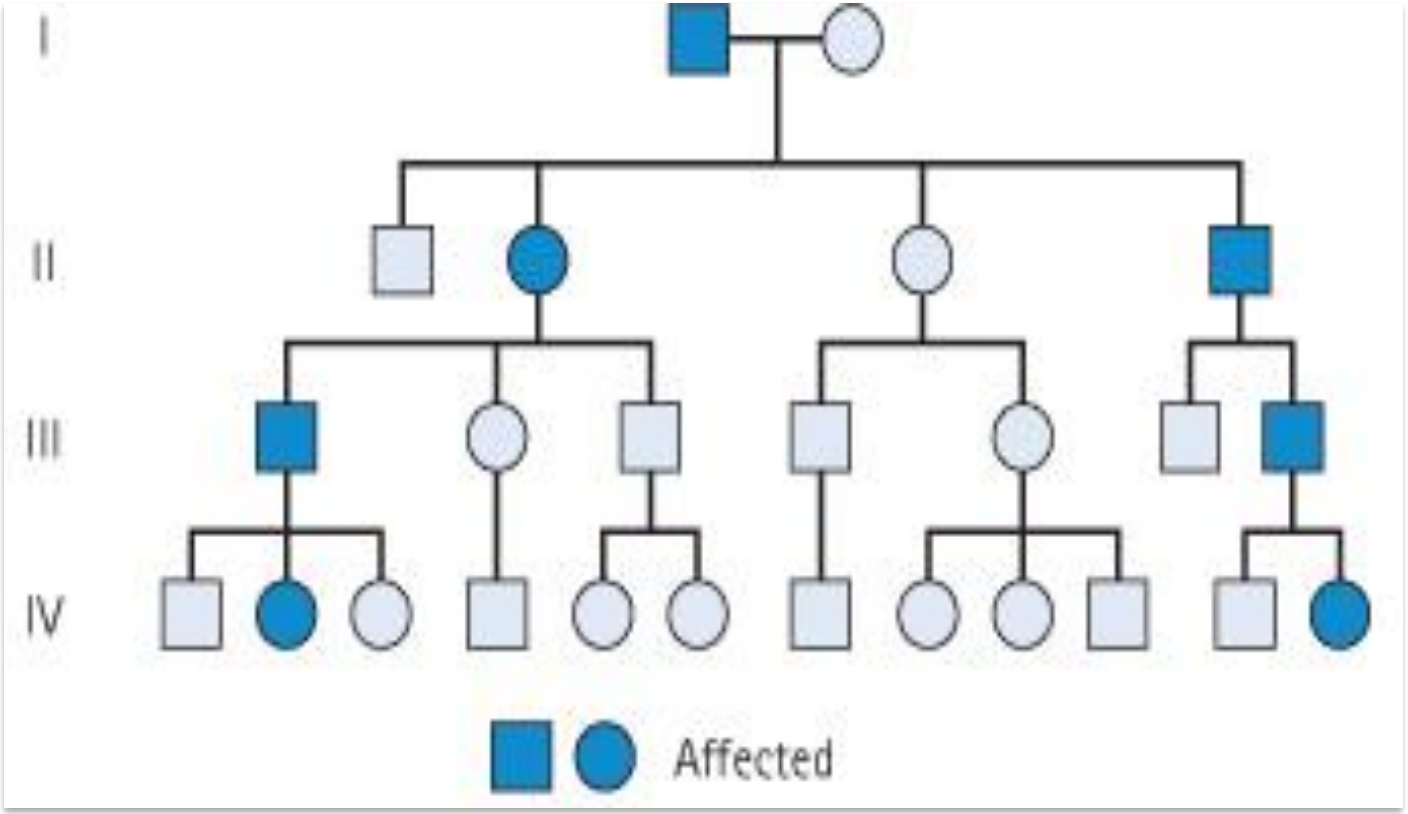


LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, Figure 10.10 Pedigree Analysis and Dominant Inheritance

Autosomal Dominant

- **The trait (character, disease) appears in every generation.**
- **Unaffected persons do not transmit the trait to their children.**
- **Examples: Huntington disease, Myotonic dystrophy, Neurofibromatosis type 1, Marfan syndrome etc.**

Family Tree of an Autosomal Dominant Mode of Inheritance



Note the presence of male-to-male (i.e. father to son) transmission

Autosomal Recessive

- **The trait (character, disease) is recessive**
- **The trait expresses itself only in homozygous state**
- **Unaffected persons (heterozygotes) may have affected children (if the other parent is heterozygote)**
- **The parents of the affected child maybe related (consanguineous)**
- **Males and female are equally affected**
- **Examples:**

  Cystic fibrosis, Phenyketonuria, Sickle cell anaemia, Thalassaemia etc.

