Chapter 2

Genetics

Patterns Of Inheritance

- The scientific study of inheritance is known as genetic.
- Genetics is the study of inheritance, the transmission of traits from parents to offspring and the expression of those traits.

Chief branches of genetics

a. Transmission genetics

b. Cytogenetics

c. Molecular genetics

d. Population genetics

e. Evolutionary genetics

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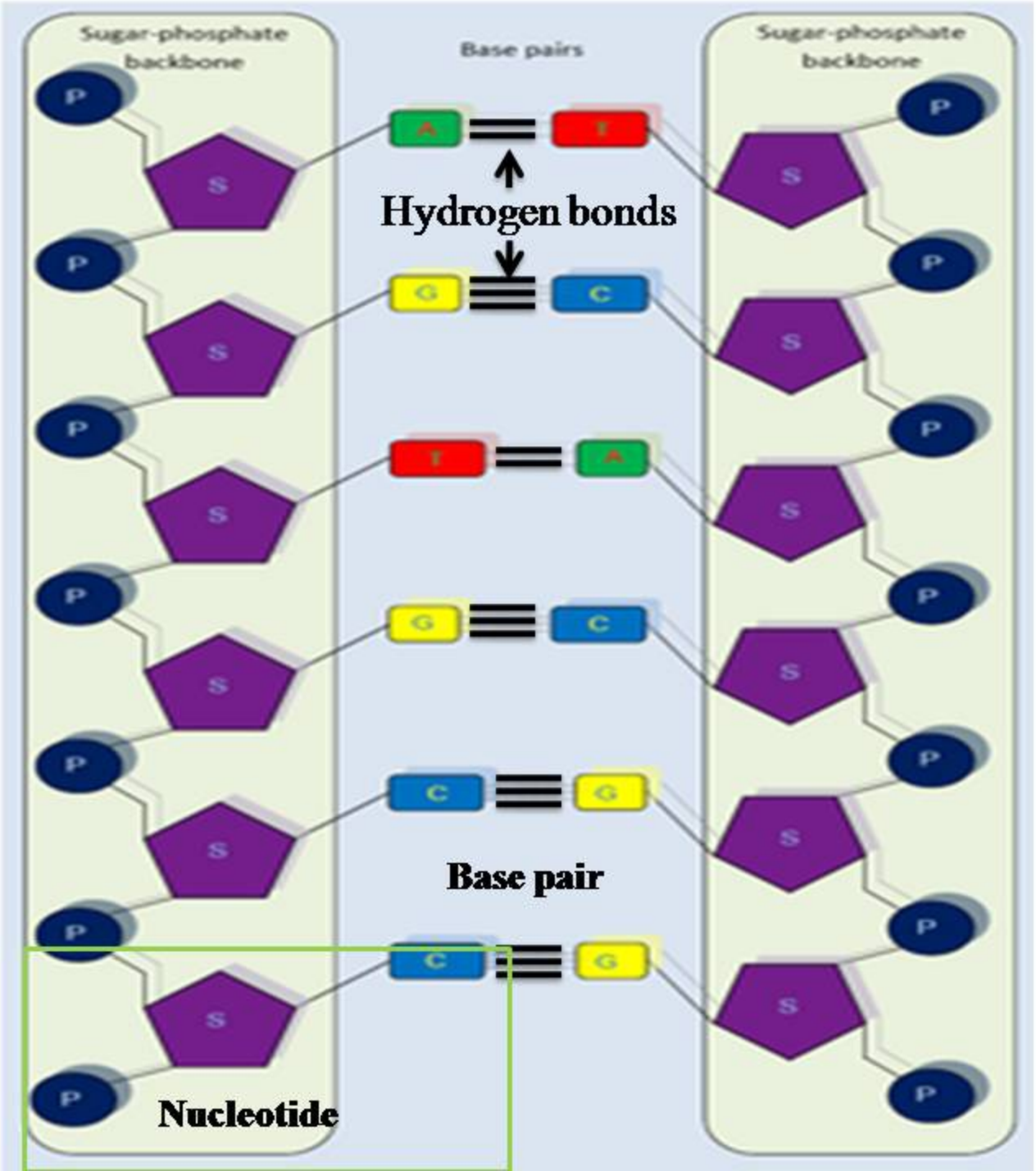
Physical nature of genes

- A gene is the basic physical and functional unit of heredity.
- Genes, which are made up of DNA, act as instructions to make molecules called proteins.
- Every organism has two copies of each gene, one inherited from each parent.


Sugar-phosphate backbone
Base pairs
Sugar-phosphate backbone
Hydrogen bonds
Base pair
Nucleotide

Gene

- DNA, or deoxyribonucleic acid is heredity material in humans and almost all other organisms.
- Nearly every cell has the same DNA.
- Most is located in the cell nucleus (where it is called nuclear DNA) but a small amount of DNA can also be found in the mitochondria (where it is called mitochondrial DNA or mt DNA)

- The DNA molecule consists of two polynucleotide chains which combine to form a double helix, similar to a spiral staricase.
- In the polynucleotide chains, the phosphate of one nucleotide is covalently bonded to the sugar of another.
- In one chain the linkages are polarized in the 3'-5' linkage, in the other they are in the reverse order -5'-3'.

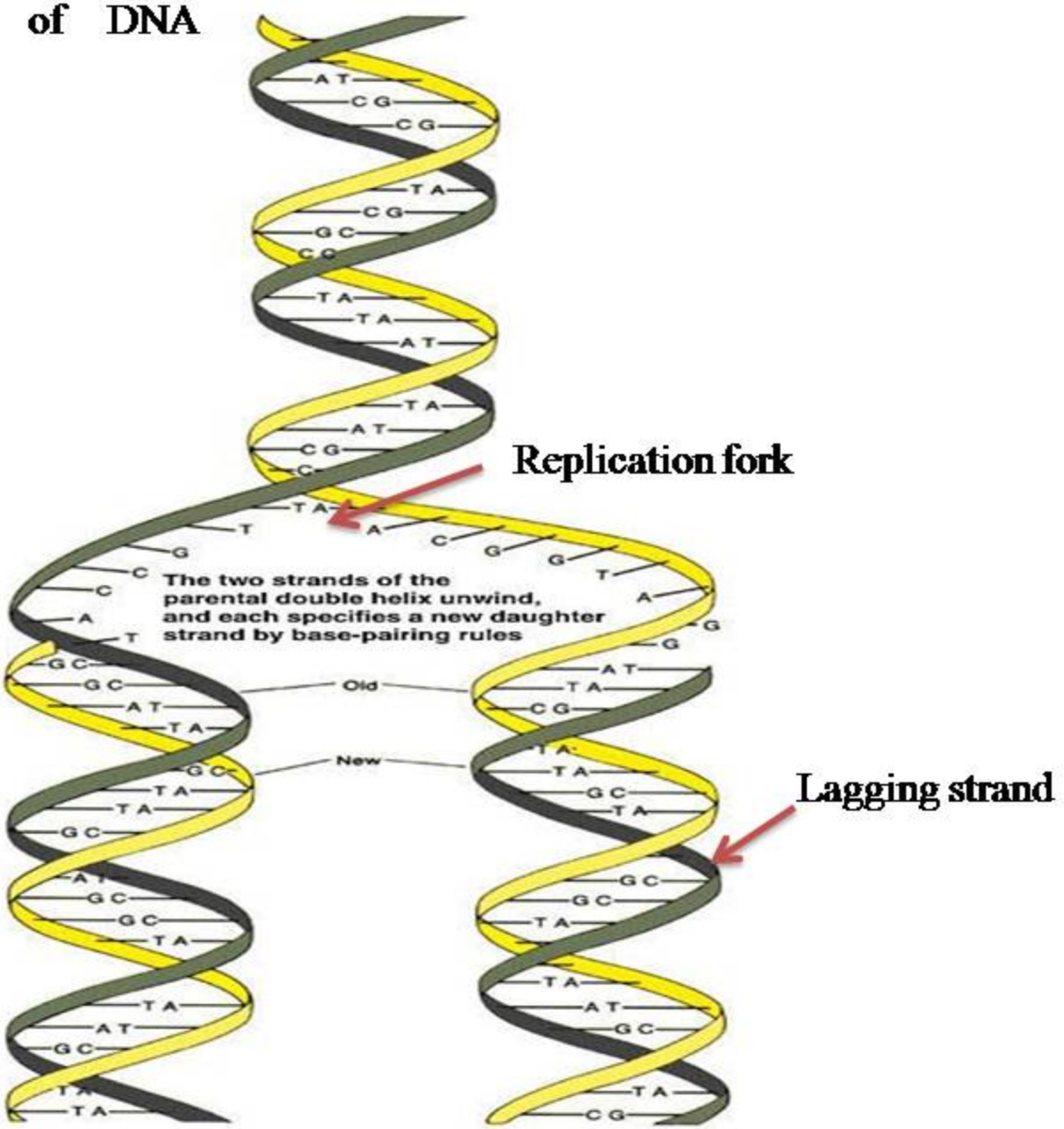
- Such an arrangement is known as reverse polarity.
- The steps of the spiral staircase consist of paired nitrogen bases in which adenine (A) always pairs with thymine (T), and guanine (G) with cytosine (C).
- Such a fitting arrangement is known as built - in complementarity.

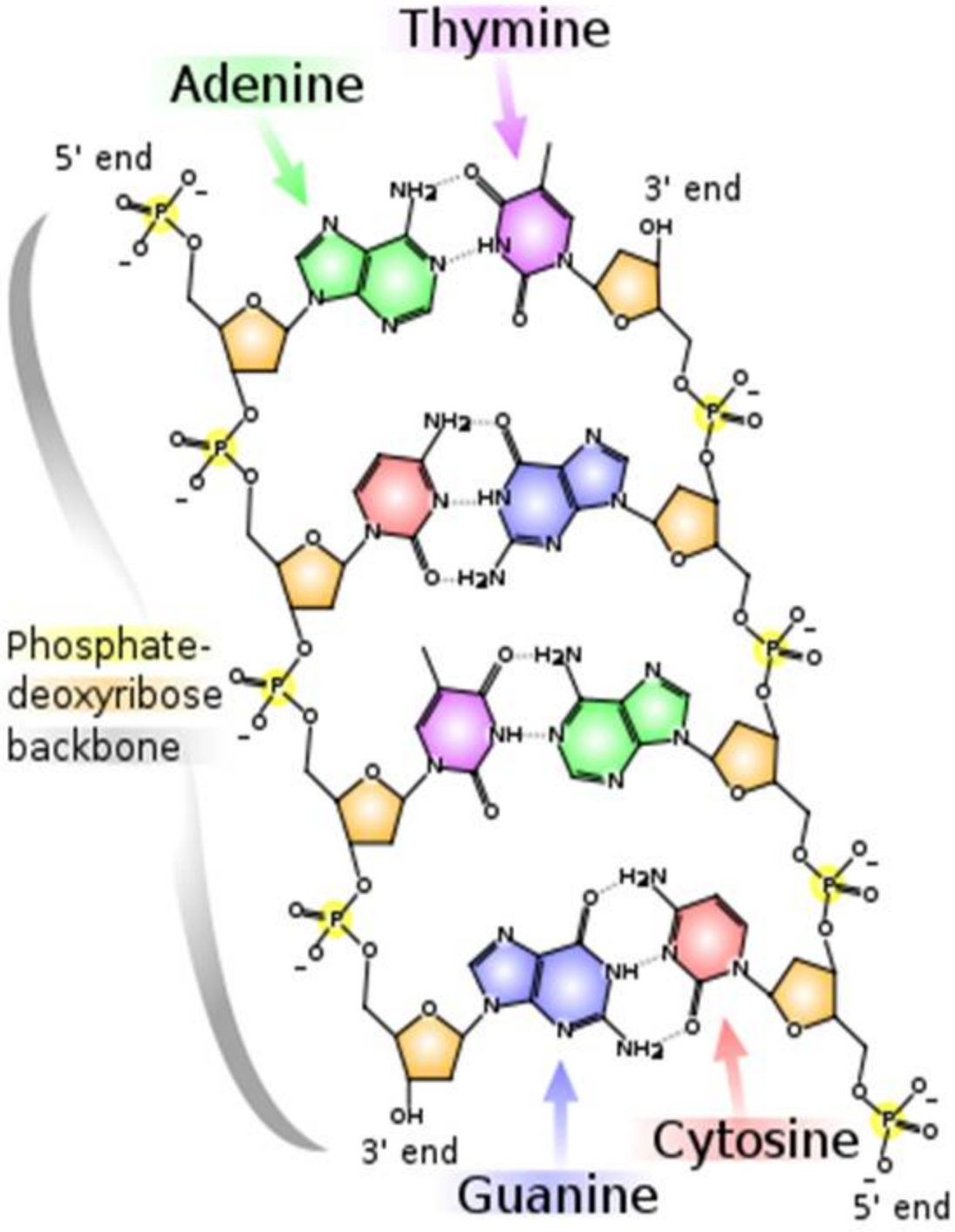
- The nitrogen bases form a core with the two spirals held together by hydrogen bonds.
- DNA forms the genes of all cells and carries the instructions required for proper development and normal function.
- The nucleotides in the DNA molecule contain the sugar deoxyribose, from which the nucleic acid gets its name.
- An important property of DNA is that it can replicate or make copies of itself.

DNA Replication

- The hydrogen bonds linking base pair together are relatively weak bonds.
- At the time of replication the 2 strands of the DNA separate along this line weakness in zipper-like fashion.
- Each single strand then becomes a template for the formation of another complementary strand by attracting free nucleotides to their complementary sites and the linking of adjacent nucleotides under the direction of the enzyme DNA- polymerase.

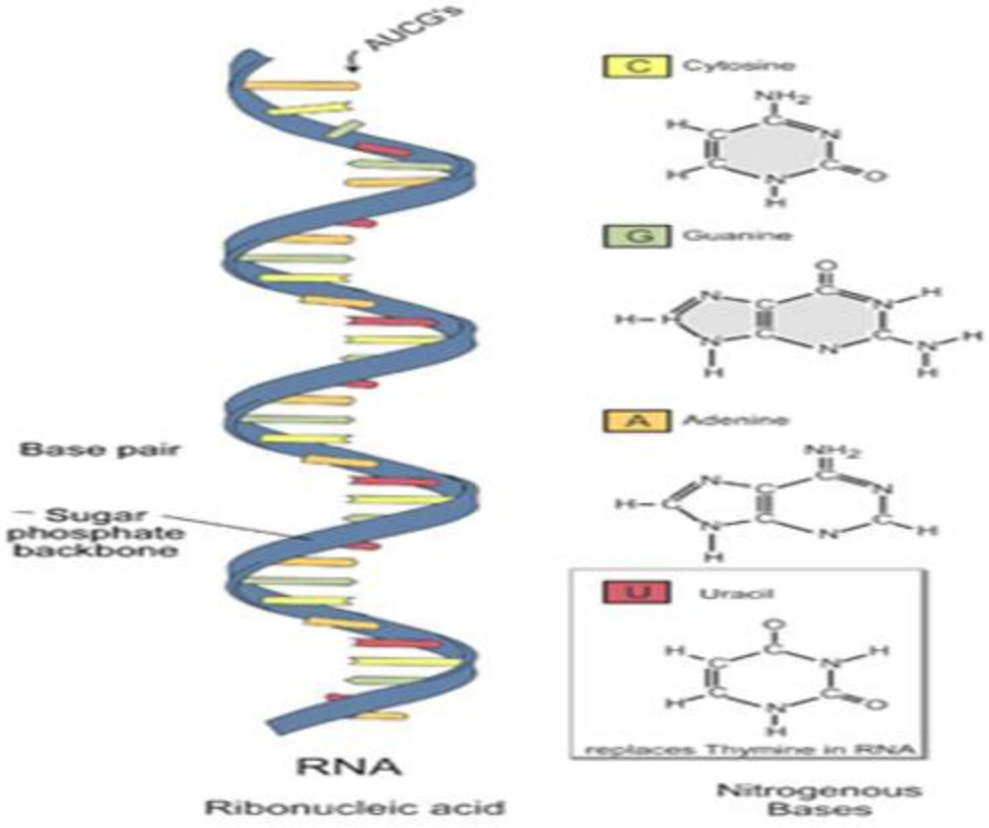
a. The mechanism of DNA replication




Thymine
Adenine
5' end
3' end
Phosphate-
deoxyribose
backbone
3' end
Cytosine
Guanine
5' end

Ribonucleic Acid (RNA)

- Like DNA, RNA consists of a long string of nucleotides linked by sugar-phosphate backbones.



