Human Genetics

Lecture 3

MODE OF INHERITANCE

Human Genetics Team

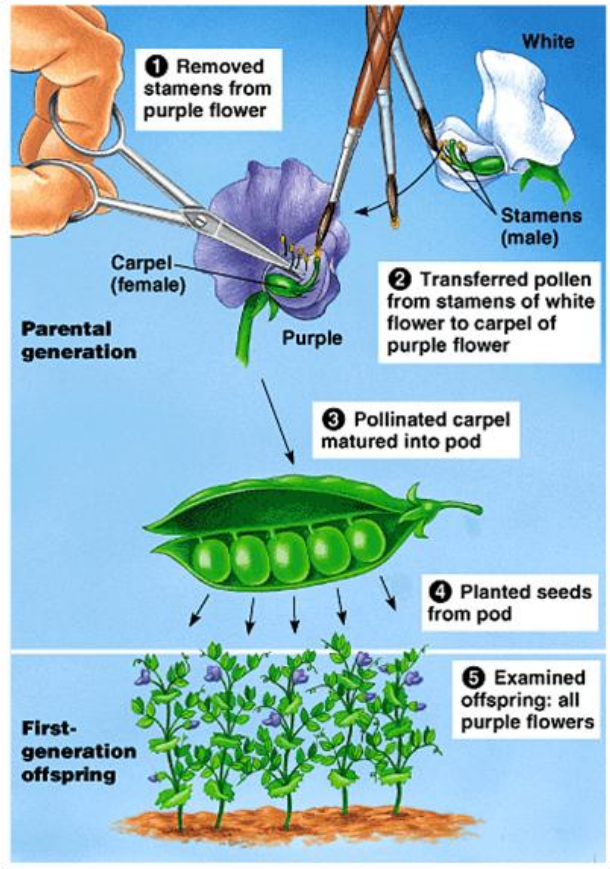
Lecture Objectives

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

Mendel was fortunate he chose the Garden Pea

(البازلاء)

- Mendel probably chose to work with peas because they are available in many varieties.
- The use of peas also gave Mendel strict control over which plants mated.
- Fortunately, the pea traits are distinct and were clearly contrasting.



To understand the picture above:

Stamen= العضو الذكري في الزهرة

Carpel = العضو الأنثوي في الزهرة

Pollen=حبيبات اللقاح

Pollinated = ملقحة

* Mendel cross-pollinated pea plants in order to study the various traits

مندل درس ٧ صفات لا غير ، ومذكوره بالجدول

	Seed shape	Seed color	Flower color	Flower position	Pod color	Pod shape	Plant height
Dominant trait	 round	 yellow	 purple	 axial (side)	 green	 inflated	 tall
Recessive trait	 wrinkled	 green	 white	 terminal (tips)	 yellow	 constricted	 short

Dominant : the trait that was **observed.** (السائد)

Recessive : the trait that **disappeared**. (المتنحي)

* Mendel's breeding experiments: Interpretation of his results

- The plant characteristics being studied were each controlled by a pair of factors, one of which was inherited from each parent.

- Homozygous : (Homo = Same) The pure-bred plants, with two identical genes.

- Heterozygous : (Hetero = Different) The hybrid F1 (First generation) plants, each of which has one gene for tallness and one for shortness .

- Allelomorphs or alleles : The genes responsible for these contrasting characteristics .

Two alleles form one gene (each gene has two alleles coming from each parent)