Punnett square showing autosomal recessive inheritance

1-) Both Parents Heterozygous:

25% offspring “affected Homozygous”

50% Trait “Heterozygous normal but carrier”

25% Normal

Mother

Father	A	a
A	AA	Aa
a	Aa	aa

(2) One Parent Heterozygous:

Female

	A	a
A	AA	Aa
A	AA	Aa

50% normal but carrier “Heterozygous”

50% Normal

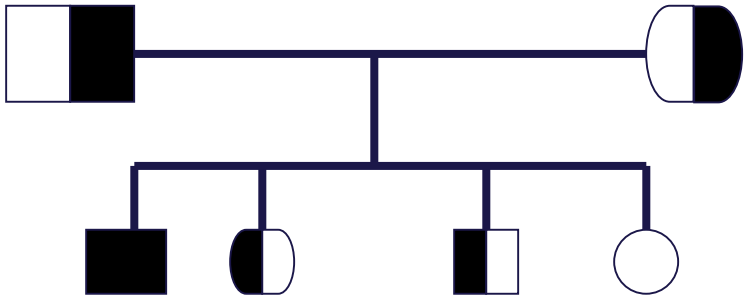
(3) One Parent Homozygous:

Female

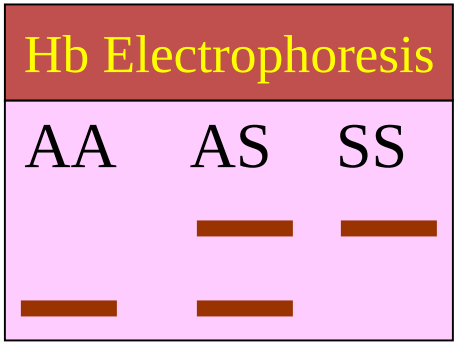
	A	A
a	Aa	Aa
a	Aa	Aa

100% offspring carriers.

Family tree of an Autosomal recessive disorder Sickle cell disease (SS)



A family with sickle cell disease -Phenotype

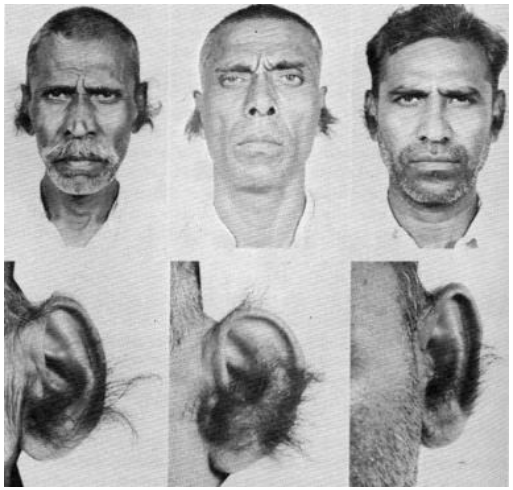


Sex – Linked Inheritance

- This is the inheritance of a gene present on the sex chromosomes.
- The Inheritance Pattern is different from the autosomal inheritance.
- Inheritance differs in males from females.

Y – Linked Inheritance

- The gene is on the Y chromosomes
- The gene is passed from fathers to sons only
- Daughters are not affected
- Hairy ears in India
- Male are Hemizygous, the condition exhibits itself whether dominant or recessive



Father

Mother	X	Y*
X	XX	XY*
X	XX	XY*

X – Linked Inheritance

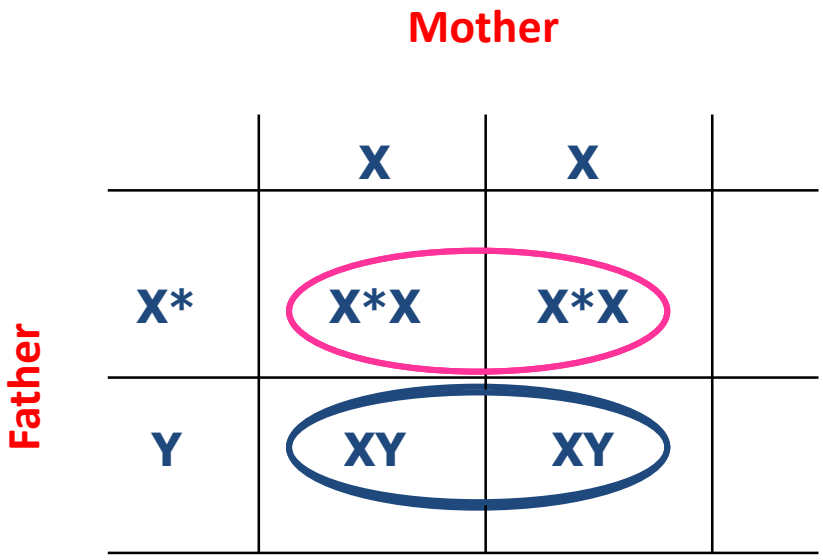
- The gene is present on the X chromosome
- The inheritance follows specific pattern
- Males have one X chromosome, and are hemizygous
- Females have 2 X chromosomes, they may be homozygous or heterozygous
- These disorders may be : recessive or dominant