Difference Between DNA and RNA

Sr. No.	DNA	RNA
1.	It usually occurs inside nucleus and some cell organelles. (Mitochondria and Chloroplast in plant)	Very little RNA occurs inside the nucleus. Most of it is found in the cytoplasm.
2.	It is double stranded	It is single stranded
3.	The sugar portion of DNA is 2-deoxyribose	The sugar portion RNA is ribose.
4.	The base present in DNA are A, G, T and C.	The base present in RNA are A, G, U and C.
5.	It replicates to form new DNA molecules	It cannot normally replicate itself.
6.	It occurs in the form of chromatin or chromosomes.	It occurs in ribosomes or forms association with ribosomes.
7.	The function of DNA is to transfer genetic information from one generation to the next.	The function of RNA is to direct synthesis of proteins in the body.
8.	Two types: intranuclear and exra nuclear.	Three different types of RNA mRNA, tRNA and rRNA.

Gregor Mendel

The Pea plant's famous traits

Mendel studied seven clearly differentiated traits, or characters, of the pea plant in pure-breeding individuals of each strain. The seven traits and the dominant and recessive forms of each are shown.

Table 14.1 The Results of Mendel's F_1 Crosses for Seven Characters in Pea Plants

Character	Dominant Trait	×	Recessive Trait	F_2 Generation Dominant:Recessive	Ratio
Flower color	Purple	×	White	705:224	3.15:1
Flower position	Axial	×	Terminal	651:207	3.14:1
Seed color	Yellow	×	Green	6022:2001	3.01:1
Seed shape	Round	×	Wrinkled	5474:1850	2.96:1
Pod shape	Inflated	×	Constricted	882:299	2.95:1
Pod color	Green	×	Yellow	428:152	2.82:1
Stem length	Tall	×	Dwarf	787:277	2.84:1

How Did Mendel Work it Out?

He studied <u>sexual reproduction</u> in Pea plants

I .Law of segregation

II. Law of independent assortment

Law of Segregation (Monohybrid) Complete Dominance

- Mendel's first law states that allelic genes in a zygote do not blend or contaminate each other but segregates and pass into different gametes.

Monohybrid cross involving

- A cross involving a single pair of allele is called a monhybrid cross.
- Mendel cross tall plant (6 ft) with dwarf plant ($1\frac{1}{2}$ ft).
- All the first filial generation or first hybrid generation (F_1) were tall.
- Of the two characters, the one expressed in the F_1 generation was called dominant while the other character which had been hidden was called recessive.

Tall (true breeding) = TT

Dwarf (true breeding) = tt

Parent	Tall	X	Dwarf
	TT		tt

Meiotic division

Gemetes (T) (t)

F_1 Tt

all tall

Example – Graden pea plant

Tall plant X Dwarf plant

All tall plants (filial generation)

F1 tall X tall(self-ertilized)

F2 787 tall : 277 dwarf (second filial generation)

F1 self-fertilized

F1 tall Tt X F1 tall Tt

Gametes (T) (t) (T) (t)

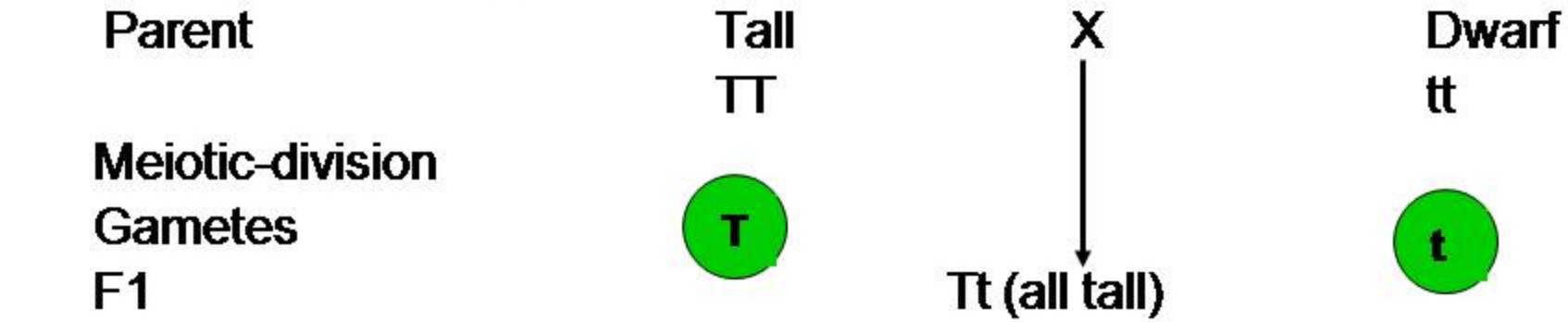
F2 Genotype TT : Tt : Tt : tt

Phenotype 1homozygous tall : 2heterozygous tall :1homozygous dwarf

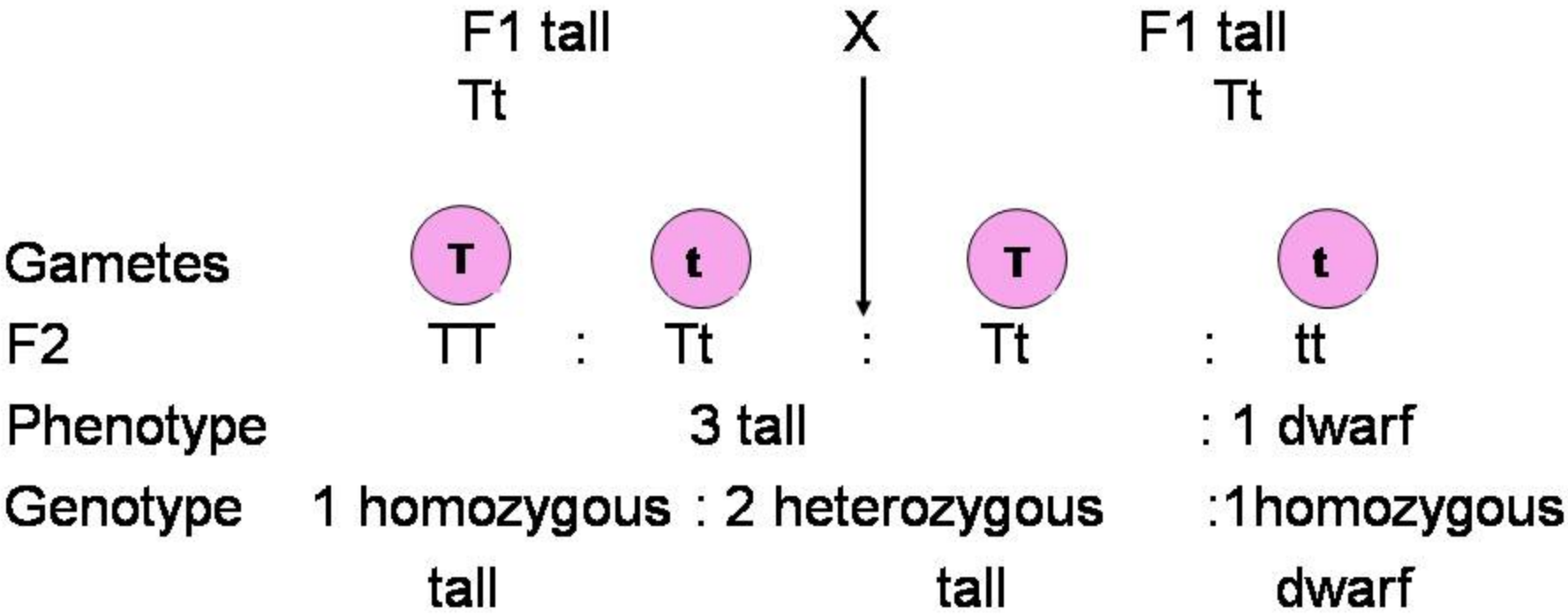
3 tall : 1 dwarf

THE GENE HYPOTHESIS

- Tall (true breeding) = T
- Dwarf (true breeding) = t



F1 self-fertilized



- Both tall and dwarf plants contain two identical gene (TT or tt) and this type of genetic constitution is known as homozygous.
- After meiotic division each gamete contains only half the number of identical genes T or t.
- The F1 offspring contain different genes Tt and such pair of gene is known as heterozygous.
- In the next generation the F2, obtain by self-pollination of F1, each of the alternative that made up the parental lines reappeared.

- In the F2 generation, both tall parents contain two different genes T and t.
- The parents produce two types of gametes.
- In each gamete only one of the two alternative genes is present: one half of the gametes will receive the gene for tallness and one half will receive the gene for dwarfness.

- These separation of the gene for tallness and dwarfness is termed as segregation.
- The concept of segregation of genes governing unit characters is known as Mendel's first law.
- Mendel concluded that the hidden character of dwarfness in the F1 generation could reappear in the F2 generation.

Back Cross or Test Cross

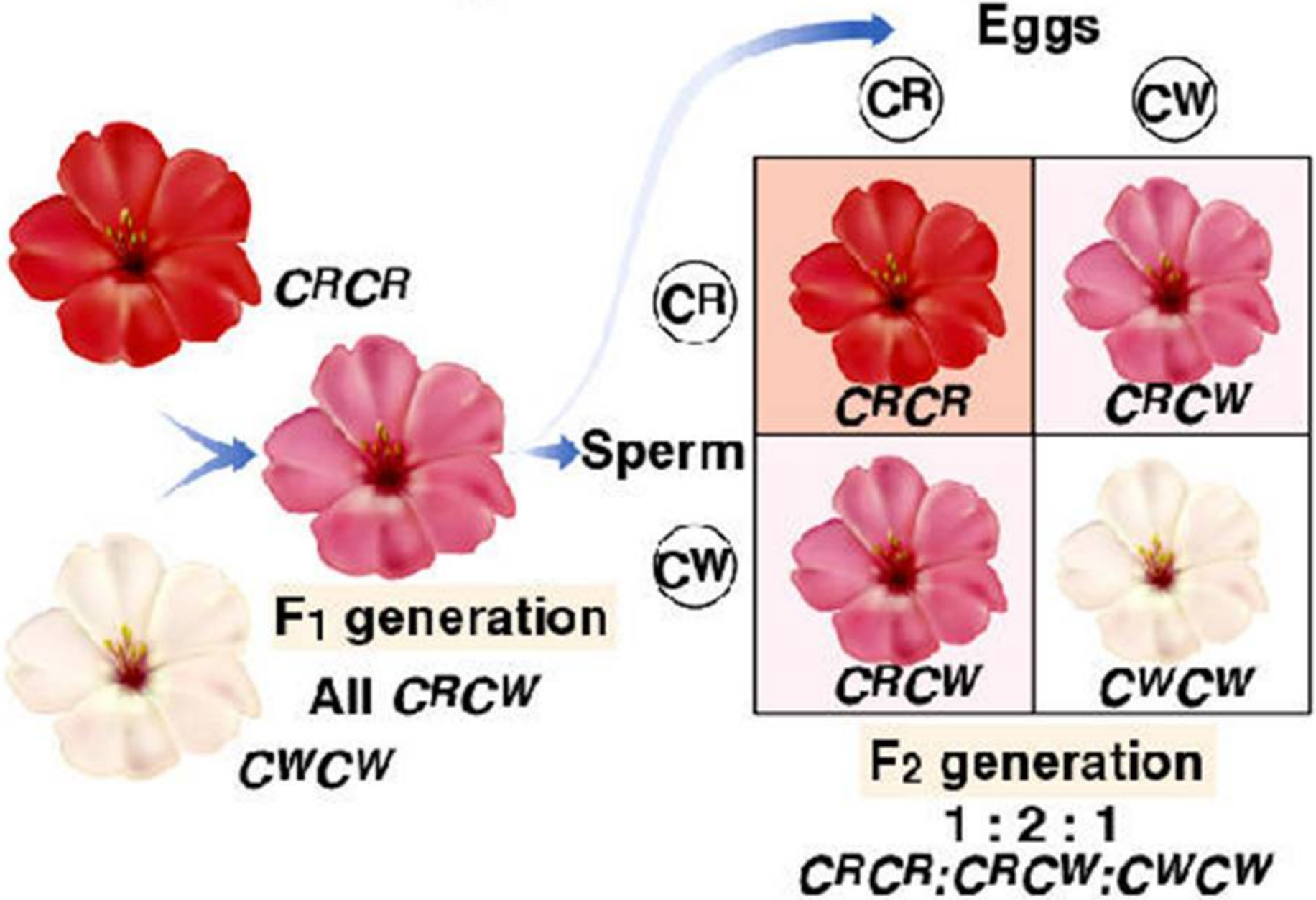
- By the gene hypothesis, we considered that F1 offspring contained two types of genetic constitutions; one was dominant gene "T" and the other recessive gene "t".
- If the consideration is true, the resulting ratio derived from a cross of F1 offspring with the recessive dwarf parent must be 1 : 1 and crossing back F1 plants to the recessive parent is called a back cross.
- Mendel crossed F1 offspring with the dwarf parent and the following result was obtained.

Back Cross (Test Cross) F1 X Double recessive

F1 offspring			X	dwarf	parent
	Tt			tt	
Gametes	T	t		t	
G:R	T t		:	tt	
P:R	87 tall		:	97 dwarf	
	1		:	1	

- Mendel's experimental results were in agreement with the results expected from the gene hypothesis.
- It is proved that genes segregated during meiosis in the formation of gametes.

Incomplete Dominance



INCOMPLETE DOMINANCE

Example – four O'clock flower

Red (true breeding) = RR

White (true breeding) = rr

Red X White

RR rr

Gametes

F1 R (Pink) r

F2 F1 Pink X F1 Pink (F1 self fertilized)

R r R r

Gametes

RR : Rr : R r : rr

Genotypic ratio 1 R : 2 r Rr : 1 rr R r

Phenotypic ratio 1 Red: 2 Pink : 1 white

- ***The F_1 offspring are pink in color. Although they are pink in external appearance, they contain red and white genes. After self fertilizing the F_1 offspring three types of offspring are obtained in a ratio of 1 : 2 : 1.***
- In this case, the phenotypic ratio of the F_2 generation corresponds to the genotypic ratio.
- Of three types of offspring, one fourth are red (like the original parent), one forth are white (like the other parent) and one half are pink (like the F_1 offspring).

- Here, the two combined genes (red gene "R" and white gene "r") are segregated and passed into different gametes at the time of meiosis in the F_2 generation.
- Thus, the characters (red and white) which have disappeared or were hidden in the F_1 generation reappeared.
- It shows that the incomplete dominant characters also behave according to Mendel's law of segregation.