* Genotypes and Phenotypes

- Homozygous dominant TT

- Homozygous recessive tt

- Heterozyous Tt

Two alleles forming one gene

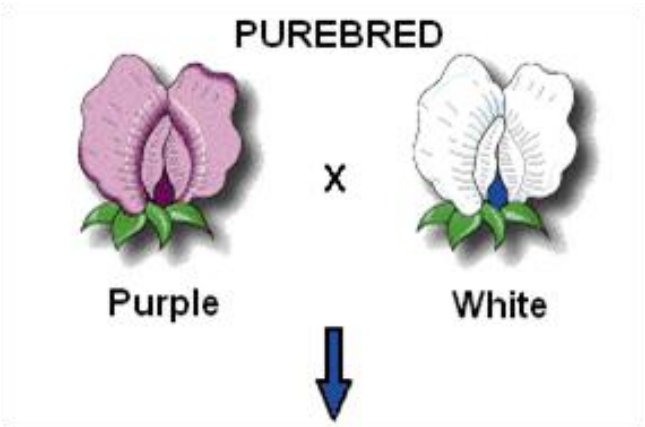
The dominant gene can have homozygous or heterozygous alleles

BUT: the recessive gene ALWAYS have homozygous alleles and can NEVER be heterozygous

* First Experiment :

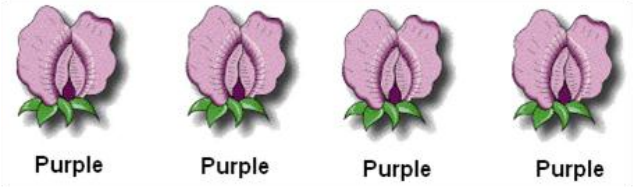
P1 generation

(Partenal generation)



F1 generation

(Filial generation)

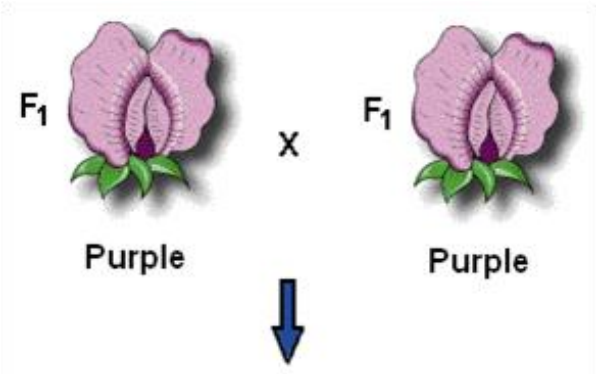


100% Purple

* Second Experiment :

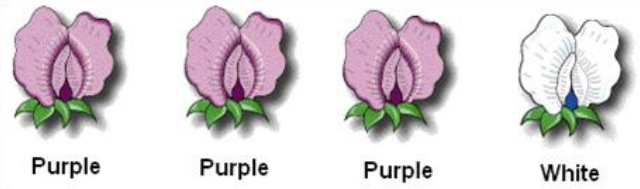
F1 generation

(First generation)



F2 generation

(second generation)



75% Purple and 25% White

* Punnett Square :

Benefit of Punnett square is used to calculate the possibility of risks for next generation

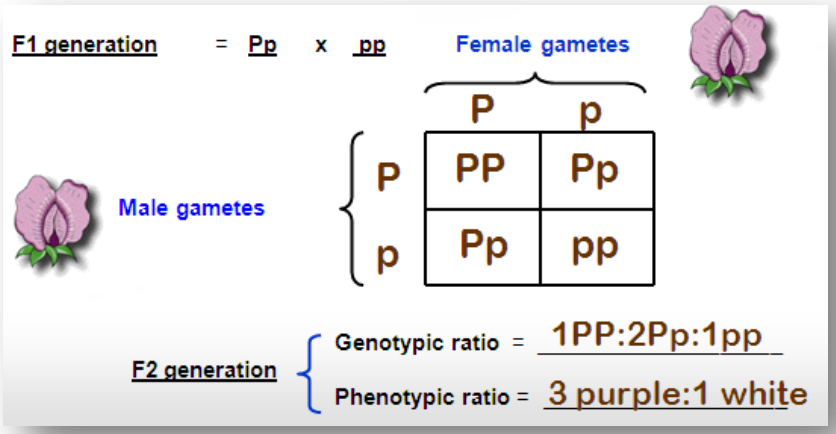
Each parent can only contribute one allele per gene

These genes are found on the chromosomes carried in the sex cells.