X – Linked Recessive Inheritance

- The incidence of the X-linked disease is higher in male than in female
- The trait is passed from an affected man through all his daughters to half their sons
- The trait is never transmitted directly from father to sons
- An affected women has affected sons and carrier daughters
- X - Linked Recessive Disorders: Albinism, Fragile X syndrome, Hemophilia, Muscular dystrophy, Retinitis pigmentosa

X – Linked Recessive Inheritance

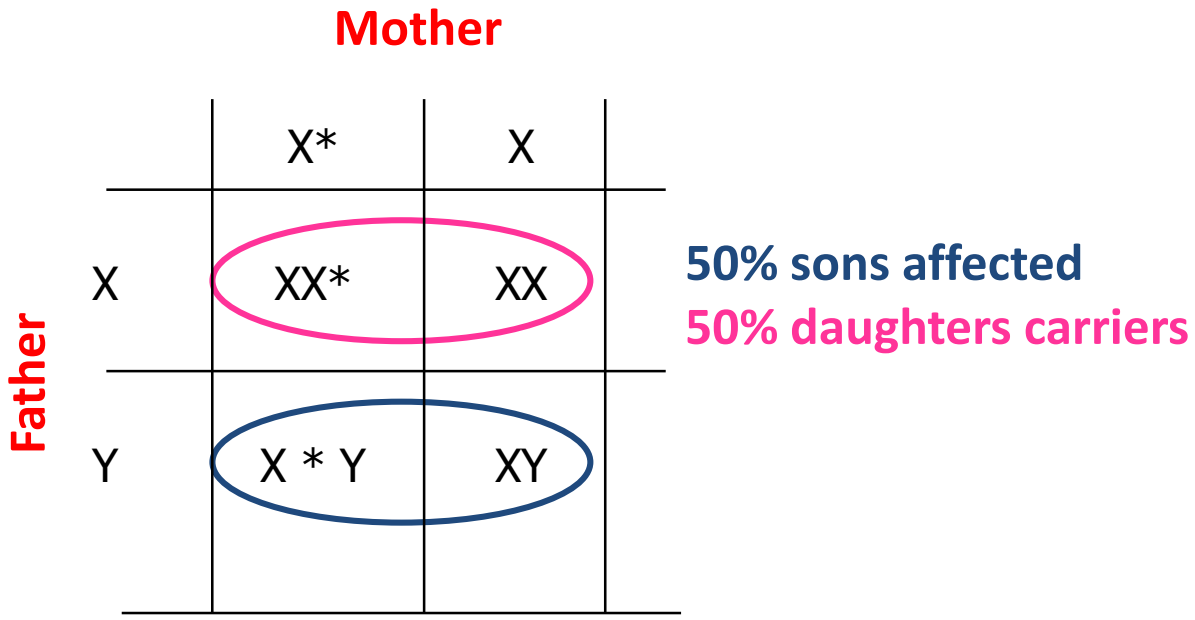
(1) Normal female, affected male



All sons are normal

All daughters carriers "not affected"

(2) Carrier female, normal male:



(3) Homozygous female, normal male:

- All daughters carriers.
- All sons affected.

X-Linked Dominant Disorders

- The gene is on X Chromosome and is dominant
- The trait occurs at the same frequency in both males and females
- Hemizygous male and heterozygous females express the disease.

Punnett square showing X – linked dominant type of Inheritance

(1) Affected male and normal female:

Mother

Father

	X	X
X*	X*X	X*X
Y	XY	XY

All daughters affected, all sons normal

(2) Affected female (heterozygous) and normal male:

Mother

Father

	X*	X
X	XX*	XX
Y	X*Y	XY

50% sons & 50% daughters are affected

TAKE HOME MESSAGE:

- An accurate determination of the family pedigree is an important part of the workup of every patient
- Pedigrees for single-gene disorders may demonstrate a straightforward, typical mendelian inheritance pattern
- These patterns depend on location of the gene locus on the chromosomal, which may be autosomal or sex chromosome-linked, and whether the phenotype is dominant or recessive