Mendel's Explanation

Mendel formed a five part hypothesis to explain these results :

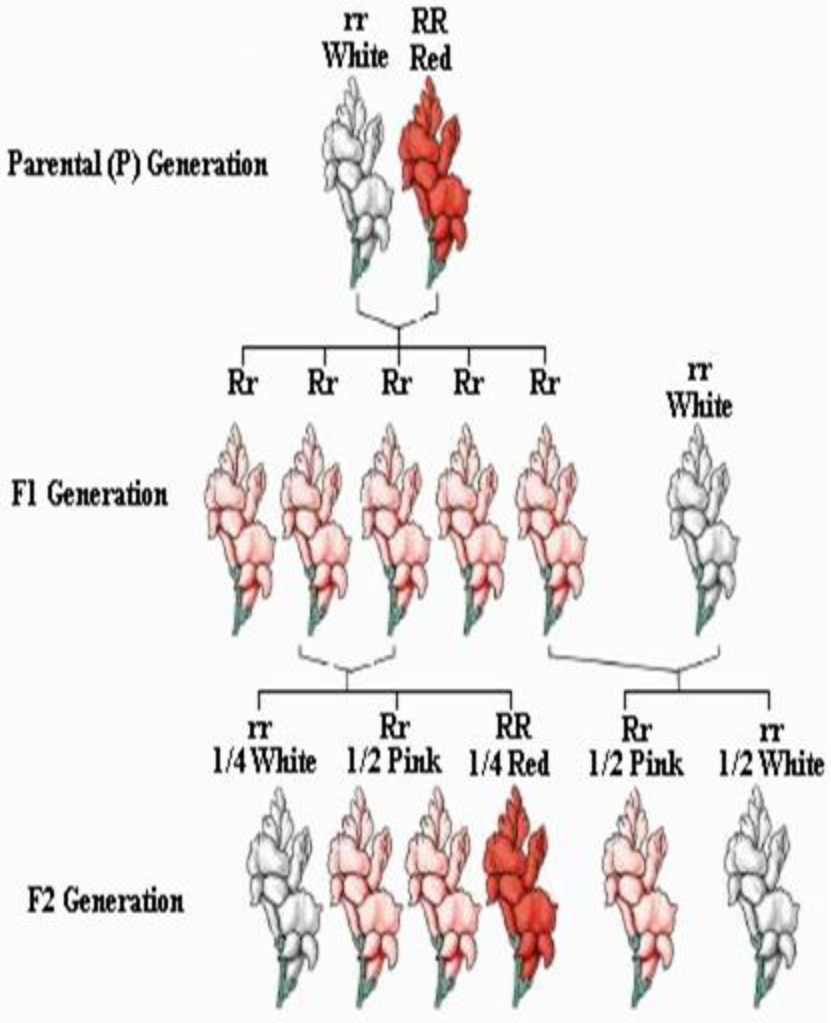
1. ***Each trait is determined by pairs of physical units***

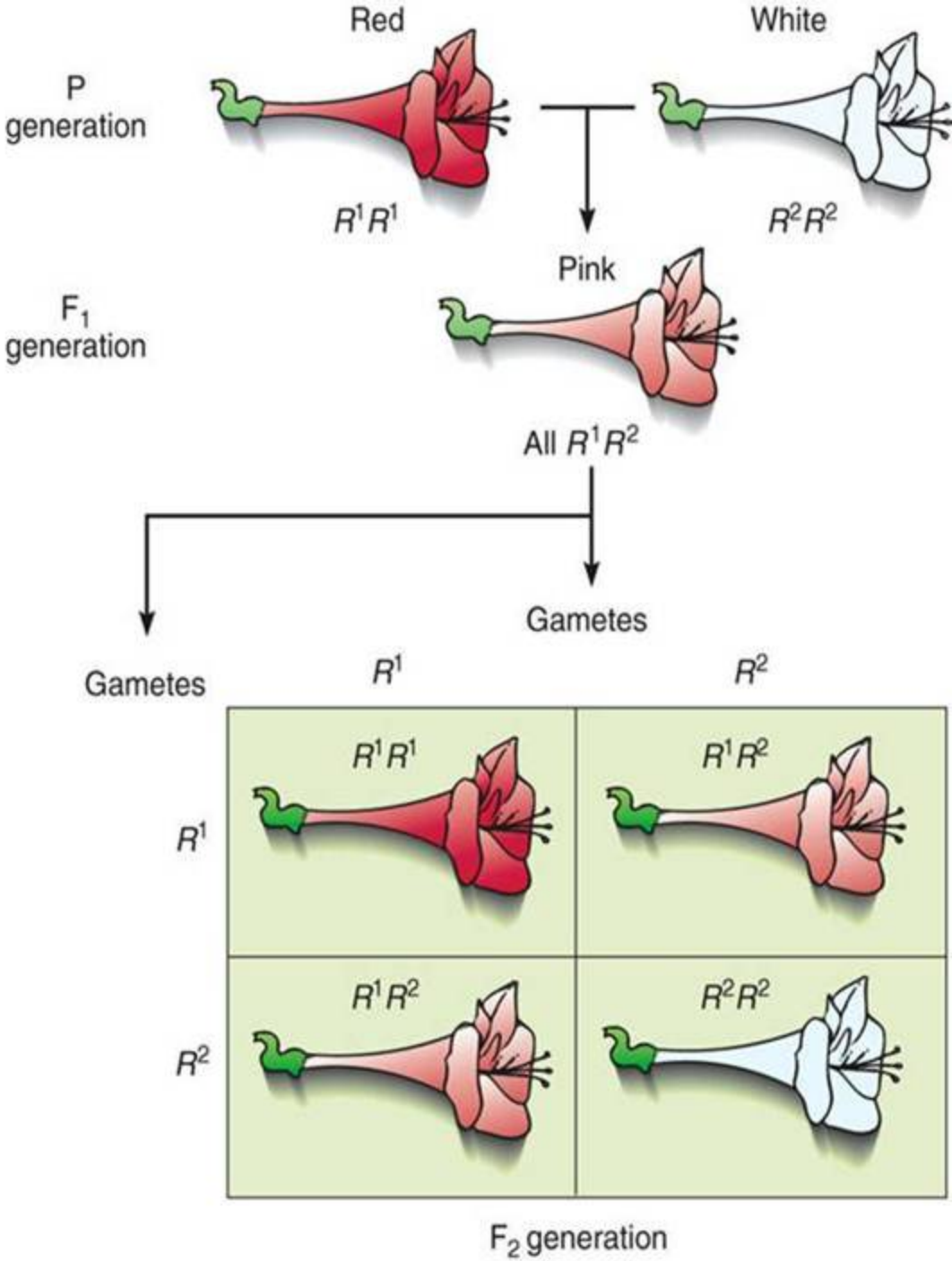
   Modern geneticists call these units genes. Each individual organism has two genes (e.g. two genes for flower colour) that together control the expression of a given trait.

2. ***Pairs of genes separate from each other during gamete formation. This is Mendel's law of segregation : each gamete receives only one of an organism's pair of genes. When a sperm fertilizes an egg, the resulting receives one gene from each parent.***

- When a red flowered plant is crossed with a white one, the F_1 offspring are all pink-flowered plants which are intermediate between red and white.
- It shows that the dominancy of red-flowered to white one is incomplete.
- This is called ***incomplete dominance.***
- ***The inheritance of incomplete dominant characters is found as mentioned above.***

3. Which member of a pair of genes becomes included in a gamete is determined by chance. Each gamete receives only one member of a pair, not both.
4. There may be two or more alternative forms of a gene. Alternative forms of a gene are called alleles One allele called the dominant allele can completely mask the expression of the other, recessive, allele. However, the domminant allele does not alter the physical nature of the recessive allele which can be passed unaltered into the individual's gametes.
5. True-breeding organisms have two of the same alleles for the trait under study, hybrids have two diferent alleles. A true-breeding or homozygous organism produces only one type of gamete. A hybrid or heterozygous individual produces equal numbers of gametes with each of the two alleles.





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Mendel's Second Law or Law of Independent Assortment

- The alleles for two or more gene on separate chromosme segregate from one another independently in meiosis.
- The linked genes may be broken apart and assorted independently of each other at random.

DIHYBRID CROSS

- A cross which involves two characters differences separable in inheritance is called a dihybrid cross.
- Mendel made a cross between a pea plant with round & yellow seeds and one with wrinkled & green one.
- In the F1 hybrids all had yellow & round seeds.
- (∴ yellow is dominant over green & the round shape is dominant over the wrinkled)

- When the F1 hybrid plants were crossed to each other (or self-fertilized), F2 generation was obtained.
- Among these seeds 3 dominant : 1 recessive was observed (seed colour and shaped).
- Mendel found that the segregation of the seed colour is independent of the shape.
- Both the parental characters appear in the F2 offspring.

- Out of seeds obtained:

  9 Round Yellow

  3 Round Green (!)

  3 Wrinkled Yellow (!)

  1 Wrinkled Green

- The sign (!) marks the new combinations of the characters, which arose through gene combination in the hybrids.
- The F2 generation from a cross involving 2 character pairs shows 4 kinds of individuals approximately in the ratio of (9/16 : 3/16 : 1/16 or 9 : 3 : 3: 1)

- Let the gene for the

  Round seed = R

  Wrinkled seed = r

  Yellow seed = Y

  Green seed = y

- In any given gamete it is a matter of chance as to whether the gene for round seed is associated with that for yellow or with that for green.
- The assortment of the gene is independent.

- When a red flowered plant is crossed with a white one, the F_1 offspring are all pink-flowered plants which are intermediate between red and white.
- It shows that the dominancy of red-flowered to white one is incomplete.
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- When F1 plants are crossed, there will be 4 kinds of gametes and 16 possible combinations of these gametes.
- The union of these gametes in fertilization is a random one.
- No selective preference being exhibited between them.
- This is shown in the chackerboard.

Law of Independent Assortment (Dihybrid)

Both Characters Completely Dominant

Round R > r wrinkled

Yellow Y > y green

Round yellow (true breeding) = R R Y Y

Wrinkled, green (true breeding) = r r y y

Round, yellow X wrinkled green

RR YY rr yy

Gametes RY r y

F1 R r Y y

All round, yellow

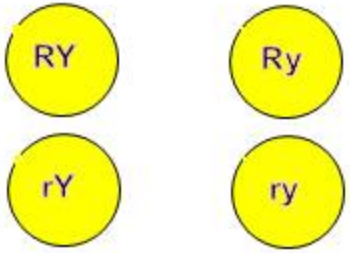
Self fertilized

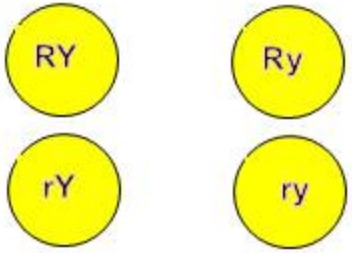
F1plant
Round, yellow
Rr Yy

X

F1 plant
Round, yellow
Rr Yy

Cametes





R → Y = RY; y = Ry

r → Y = rY; y = ry

Q / P	RY	Ry	rY	ry
RY	RRYY	RRYy	RrYY	RrYy
Ry	RRYy	RRyy	RrYy	Rryy
rY	RrYY	RrYy	rrYY	rrYy
ry	RrYy	Rryy	rrYy	rryy

BY RATIO METHOD

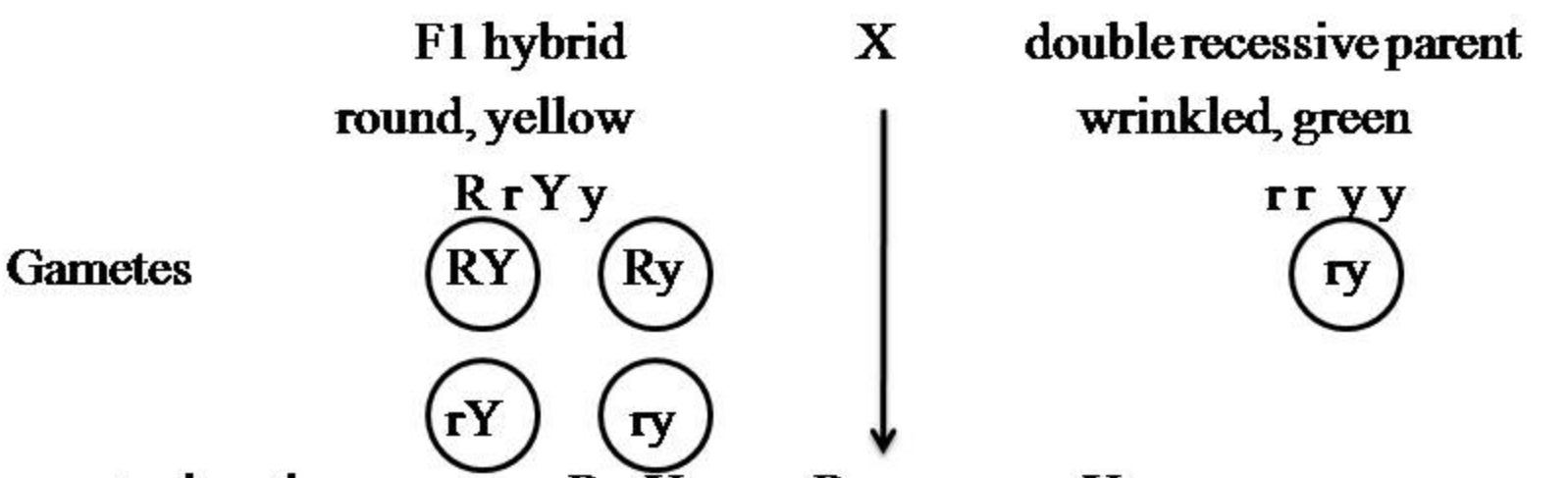
R r	X	Rr	=	3 R _	:	1 r
Y y	X	Y y	=	3 Y _	:	1 y

Genotypic ratio = 9 R Y : 3 r Y : 3 R y : 1 r y

Phenotypic ratio = 9 round, yellow : 3 wrinkled, yellow :
3 round, green : 1 wrinkled, green

Back Cross (Test Cross)

- If the genes assort independently, the plants grown from the round, yellow seeds of the F1 generation will produce four types of gametes with the genes RY, Ry, rY, ry.
- The wrinkled, green parent (both charactes recessive) forms only one kind of gamete with the genes ry.
- The expected ratio by the union of the these gametes must be 1 : 1 : 1 : 1 as follows :



genotypic ratio R r Y y : R r y y : r r Y y : r r y y

phenotypic ratio round, yellow : round, green : wrinkled, yellow : wrinkled, green

1 : 1 : 1 : 1

Mendel's experimental results are as follows:

Round, yellow	=	55	=	1
Round, green	=	51	=	1
Wrinkled, yellow	=	49	=	1
Wrinkled, green	=	52	=	1

- The above expected ratio corresponds to the experimental ratio and it confirms Mendel's theory. (law of independent assortment).

LINKAGE AND CROSSING OVER

- Mendel's principle of independent assortment applies both to genes and to chromosomes.
- The maternal and paternal chromosomes are distributed independently to the gametes at meiosis.
- So the genes which are located on the chromosomes undergo independent assortment and produce Mendelian ratio.

- But most organsims contain thousands of genes and only a few chromosomes.
- In *Drosophila, for example, hundreds of genes have been studied, yet there are only four pairs of chromosomes.*
- *When a chromosome contains thousands of genes, they cannot assort independently and some genes of a particular chromosome tend to remain together from generation to generation.*

- *Such a phenomenon where genes tend to remain together in inheritance is known as linkage.*
- ***Linkages can be demonstrated as follows:***
- In maize colour gene C is dominant over colorless c, whereas normal or full endosperm, gene 'S', is dominant over shrunken 's'.
- When colored full maize was corssed with colorless shrunken, colored full offspring were obtained in the F1 generation.