Offspring will inherit 2 alleles to express that gene .

CROSS: Two F1 generation offspring with each other .

The dominant allele (capital letter) will always overpower the recessive allele (small letter)



* Law of Dominance:

In the monohybrid cross (mating of two organisms that differ in only one character), one version disappeared.

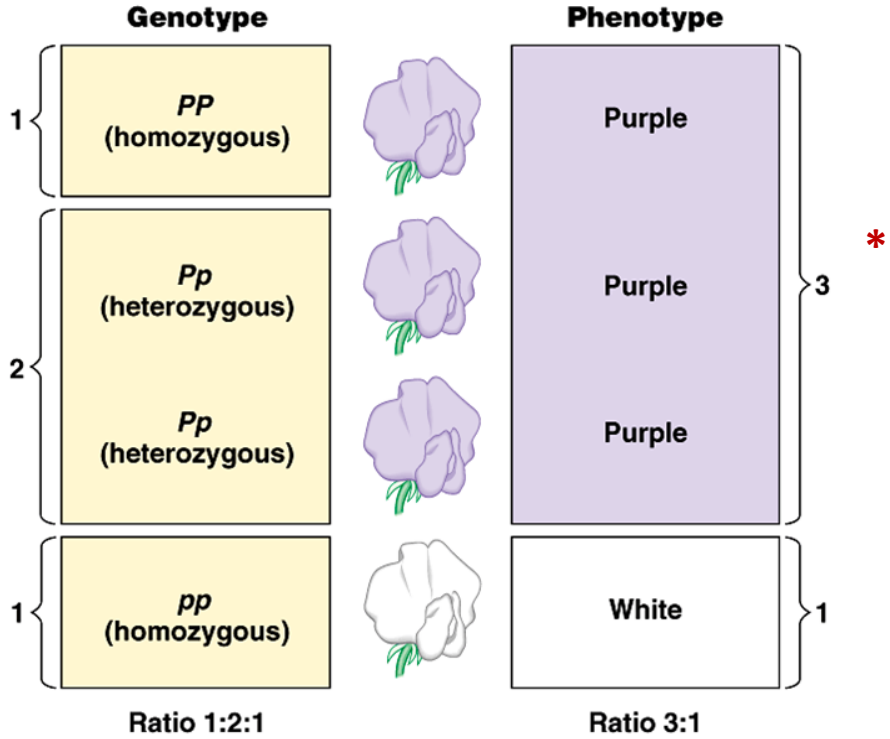
قانون السائد : لما تتزاوج زهره بيضاء نقية (صفة متنحية) مع زهره بنفسجيه نقية (صفة سائدة) في الجيل الأصلي (الأبوين) يكون الناتج: 100% أزهار بنفسجية (غير نقية Pp)

وعند تزاوج الجيل الاول زهره بنفسجيه (غير نقية Pp) مع زهره اخرى بنفسجيه (غير نقية Pp) ينتج لدينا 3 ازهار بنفسجيه وواحده متنحيه بيضاء 3:1

3 purple flowers: Only one is homozygous PP and 2 are heterozygous Pp

1 white flower: ALWAYS homozygous pp

* Genotype versus phenotype :



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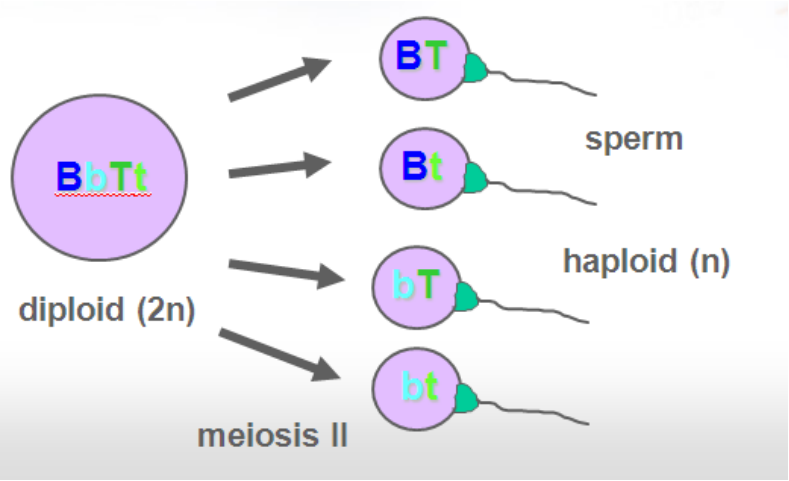
Mendel's 3rd Law of Inheritance :



Phenotypic ratio: 9 round, green: 3 round, yellow: 3 wrinkled, green: 1 wrinkled, yellow → (9: 3:3:1)

Genotypic ratio:

1RRGG: 2 RRGg: 2 RrGG: 4 RrGg: 1 RRgg: 2 Rrgg: 2 rrGg: 1 rrGG: 1 rrgg

	RG	Rg	rG	rg
RG	RRGG	RRGg	RrGG	RrGg
Rg	RRGg	RRgg	RrGg	Rrgg
rG	RrGG	RrGg	rrGG	rrGg
rg	RrGg	Rrgg	rrGg	rrgg

2 pair mix cross the system will be 9:3:3:1

What is the difference between mendel's first law third law?

First law: he studied the characteristics of only ONE trait for example : the color of the flowers

Third law: he studied TWO traits for example: the color of flowers + shape of the seed

THE LAW OF UNIFORMITY :

It refers to the fact that when two homozygotes with different alleles are crossed, all the offspring in the F1 generation are identical and heterozygous.

The characteristics do not blend, as had been believed previously, and can reappear in later generations.

يشير القانون الى عندما تُلقح زهرتان كلهما نقيتان لكنهم مختلفتان في الطراز الجيني يعني وحدة بيضاء و وحدة حمراء صفة وحدة إلي راح تظهر ف الجيل الأول و هي الصفة السائدة وكلها هجينة

THE LAW OF SEGREGATION :

It refers to the observation that each individual possesses two genes for a particular characteristic, only one of which can be transmitted at any one time.

Rare exception this rule can occur when two allelic genes fail to separate because of chromosome non-disjunction at the first meiotic division

أن الصفة الوراثية تمثل بزوج من الجينات ينعزلان عن بعضهما عند تكوين الأمشاج و يحتوي كل مشيج على جين واحد فقط من هذا الزوج

* THE LAW OF INDEPENDENT ASSORTMENT :

It refers to the fact that members of different gene pairs segregate to offspring independently of one another.

In reality, *this is not always true*, as genes that are close together on the same chromosome tend to be inherited together, i.e. they are "linked"