- When the F1 colored full plants were crossed with double recessive plants, four types of offspring in the ration of 1: 1: 1: 1 would be obtained if the genes of F1 plant assorted independently in accordance with Mendel's second principle.
- But when the actual cross was made the expected ratio was not realized.
- Instead of this ratio the following result was obtained:

Color = CC

Full = SS

Colourless = cc

Shrunken = ss

Coloured full x Colourless shrunken

$\frac{CS}{CS}$ $\frac{cs}{cs}$

CS cs

$\frac{CS}{cs}$

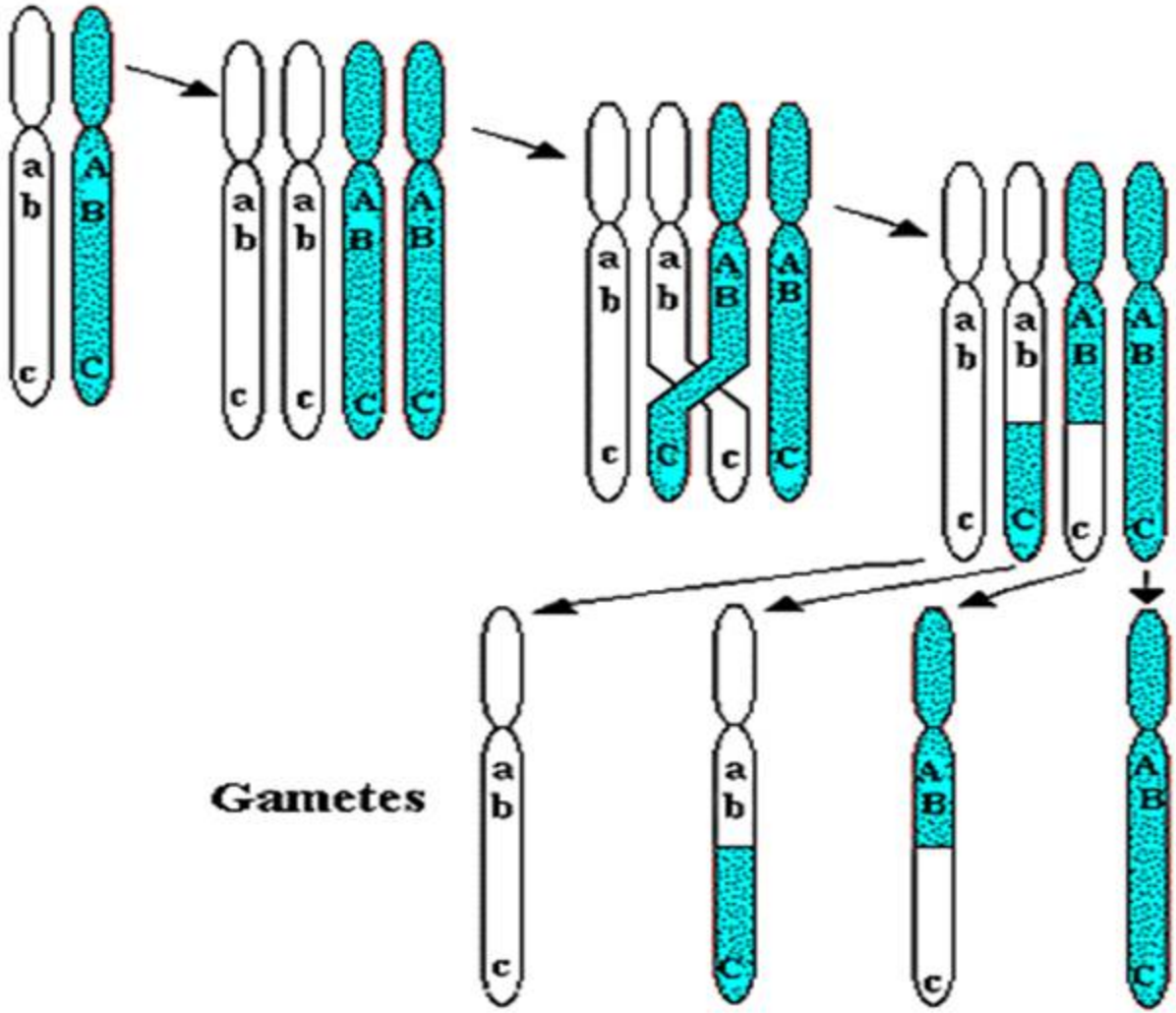
F1 (coloured full)

F1 coloured full x double recessive

$\frac{CS}{cs}$ $\frac{cs}{cs}$

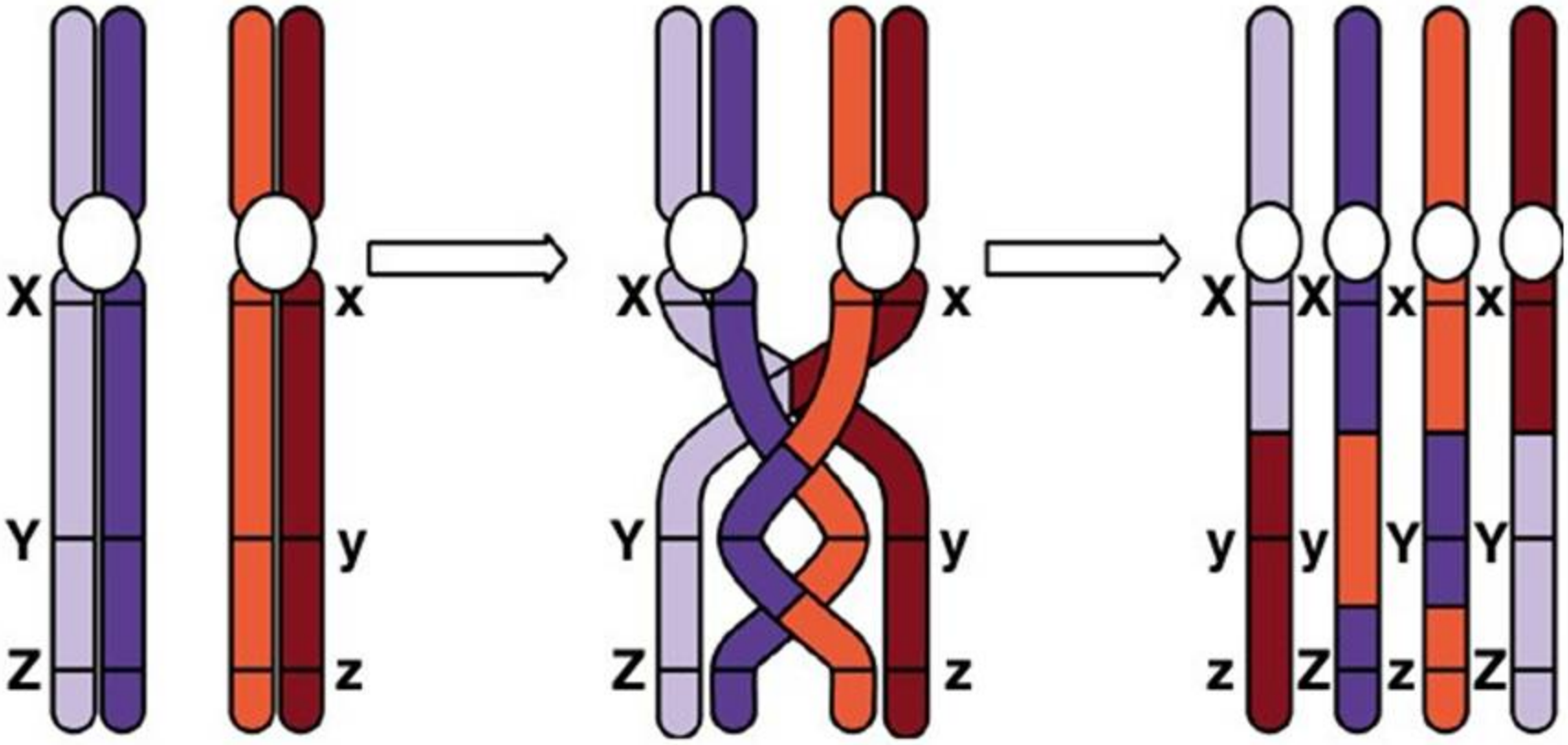
CS Cs cS cs cs

$\frac{CS}{cs}$	coloured full	=	4032	parental combination
$\frac{cS}{cs}$	colourless full	=	149	recombination
$\frac{Cs}{cs}$	coloured shrunken	=	152	recombination
$\frac{cs}{cs}$	colourless shrunken	=	4035	parental combination
	Total	=	8368	



Crossing-over and recombination during meiosis

Crossing over during meiosis



- In independent assortment the parental combination CS and cs and recombination Cs and cS would be equally frequent.
- But in the experiment shown the situation is as follows : -

Parental combination CS 4032 + cs4035 = 8067 or

about 96.4 percent of the total

Recombination or crossing over Cs 152 + cS 149 = 301

or about 3.6 percent

- In the above result the parental combinations are more frequent than the recombination.
- This result demonstrates that the two pairs of genes C- c and S - s have not assorted independently and they remain combined or linked in 96.4 percent of the offspring.
- The above example shows that linkage is caused by genes being carried in the same chromosomes.

- If the chromosomes remain intact in inheritance, the two linked genes located in the same chromosome should remain together in all cases.
- But there are recombinations in about 3 percent.
- The formation of recombinations is due to interchange of sections of homologous chromosomes at meiotic division in the formation of gametes.
- This interchange of sections of homologous chromosomes is known as *crossing over and is found as a X shaped attachment, called chiasma seen under the microscope.*

The Expression and Interaction of Genes

- Mendel's laws of segregation and independent assortment were confirmed by other investigators in 1900, some exceptions were still found.
- These exceptions were expressed because of the blending or mixing of the heredities of the parents in the offspring or interaction of genes.
- Thus, Mendelian ratios such as 3 : 1, 9 : 3 : 3 : 1 etc, do not occur in all crosses. Some examples of expression and interaction of genes may be explained as follows :

Complementary Genes (9 : 7)

- Two genes which are similar in their individual effect, but are both necessary to the production of another and different character may be called complementary.

- Example - sweet pea
- The complementary genes were illustrated by Bateson and Punnette.
- They crossed two white (varieties) which were collected from different areas and found that the F1 offspring were all purple.
- After allowing the F1 purple offspring to undergo self fertilization, they realized that there were two types of offspring in a ratio of 9 purple: 7 white which indicates that two pairs of genes are involved.
- Thus the F1 offspring contained two different pairs of dominant genes which are heterozygous in condition.

- We can explain complementary genes by gene symbols as follows :
- "C" represents the color genes and "P" for the purple one.
- Both dominant genes are necessary to express purple color.
- Plants lacking one of these dominant genes will be white.

White C C p p or c c P P or c c p p

Purple C-P-

Complementary Genes

Genotype of White = C C p p **or** c c P P **or** c c p p

Genotype of Purple = C-P-

White C C p p **X** White c c P P

Gametes: Cp × cP

F1: C c P p all purple

F2 = F1 Purple C c P p **X** F1 Purple C c P p

Gametes: CP, Cp, cP, cp × CP, Cp, cP, cp

Checkerboard Method

P \ Q	CP	Cp	cP	cp
CP	CCPP	CCPp	CcPP	CcPp
Cp	CCPp	CCpp	CcPP	Ccpp
cP	CcPP	CcPp	CcPP	ccPp
cp	CcPp	Ccpp	ccPp	ccpp

- In the above checkerboard, out of 16 squares, the 9 squares containing *both dominant genes will give purple character and the remaining 7 squares containing one type of dominant gene or lacking of both types of dominant will express white character.*
- By studying the above records, we realize that purple offspring always contain both types of dominant genes, either homozygous or heterozygous in condition.
- Therefore we can conclude that to obtain purple offspring both types of dominant genes are required or both dominant genes (gene "C" and gene "P") are complementing each other in their effect on the same character.

Epistasis (Greek Word, Stopping or Suppressing)

The term epistasis is used to describe the effects of non - allelic genes on each other's expession

Two types of epistasis,

1. Dominant Epistasis (12 : 3 : 1)
2. Recessive Epistasis (9 : 3 : 4)

Dominant Epistasis (12 : 3 : 1)

Dominant epistasis results when only one dominant gene of a pair of alleles is necessary to influence the expression of a second pair of alleles. e.g. Summer squash.Colour of summer squash - usually , white , yellow and green.

When crosses, White X Green

Yellow x Green

White x Yellow

Dominant Epistasis (12 : 3 : 1)

Colour of summer squash – usually, white, yellow and green.

When crosses , White x Green

Yellow x Green

White x Yellow

True breeding White x Green

↓

F_1 White

↓

F_2 12white : 3yellow : 1green

12 : 3 : 1

W = white colour gene

Y = yellow colour gene

White = W- - -

Yellow = ww Y- -

Green = ww yy

True breeding

White
WW YY

x

Green
ww yy

WY

wy

Ww Yy (White)

F_1 White
Ww Yy

x

F_1 White
Ww Yy

WY Wy wY wy

same as on left hand side

0_+ \ 0	WY	Wy	wY	wy
WY	WW YY	WWYy	WwYY	WwYy
Wy	WWYy	WWyy	WwYy	Wwyy
wY	WwYY	WwYy	wwYY	wwYy
wy	WwYy	Wwyy	wwYy	wwyy

12 White : 3Yellow : 1Green

- Here the dominant allele W is able to express itself in the presence of either Y or y.
- Thus the genotypes WY and Wy produce the same phenotype whereas wY and wy produce two additional phenotypes, i.e. yellow and green.
- When the dominant allele, for example, the W allele produces a certain phenotype regardless of the allelic condition of the other (Y), the W allele is said to be dominant epistatic.
- In this case the classical 9 : 3 : 3 : 1 ratio becomes modified into a 12 : 3 : 1 ration.

Recessive Epistasis (9 : 3 : 4)

When a pair of homozygous recessive genes supresses the expression of genes of the other pair, the phenomenon is known as Recessive Epistasis.

Recessive Epistasis (9 : 3 : 4)

e.g. Mice , Typical mice

Black x Albino

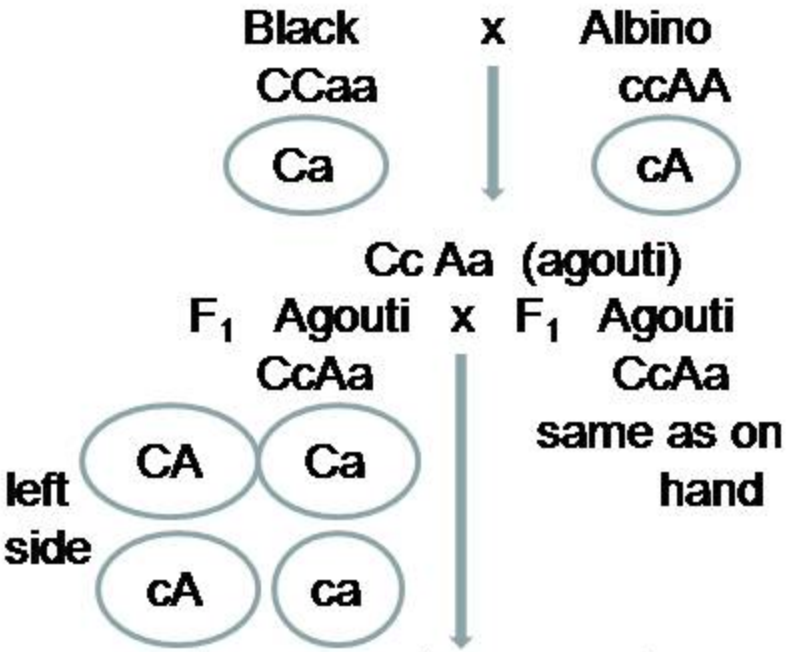
F_1 Agouti

F_2 9 agouti :3 black : 4 albino

genotype for Agouti = C_A_

genotype for black = C_aa

genotype for albino = ccA_ , ccaa



0+ 0	CA	Ca	cA	ca
CA	CCAA	CCAa	CcAA	CcAa
Ca	CCAa	**CCaa**	CcAa	**Ccaa**
cA	CcAA	CcAa	ccAA	ccAa
ca	CcAa	**Ccaa**	ccAa	ccaa

9 agouti : 3 black : 4 albino

Recessive Epistasis (9 : 3 : 4)

Parents: CCaa Coloured × ccAA Albino

Gamete: Ca × cA

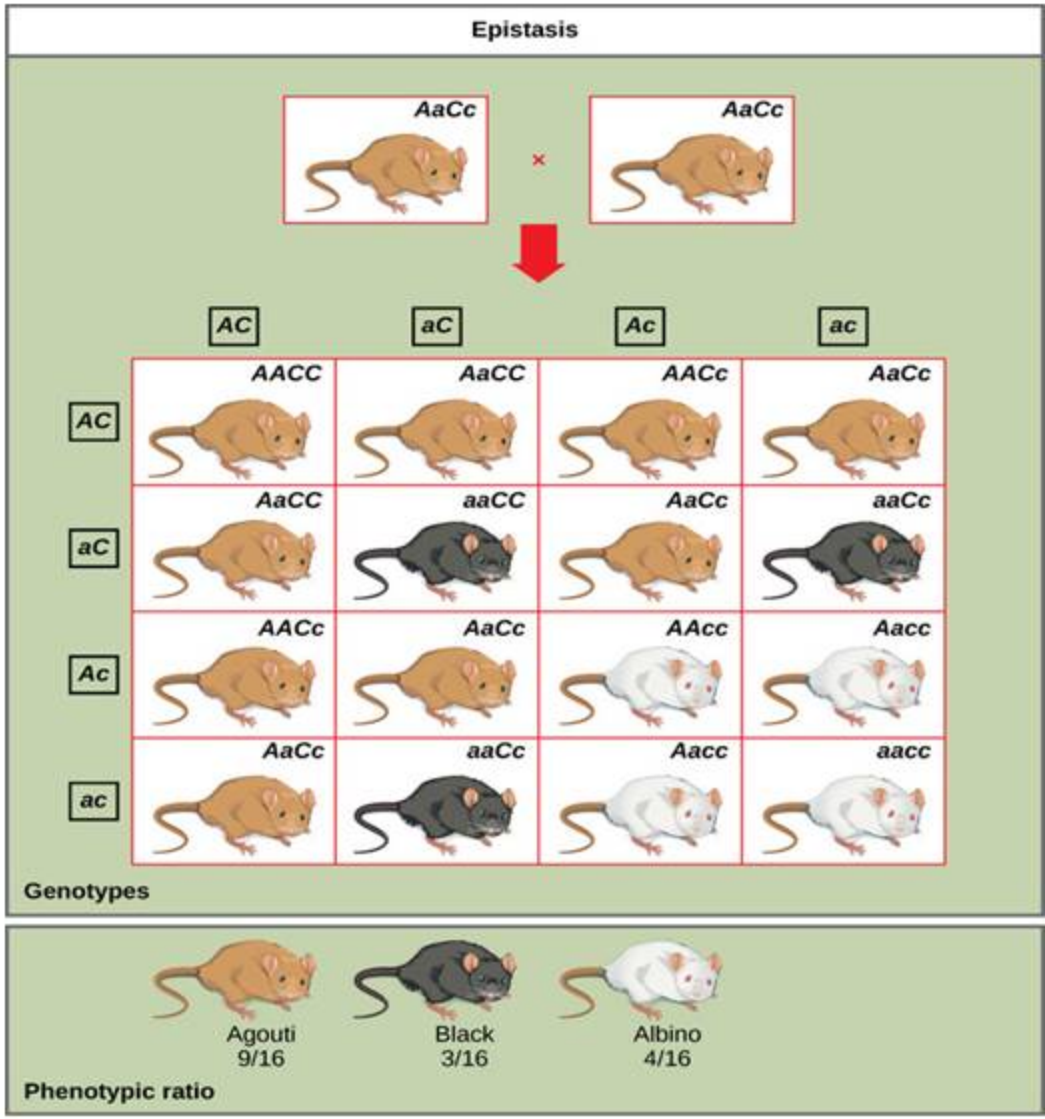
F_1: CcAa

Agouti

Selfing of F_1

Gametes → / ↓	CA	Ca	cA	ca
CA	CCAA Agouti	CCAa Agouti	CcAA Agouti	CcAa Agouti
Ca	CCAa Agouti	CCaa Coloured	CcAa Agouti	Ccaa Coloured
cA	CcAA Agouti	CcAa Agouti	ccAA Albino	ccAa Albino
ca	CcAa Agouti	Ccaa Coloured	ccAa Albino	ccaa Albino

F_2 Generation



- In the above ration, 9 offspring are agouti.
- To express agouti both dominant genes C and A are required.
- Three offspring contain dominant gene C and recessive gene a and they become black.
- In the remaining 4 offspring, two different genotypes are found i.e. cA and ca.
- Here although A genes are present in the genotype ccA they cannot express their character due to the presence of recessive genes cc.
- Thus this phenomenon is known as Recessive Epistasis.

Lethat Genes (2 : 1)

The gene that produces death is called lethal genes.

Eg. Mice

Yellow x Yellow

↓

Non yellow

Here phenotypically yellow parents produce non yellow offspring. Therefore both parents must be genetically heterozygous. The inheritance of mice can be explained as follows: -

A = a dominant gene for yellow

a = its recessive allele for non yellow (black)

Yellow = $A^y a$

non yellow = a a

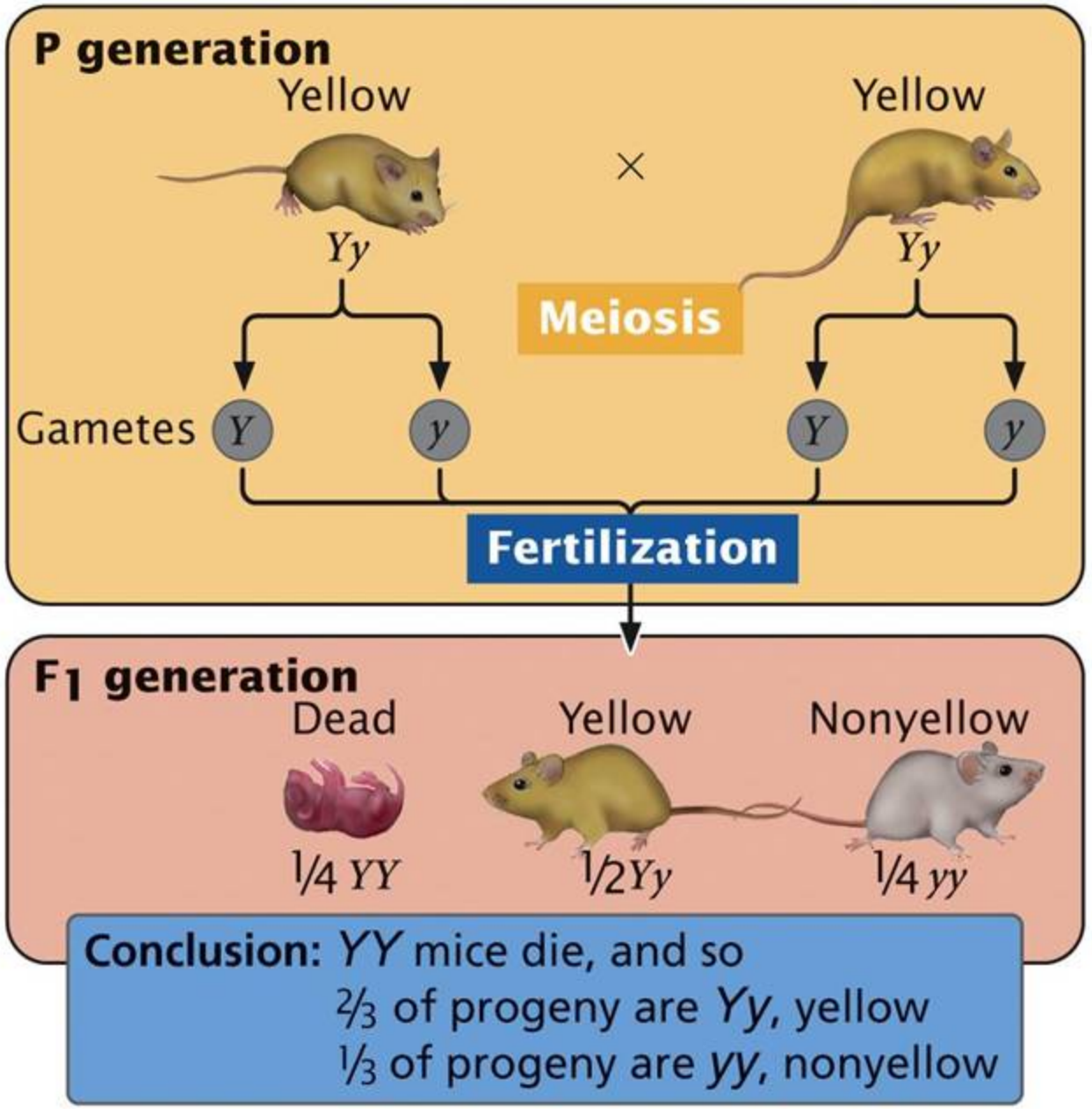


Fig_05-04 *Genetics, Second Edition* © 2005 W.H. Freeman and Company

The gene that produces death is called lethal gene e.g Mice

Yellow x Yellow

↓

Non yellow

A = a dominant gene for yellow

a = its recessive alleles for non yellow (black)

Yellow = A^Y a

non yellow = a a

Yellow x Yellow

$A^Y A^Y$: A^Y a : A^Y a : aa

(Die)

genotype 2A^Y a : 1aa

phenotype 2 Yellow : 1non yellow (black)

Thus a mouse homozygous for A^y die before birth. The allele A^y is lethal in homozygous condition. Thus ratio is a modification of Mendel's monohybird ratio 3 : 1 .

Multiple Alleles

- By studying the Mendelian law of segregation we know that a pair of genes contains two different alleles.
- Sometimes there may be more than two alternative forms of a gene; such alleles are known as multiple alleles.
- e.g coat colour in rabbits and blood groups in human beings.

The O, A, B Blood Groups in Man

- In human blood there are two antigens and antibodies.
- The two antigens are antigen A and antigen B.
- The two antibodies are antibody A and antibody B.
- The antigens are present in the red blood cells and the antibodies in the serum.

Regarding the antigen property of the blood all human beings can be classified into 4 groups,

- those with antigen A (group A), those with antigen B (group B),
- those with both antigen A and B (group AB) and those with neither antigen (group O).

The antibodies present together with the antigens are found as follows :

1. Antigen A with antibody B
2. Antigen B with antibody A
3. Antigen AB has no antibodies
4. Antigen nil (group O) with antibody A and B.

The above four blood groups may be tabulated as follows :

Blood group	Antigen	Antibody
A	**A**	**B**
B	**B**	**A**
AB	**AB**	**Nil**
O	**Nil**	**A and B**

- There is an agglutination reaction between similar antigen and antibody (e.g, antigen A agglutinates the antibody A and antigen B agglutinates the antibody B).
- Thus, transfusion can be considered safe as long as the serum of the recipient does not contain antibodies for the blood cell antigens of the donor.
- The following table shows the receivers and donors in the transfusion of blood of different O - A - B types.

Universal Receiver

Blood Group	A Antibody B	B Antibody A	AB Antibody Nil	O Antibody A & B
A	✔	✘	✔	✘
B	✘	✔	✔	✘
AB	✘	✘	✔	✘
O	✔	✔	✔	✔

Universal Donor

Inheritance of Blood Groups

The evidence shows that the blood group properties are determined by a series of 3 multiple alleles I^A, I^B and i.
"I^A" is the gene for the production of antigen A.

"I^B" for antigen B and

"i" for neither antigen.

I^A and I^B are codominant and on the other hand I^A and I^B show complete dominance over "i". The genetypes which produce the four blood types,

Blood Groups	**Genotypes**
AB	I^AI^B
B	I^BI^B or I^Bi
A	I^AI^A or I^Ai
O	ii

Importance of Classification of Blood Groups A, B, AB, and O

a. Transfusion of the blood

b. Legal case of disputed parents

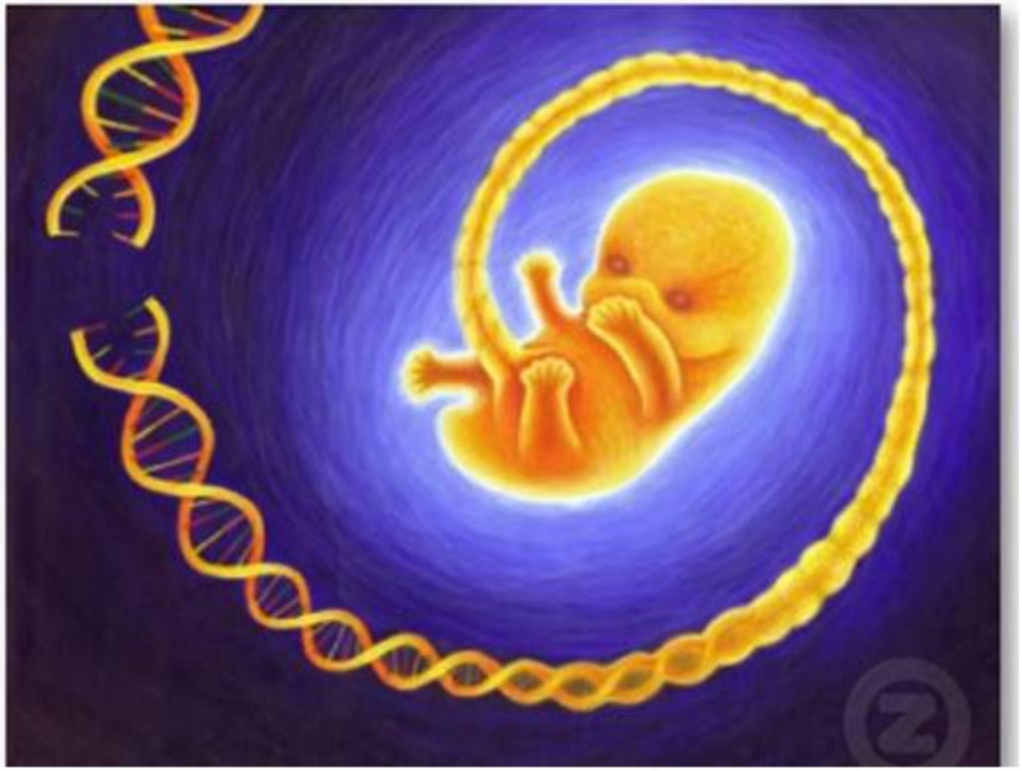
c. Disputed paternity

The Rhesus (Rh) Alleles in Man

- The blood of the rhesus monkey was injected into a rabbit.
- When the serum of the rabbit injected with the blood of the rhesus monkey was mixed with human blood the red cells of about 85% of the population of New York City were agglutinated.
- The antigen responsible for the agglutination of blood was called the rhesus factor.
- This rhesus factor is a result of a dominant gene capital "R" Therefore Rh positive equals "RR" or Rr" and Rh negative equals rr".

- This Rh factor was discovered by Levine while studying a characteristicform of anemia known as erythroblastosis fetalis.
- This disease occurs in new-born infants.
- The origin of the disease was explained as follows:
- The infant suffering from anaemia is Rh positive and his father also Rh positive. But his mother is Rh negative.
- The mother and the son are connected by the placenta.
- Because of this connection, there is blood circulation between both of them.

- Therefore, the antigens of the fetus and antibodies of the mother combine forming anti - Rh ahtibodies.
- These anti Rh antibodies gain sufficient strength in the mother's blood and attack the red blood cells of the fetus.
- Thus, the unborn child becomes hemolytic and anaemic.
- If this reaction is serious, it causes death of the unborn infant or abortion of the fetus.



Father

Rh^+

Anti-Rh antibody

Mother

Rh^-

antigen

antibody

Son

Rh^+

- The Rh factor has important significance in transfusion.
- Let us assume that an Rh negative person has been injured in an accident and is in serious need of immediate transfusion.
- A donor of suitable A, B, O group is found and the transfusion is given.
- If the donor, however happens to be Rh positive, there will be no reaction.
- But the presence of Rh antigens will stimulate the recipient to generate Rh antibodies.

- Now let us suppose that this same person needs another transfusion one year later and the same donor is selected.
- This time the Rh antibodies formed in the recipient will react with Rh antigen and the recipient will die.
- So an Rh negative person should not be given a transfusion from a Rh positive person even though it may be the first transfusion.