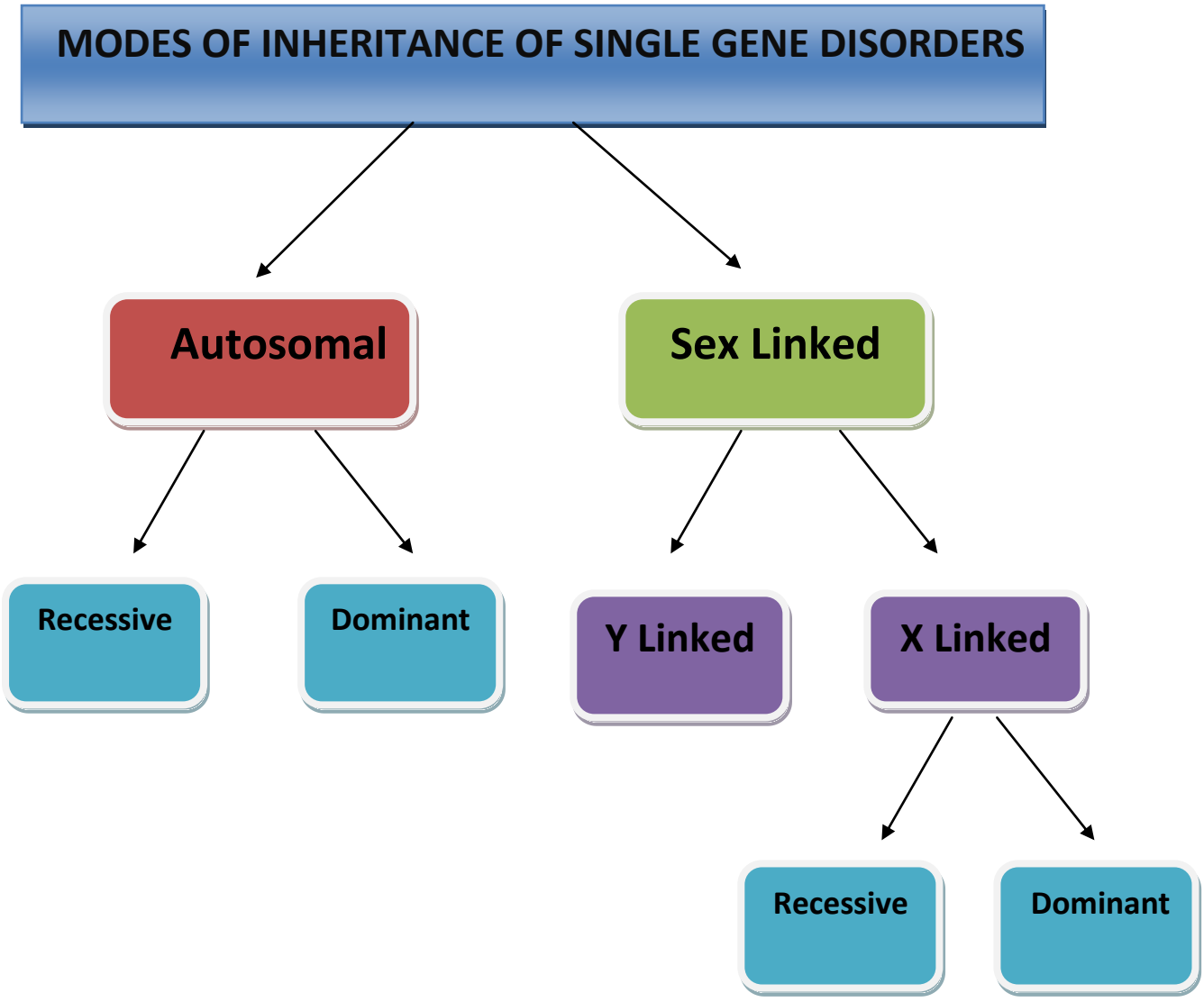
كل زوج من الجينات الخاصة بالصفات المختلفة يتوزع توزيعا حرا و مستقلا عند تكوين الأمشاج

* MENDELIAN INHERITANCE (simple pattern of inheritance)

- Over 16,000 traits/disorders in humans exhibit single gene unifactorial or Mendelian inheritance.

- A trait or disorder that is determined by a gene on an autosome is said to show autosomal inheritance.

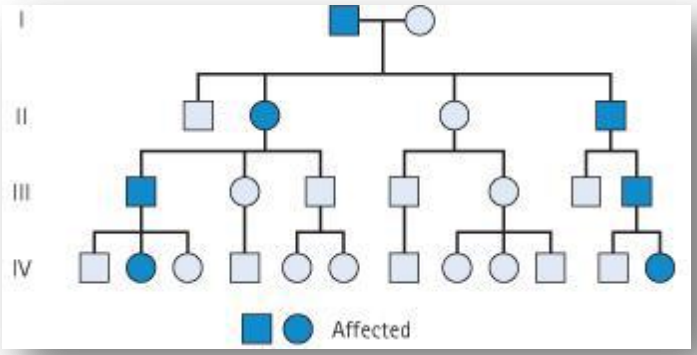
- A trait or disorder determined by a gene on one of the sex chromosomes is said to show sex-linked inheritance.