Inheritance of Rh Blood Groups

Follows simple Mendelian rules — Gene R = produces Rh antigen; r = no Rh antigen; R > r

Genotypes Rh^+ person = RR or Rr

Rh^- = rr

Marriage between Rh^+ man and Rh^- woman

Rh^+ X Rh^-

RR or Rr, rr

Gametes (R) (r) (r)

Rr	: rr	:	Rr	:	rr
Rh^+	Rh^-	:	Rh^+		Rh^-
1st child	2nd child		3rd child		4th child

Hemolytic disease of new born (HDN)

- The children with HDN may be mildly affected with jaundice or may be severely affected and require exchange transfusion.
- The first pregnancy (Rh^+) escape because immunization of the mother does not occur until the temination of pregnancy.
- But when another incompatible pregnancy occurs the antibodies cross from the maternal into the fetal circulation and destroy the fetal cells producing hemolytic disease of new born (HDN).

M-N Blood Groups

M-N blood groups were discovered by **Landsteiner and Levine.**

They found antigen M and antigen N in the blood.

Blood containing antigen M was named as M blood group

Blood containing antigen N" was named as N blood group

Blood containing M & N was named as MN blood group

There are no natural M or N antibodies in the serum.

Autosomes and Sex Chromosomes

- For most chromosomes, the maternal and paternal copies of the chromosomes are exactly alike in terms of length, shape and the sequence of genes they carry.
- But in humans and many other organisms, this is not true for the chromosomes (X and Y) that determine the sex of the organism.
- In humans for example, males have one X chromosome and one Y chromosome, whereas females have two X chromosomes.

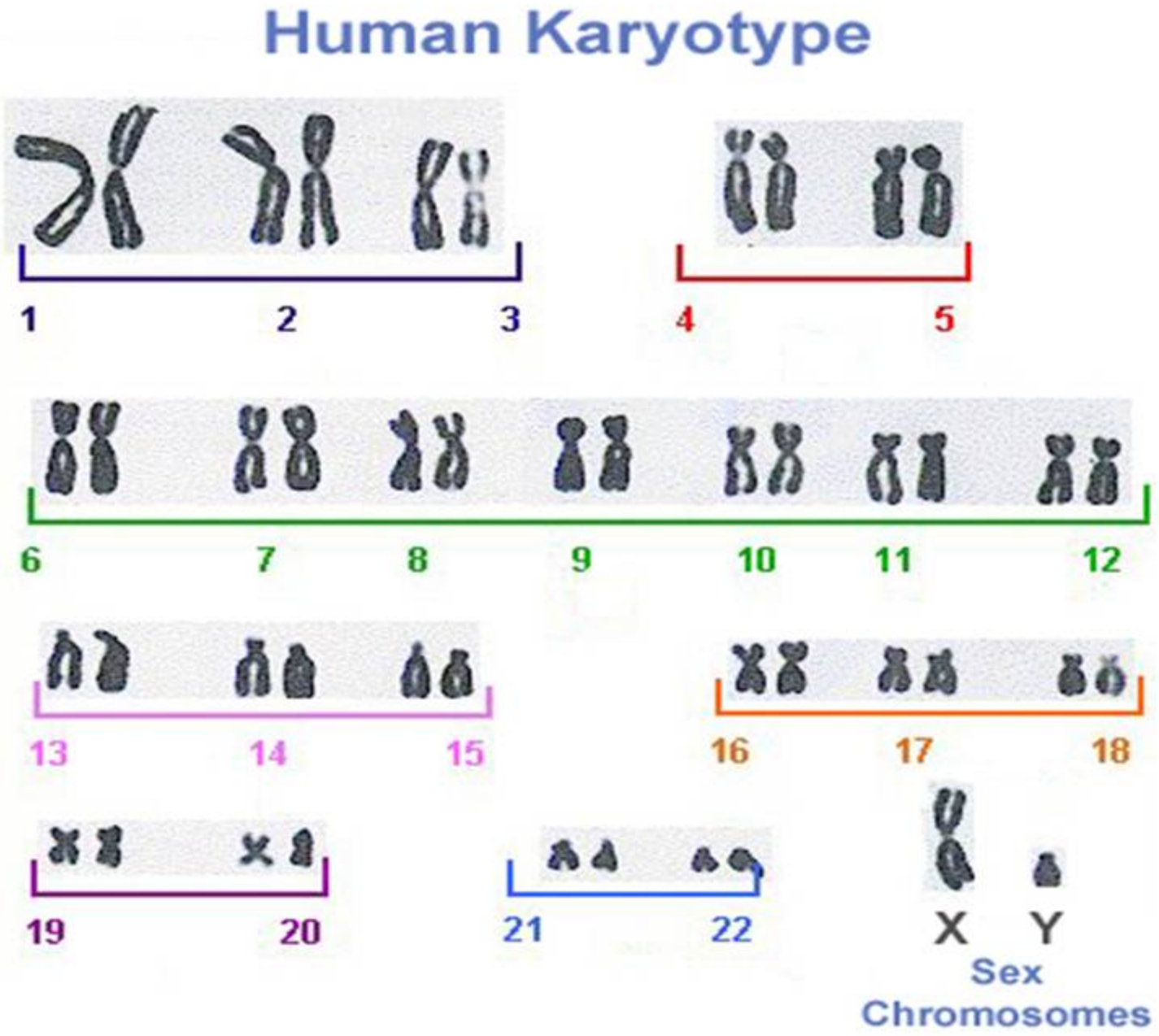
- The Y chromosome in humans is much smaller than the X chromosome, and does not contain the same set of genes.
- In other organisms, such as birds, butterflies and some fish, the males have two identical chromosomes (ZZ), whereas the females have one Z chromosome and one W chromosome.
- As in humans, gender (sex) in ***Drosophila is also determined by XX and XY chromosomes.***

- In this case the X chromosome is rod-shaped, while the Y chromosome is hooked.
- Chromosomes that determine gender are called sex chromosomes; the other chromosomes are known as autosomes.

  In man, there are 23 pairs of chromosomes :

  1 pair of sex chromosomes and 22 pairs of autosomes

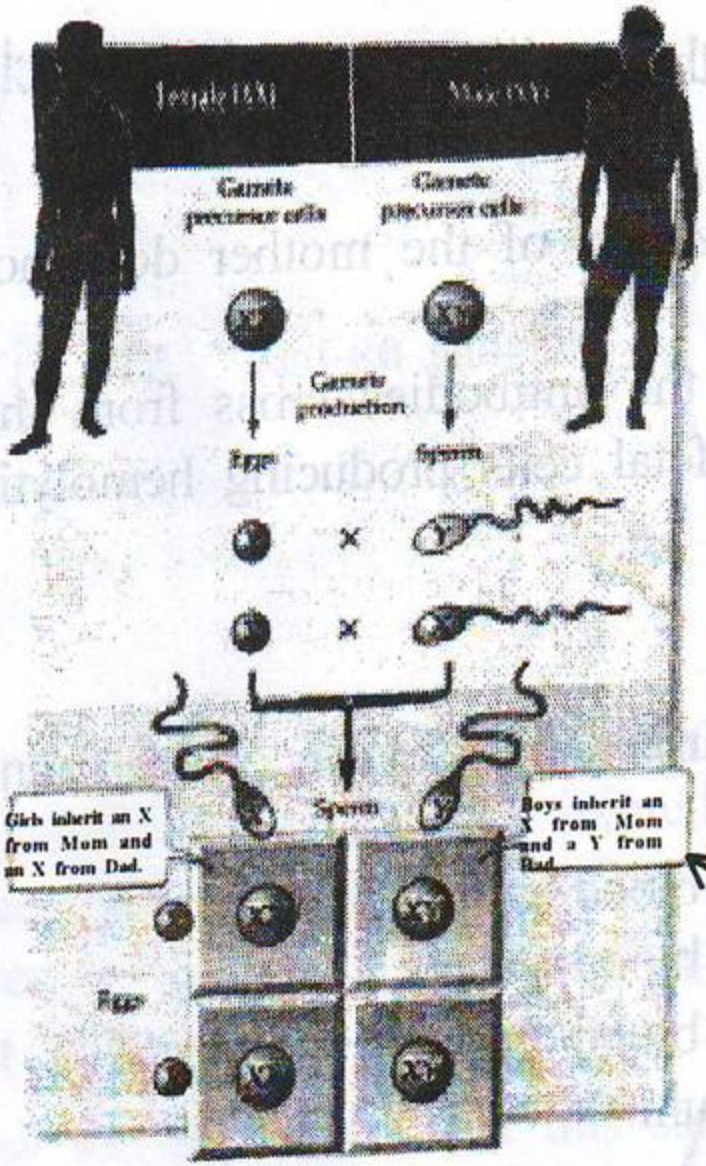
Autosomes and Sex Chromosomes

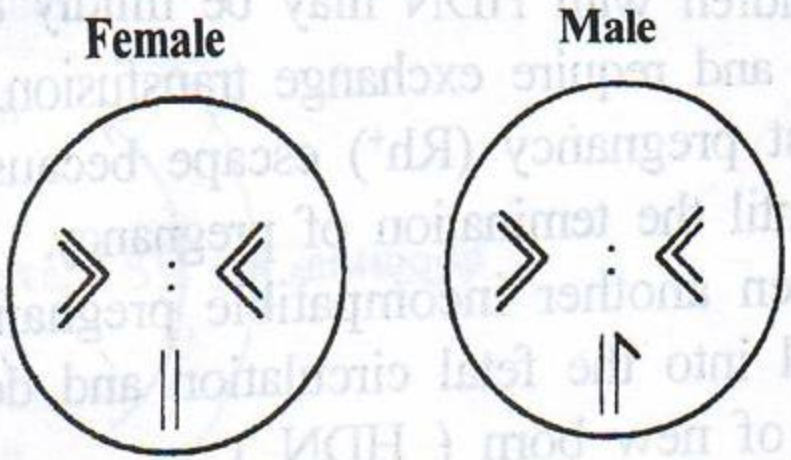


Sex Chromosomes and Sex Determination

- The Y chromosome determines maleness in humans.
- Having only one X chromosome, as both XY males and XO females does not automatically lead to maleness.
- In most respects XO individuals are clearly female.
- On the other hand the Y chromosome produces the male phenotype, no matter how many X chromosomes are present.
- Even the rare XXXY or XXXXY person is male.
- Explicit instructions on the Y chromosome are required to produce the male.

Sex Chromosomes and Sex Determination





Chromosome of *Drosophila melanogaster.*

Fig. 2.6 Sex Determination in Humans, Human fem
have two X chromosomes, while human m
have one X and one Y chromosome.

Female

Autosomes	2 pairs of V – shaped cromosomes
	1 pair of dot – shaped chromosomes
Sex-chromosome	1 pair of rod shaped chromosomes

Male

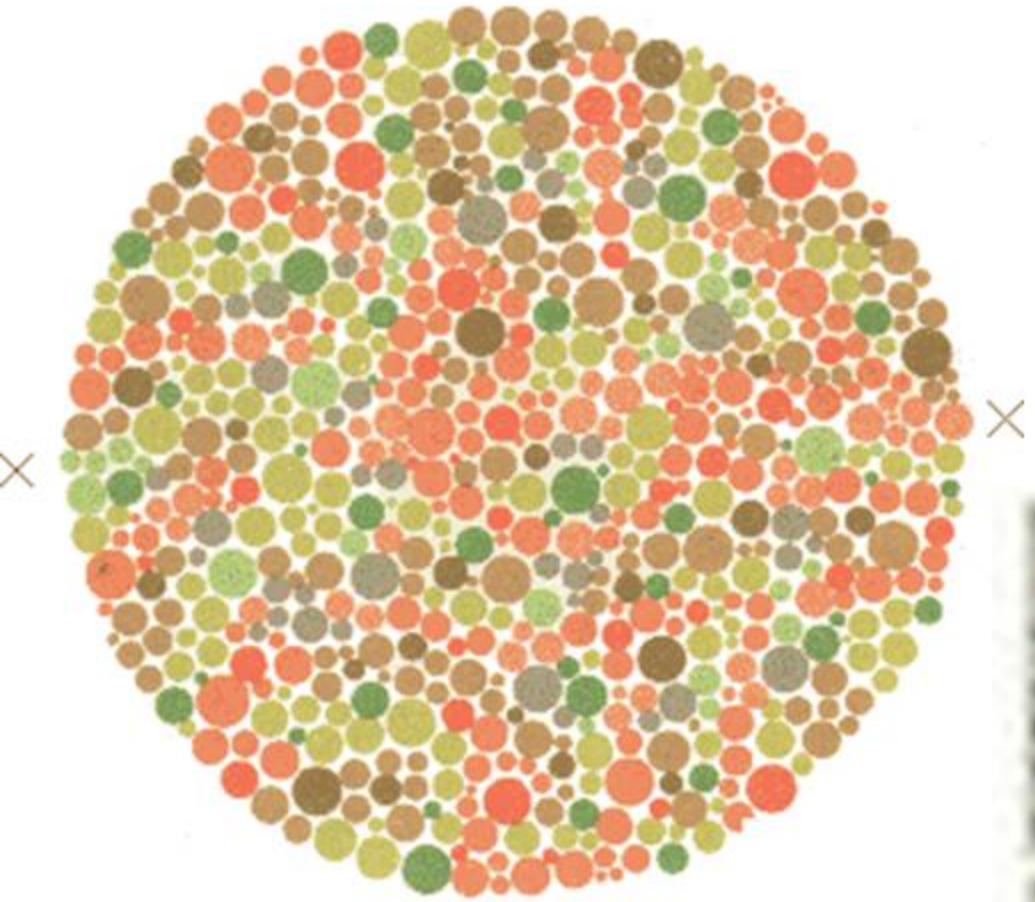
Autosomes	2 paird of V – shaped chromosomes
	1 pair of dot – shaped chromosomes

In *Drosophila,* sex-chromosome only 1 rod-shaped chromosome and the other with a hook. The rod like chromosomes are called X chromosome while the unlike rod with hook on it is called Y. chromosome, Both types are called sex chromosomes. The rest of the chromosomes are called autosomes.

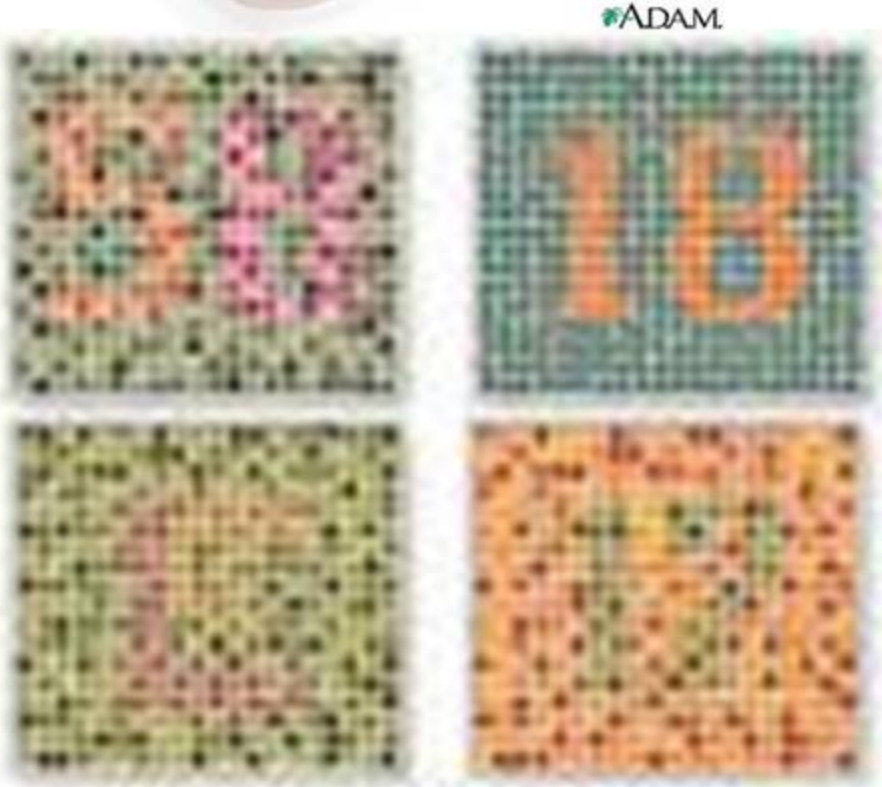
Sex-Linked Genes in Man (Criss cross inheritance)

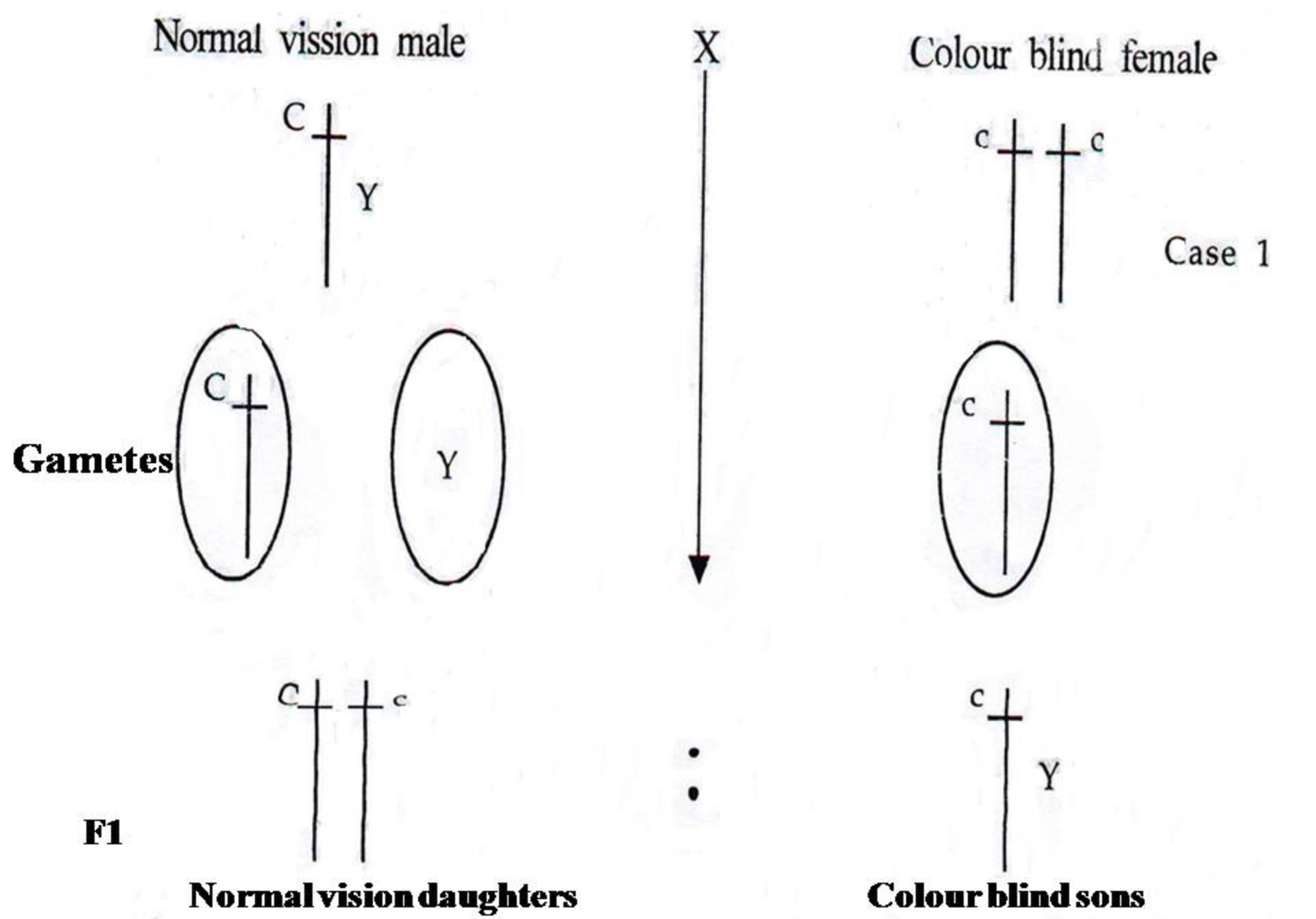
- The commonest sex-linked gene in man is red-green colour blindness.
- This red-green colour blindness is due to a recessive gene which is located on the X chromosome.
- When a colour blind woman is married to a man with normal vision all the sons are colour blind and all daughters have normal vision.

Sex-Linked Genes in Man (Criss cross inheritance)



In male pattern baldness, hair recedes in an "m" shape, the crown bald patch eventually meeting the top points to form a horseshoe shape

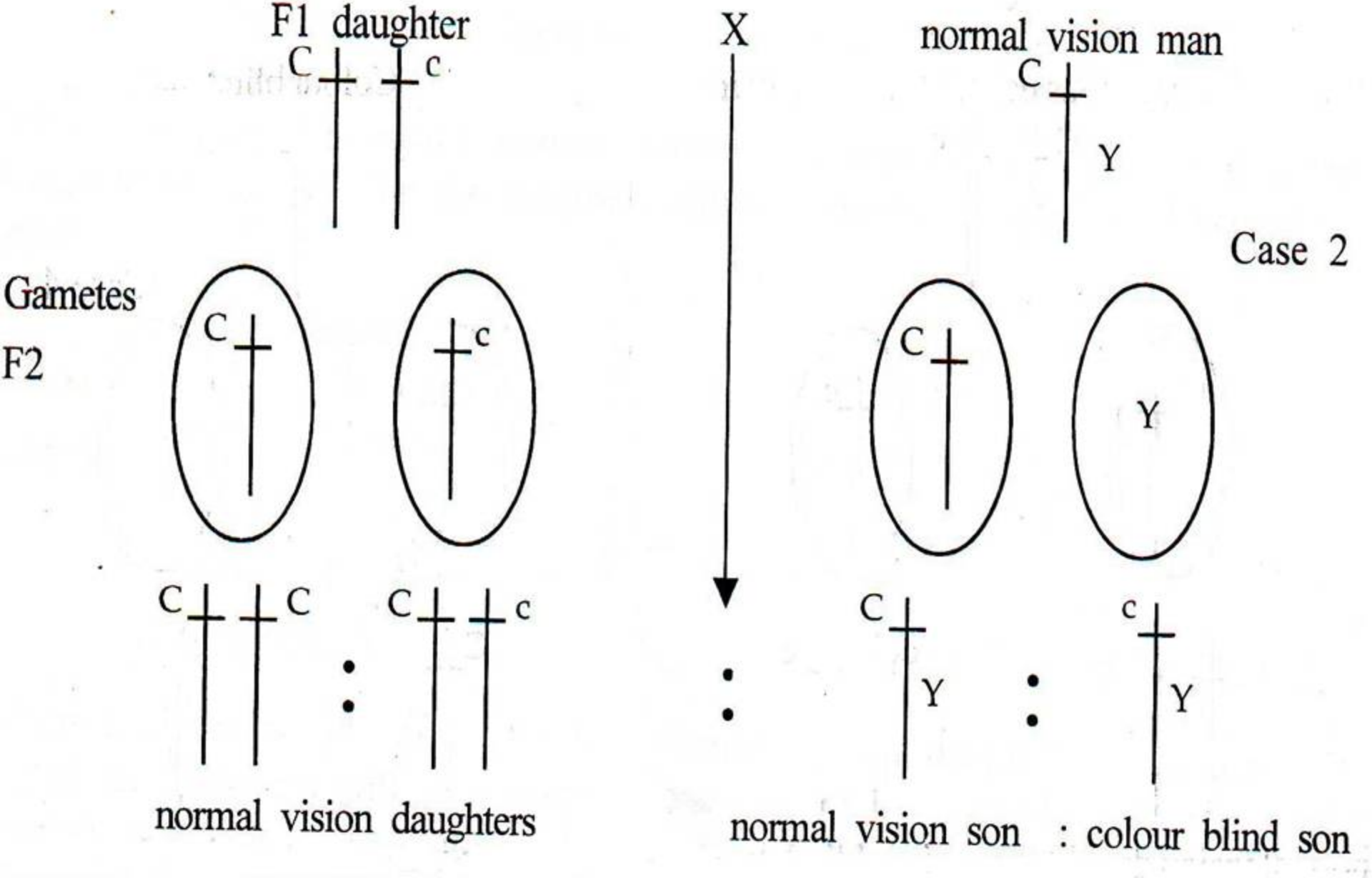



Normal vission male
X
Colour blind female
C
Y
c
c
Case 1
Gametes
C
Y
c
C
c
c
Y
F1
Normal vision daughters
Colour blind sons

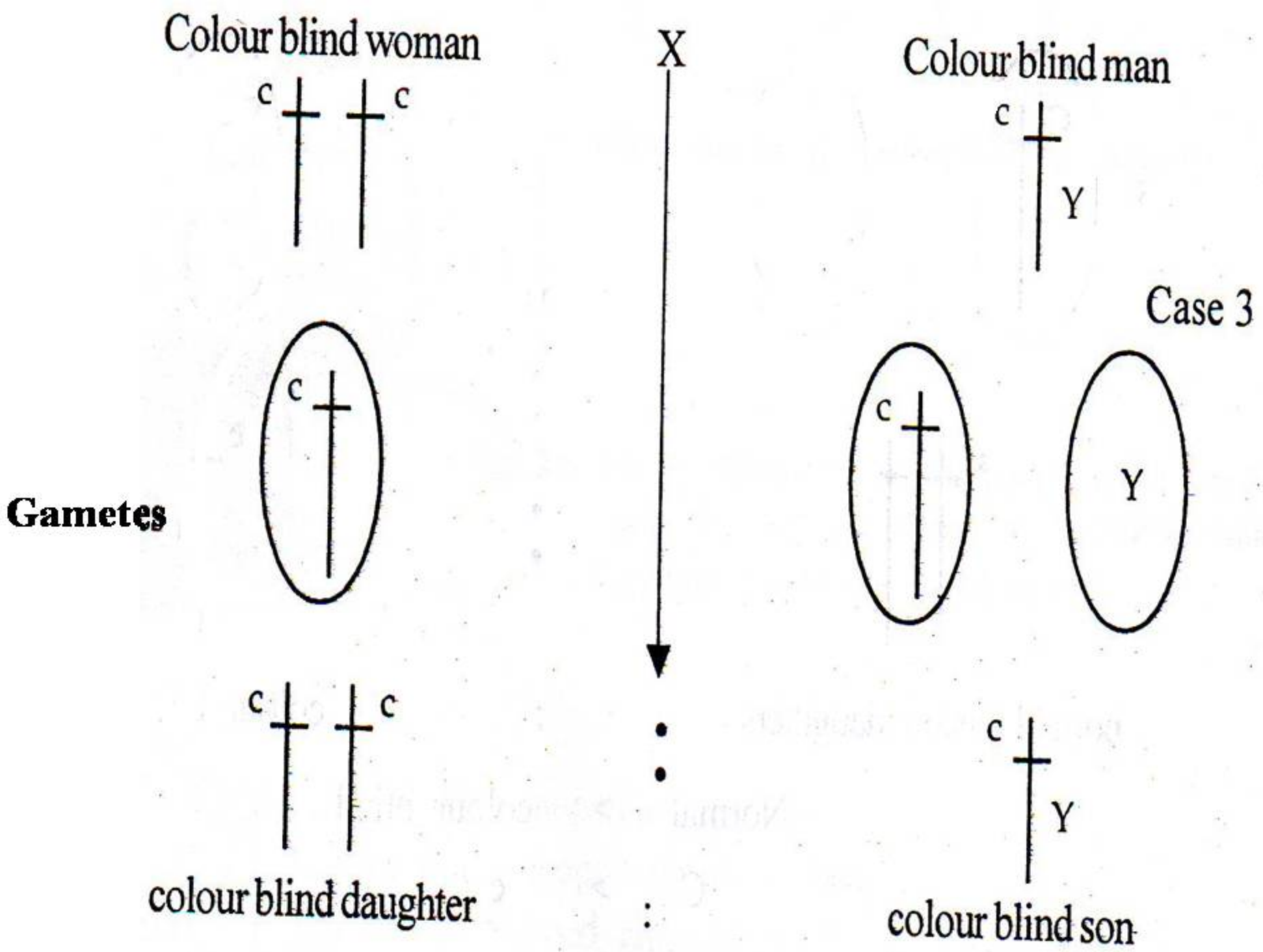
- In the above Case 1 the father transmits his X chromosome to all daughters but none of his sons.
- The mother passes one of her two X chromosomes to each of her children.
- Therefore all the sons are colour blind and the genotypes of the daughters are heterozygous for normal vision.