* Autosomal Dominant Inheritance :

- The trait (character, disease) appears in every generation.

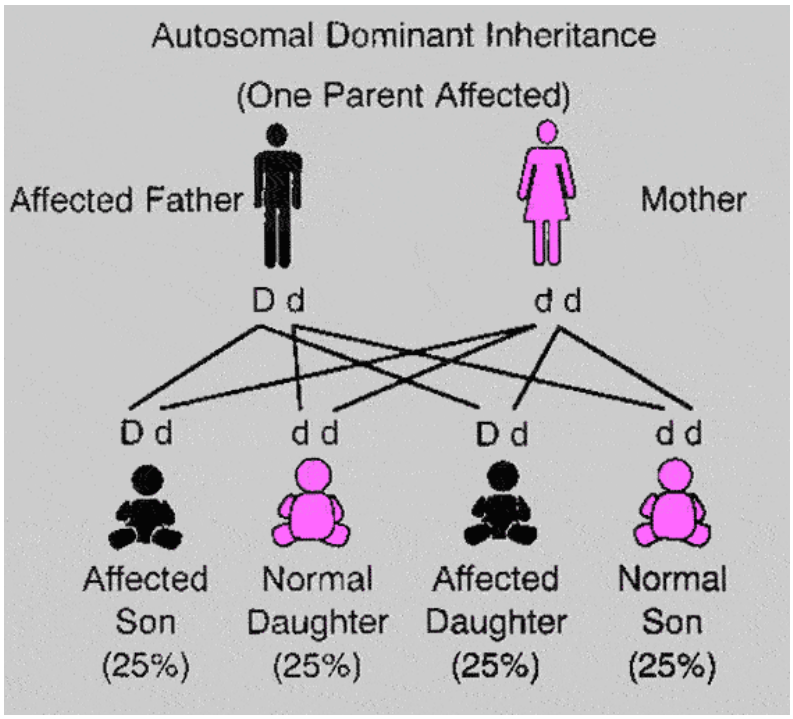
- Unaffected persons do not transmit the trait to their children.



***Note the presence of male-to-male**

(i.e. father to son) transmission.

To understand more:



* Examples of Autosomal dominant disorders:

- Familial hypercholesterolemia (LDLR deficiency)

- Adult polycystic kidney disease

-Huntington disease

Myotonic dystrophy

- Neurofibromatosis type 1

- Marfan syndrome

* Autosomal Recessive Inheritance :

- 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

(الأقارب)- The parents of the affected child maybe related . (consanguineous)

-Males and female are equally affected.

-

(1) Both Parents Heterozygous:

25% offspring affected Homozygous"

50% Trait "Heterozygous normal but carrier"

25% Normal

	A	a
A	AA	Aa
a	Aa	aa

(2) One Parent Heterozygous

50% normal but carrier "Heterozygous"

50% Normal

	A	a
A	AA	Aa
A	AA	Aa

(3) One Parent Homozygous:

100% offsprings carriers.

	A	A
a	Aa	Aa
a	Aa	Aa

* Examples of Autosomal Recessive Disorders:

-Cystic fibrosis

- β-Thalassaemia

- Phenyketonuria

- Recessive blindness

- Sickle cell anaemia

- Mucopolysaccharidosis

* 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 is different in the males and females.

Y – Linked Inheritance

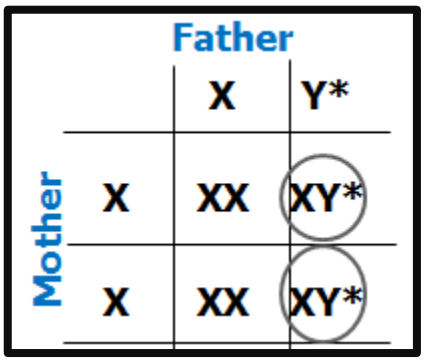
- The gene is on the Y chromosomes.

- 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.



X – Linked Inheritance

- >1400 genes are located on X chromosome

(~40% of them are thought to be associated with disease phenotypes)

X-linked inheritance in male & female

** X_H is the normal allele, X_h is the mutant allele

	Genotype	Phenotype
males	X_H X_h	Unaffected Affected
females	X_H/X_H	Homozygous unaffected
	X_H/X_h	Heterozygous
	X_h/X_h	Homozygous affected

You can see here (females) that it takes two recessive allels to be affected with the disease unlike males who are hemizygous one recessive will express the disease

- 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

an Genetics Team

- The incidence of the X-linked disease is higher in male than in female. **(because they are Hemizyous)**

- 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. **(because sons only get "Y" chromosome from their father)**

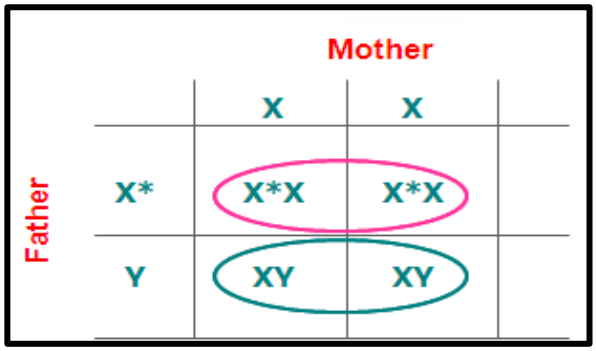
- An affected women has affected sons and carrier daughters.

(since they are affected they have only recessive alleles let's say for example "rr", so their sons will definitely get an r which will affect the sons, on the other hand daughter will get also an "r" but they are not hemizygous so depending on the other allele that they will get from their fathers they either become Carrier "Rr" or if the father is affected too they will become affected also "rr".)

(1) Normal female, affected male :-

All sons are normal

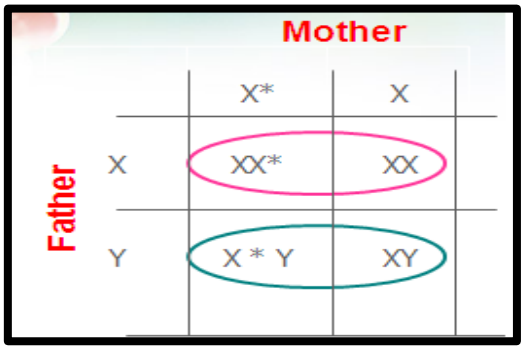
All daughters carriers "not affected"



2) Carrier female, normal male:-

50% sons affected

50% daughters carriers



(3) Homozygous female, normal male:

- **All daughters carriers.**
- **All sons affected.**

X - Linked Recessive Disorders

- Albinism (Ocular) - Fragile X syndrome - Hemophilia A and B
- Lesch–Nyhan syndrome
- Mucopoly Saccharidosis 11 " Hunter's syndrome "
- Muscular dystrophy (Duchenne and Beeker's)
- G-6-PD deficiency
- Retinitis pigmentosa

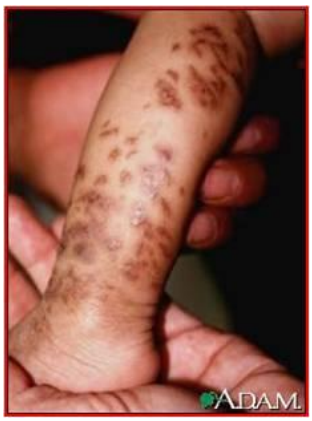
X - Linked dominant Disorders

-Incontinentia pigmenti (IP)

Lethal in males during the prenatal period

Lethal in hemizygous males before birth:

Exclusive in females (because its lethal in males before birth)



Affected female produces:

affected daughters

normal daughters

normal sons

} in equal proportions (1:1:1)

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 the chromosomal location of the gene locus, which may be autosomal or sex chromosome-linked, and whether the phenotype is dominant or recessive.

- **Other atypical mode of inheritance will be discussed next lecture.**