Normal > colour blind

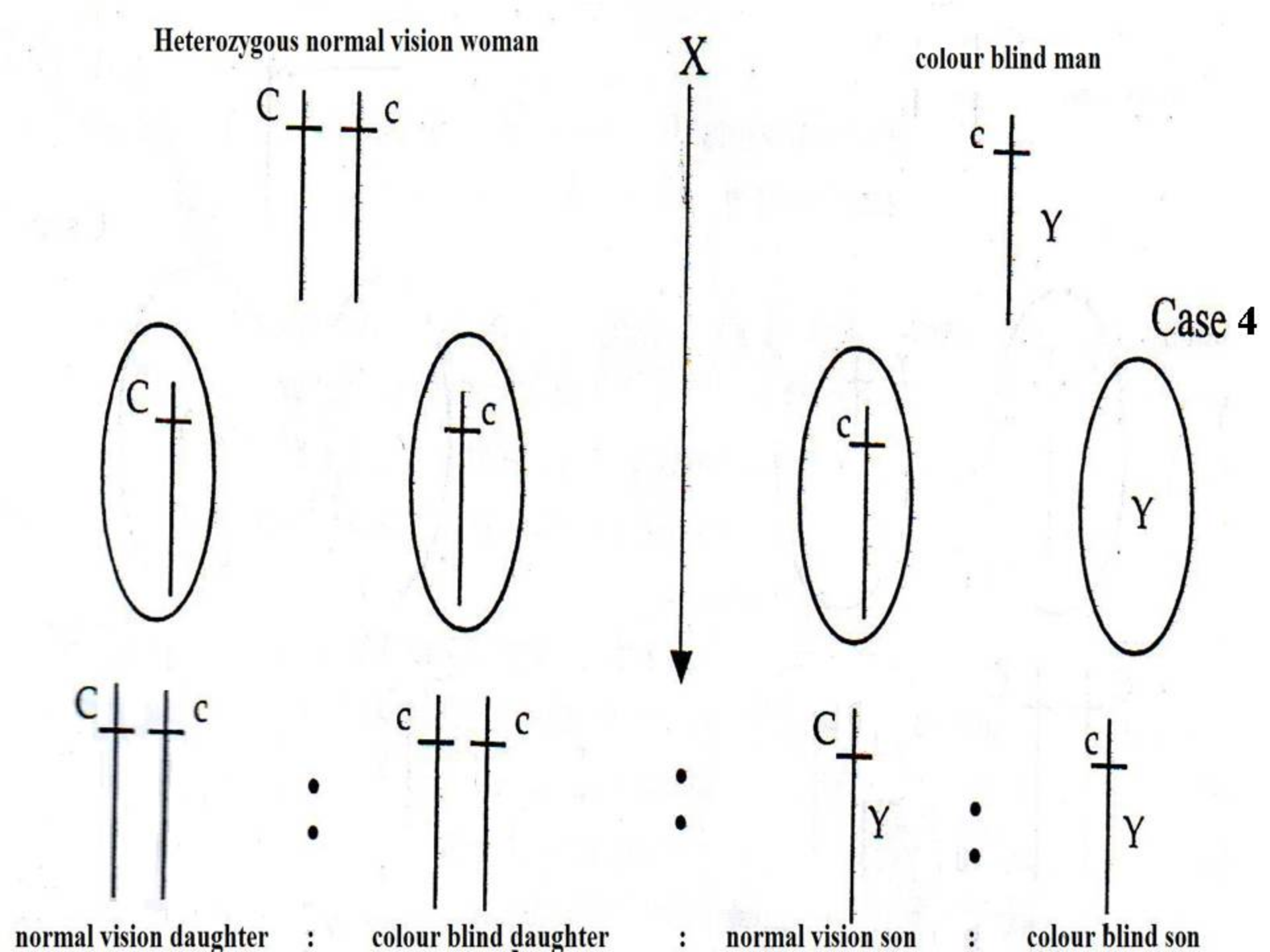
C > c



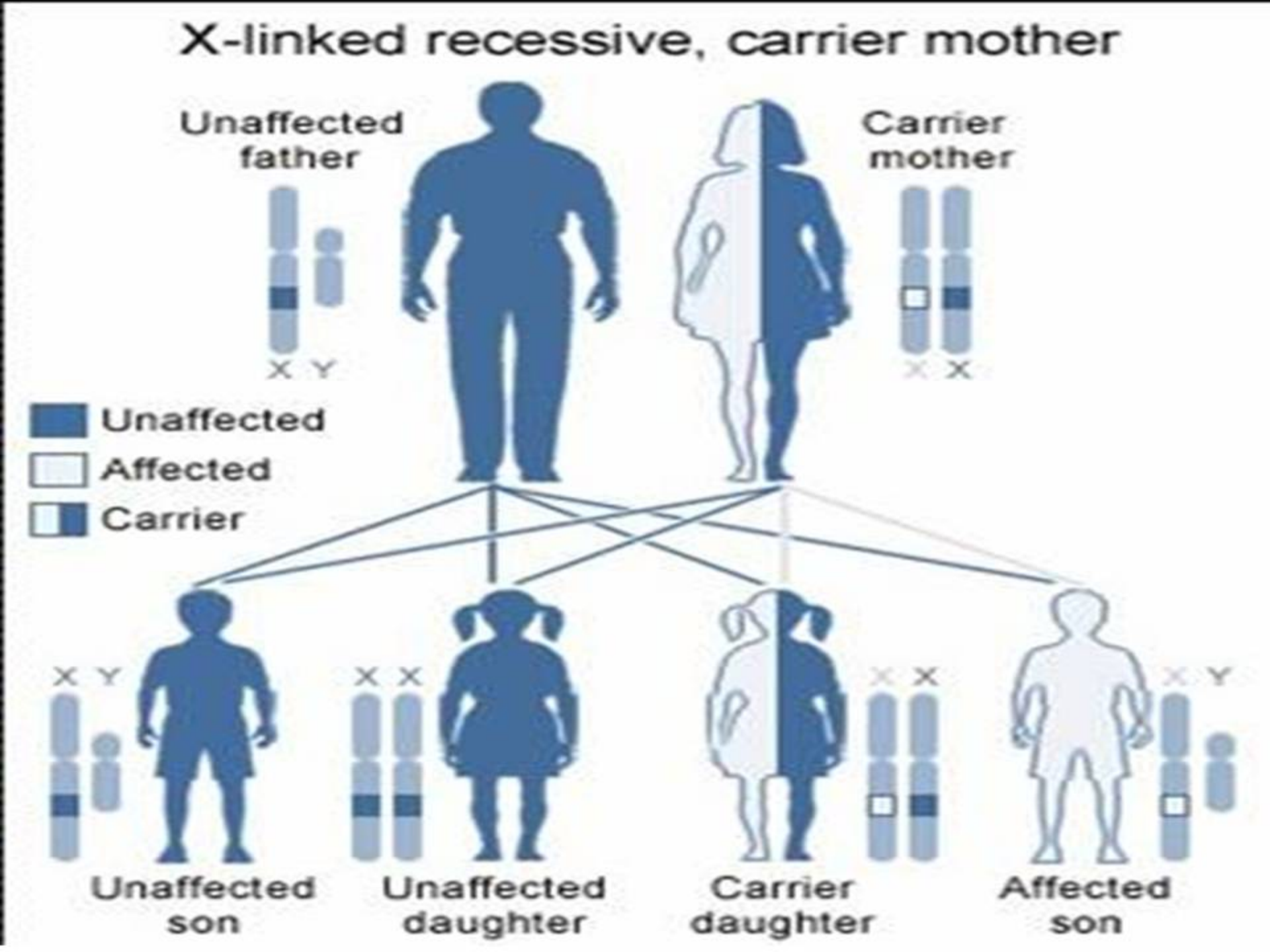
- When the F1 normal vision daughter (heterozygous normal vision) marries a normal vision man, they again produce all normal girl children but among the boys half are normal vision and the other half colour blind.


Colour blind woman
X
Colour blind man
c
c
c
Y
Case 3
Gametes
c
c
Y
c
c
c
Y
colour blind daughter
colour blind son

- A colour blind daughter can be produced only if a colour blind man happens to marry a homozygous colour blind woman or a heterozygous normal vision woman.


Heterozygous normal vision woman
X
colour blind man
C
c
c
Y
Case 4
C
c
c
Y
C
c
c
c
C
Y
c
Y
normal vision daughter : colour blind daughter : normal vision son : colour blind son

- The above experiment (Case 4) shows that colour blindness is due to a recessive gene which is carried in the X chromosome and the chromosome contains no gene for colour blindness.
- Thus colour blindness occurs more often in men than in women because men receive an X chromosome from their mother.


X-linked recessive, carrier mother
Unaffected father
Carrier mother
X Y
X X
Unaffected
Affected
Carrier
X Y
X X
X X
X Y
Unaffected son
Unaffected daughter
Carrier daughter
Affected son

Hemophilia

- Another type of sex-linked gene is hemophilia (Bleeder's disease) in man.
- Hemophilia is due to a recessive gene. It is also a sex-linked gene.
- Hemophilic men produce dughters all of whom are normal but have a hemophilic gene in their X chromosome, obtained from their fathers.

- These women also transmit the hemophilic gene to their sons.
- Thus hemophilia also occurs more often in men than in women.
- Hemophilic daughers and grand daughters can be produced only when heterozygous normal women marry hemophilic men.

Normal gene = H

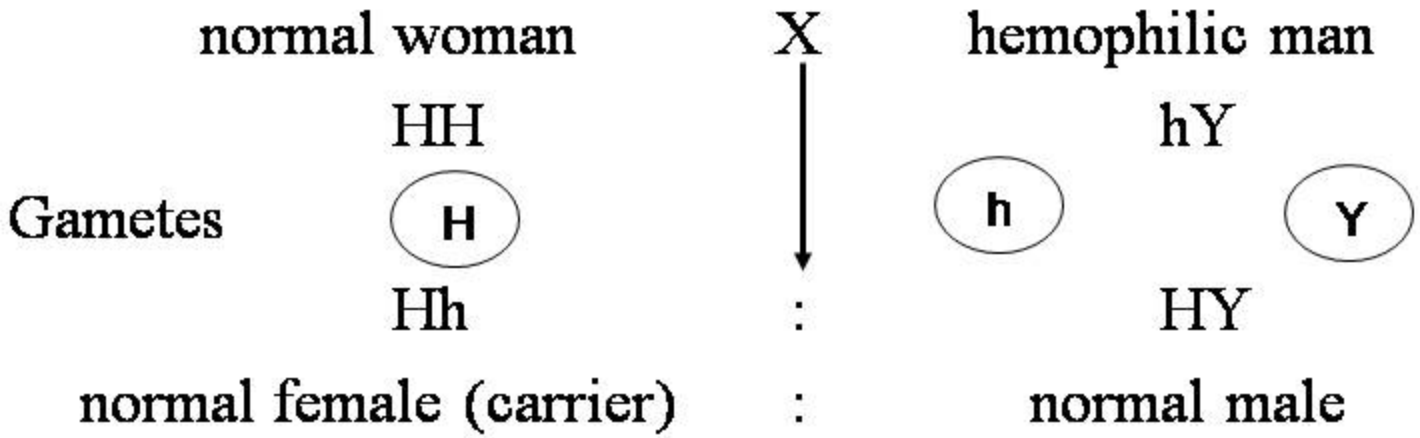
Hemophlia = h

Normal woman = HH or Hh

Normal man = HY

Hemophilic woman = hh

Hemophilic man = hY



- When a homozygous normal woman marries a hemophilic man, all their sons and daughters are normal. But the daughters, although normal are carriers of hemophilic genes.

F1 female Hh x normal man HY

Gametes: H, h | H, Y

HH : Hh : HY : hY

normal female : normal male : hemophilic male

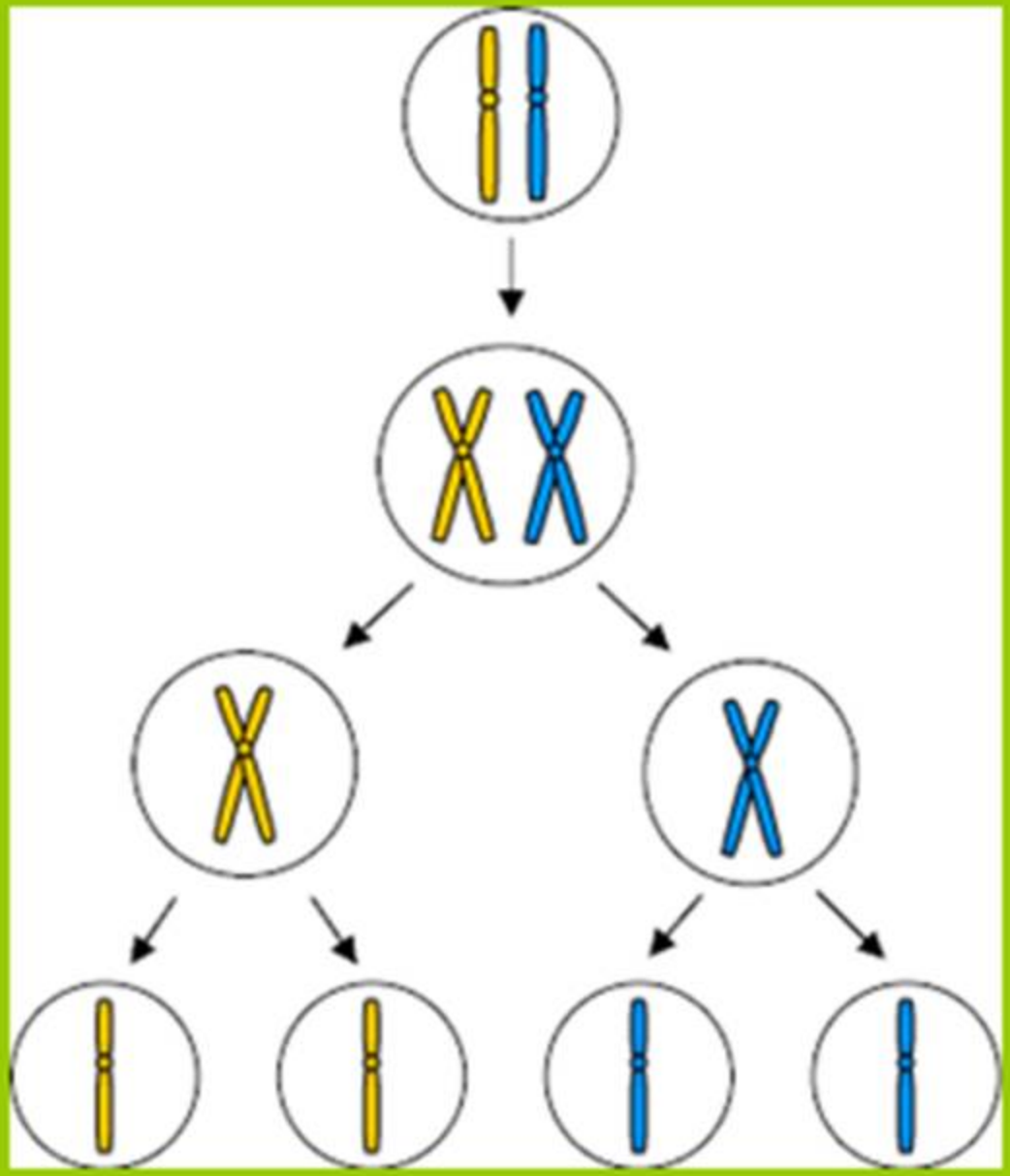
Hh or hh x hY

H, h, h | h, Y

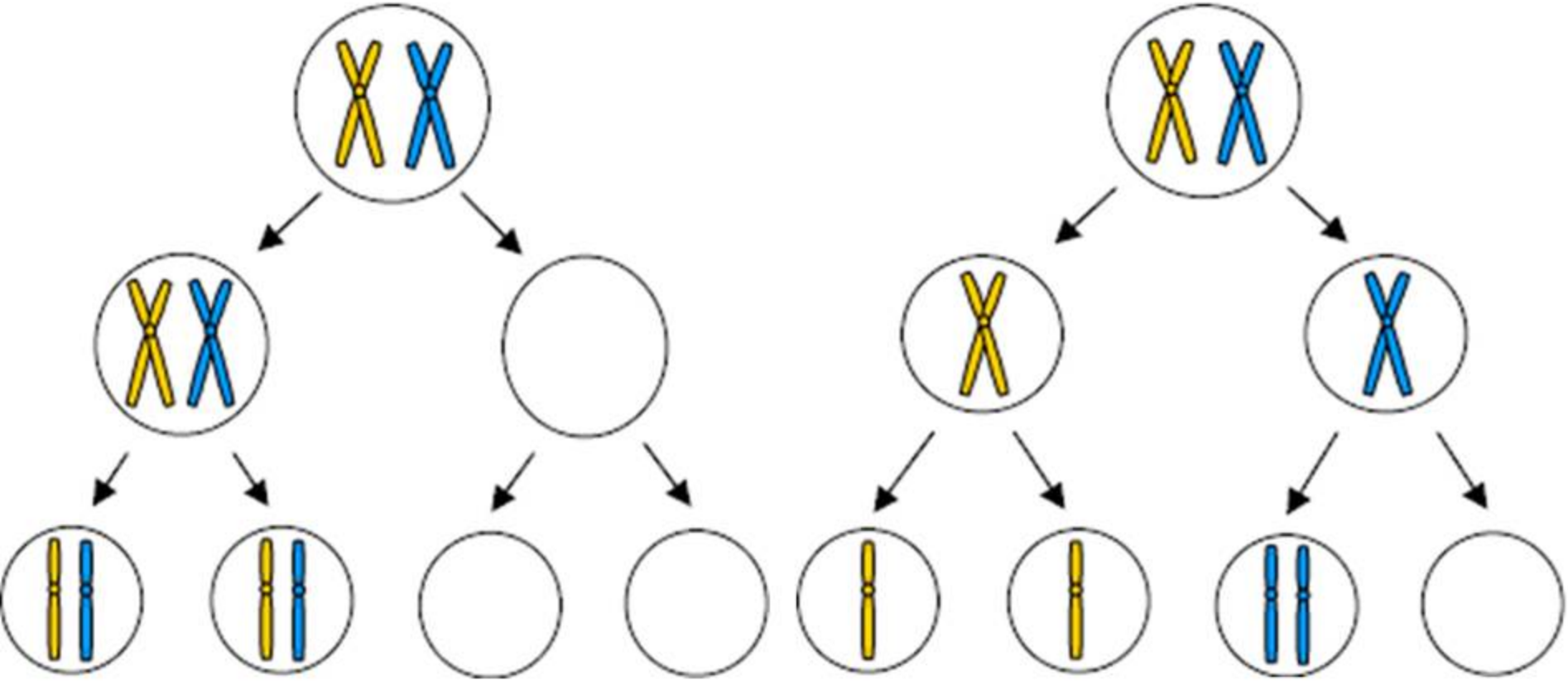
Hh : hh : HY : hY : hh : hY

normal female : normal male

- When a carrier woman marries a normal man, all her daughters are normal but 1/2 of the daughters will be carriers.
- In the case of sons, the ratio of normal-hemophilic condition is in the ratio of 1 : 1.
- Hemophilic daughters are produced when the mother is a carrier or hemophilic and the father is hemophilic. Hemophilic women are very rare.

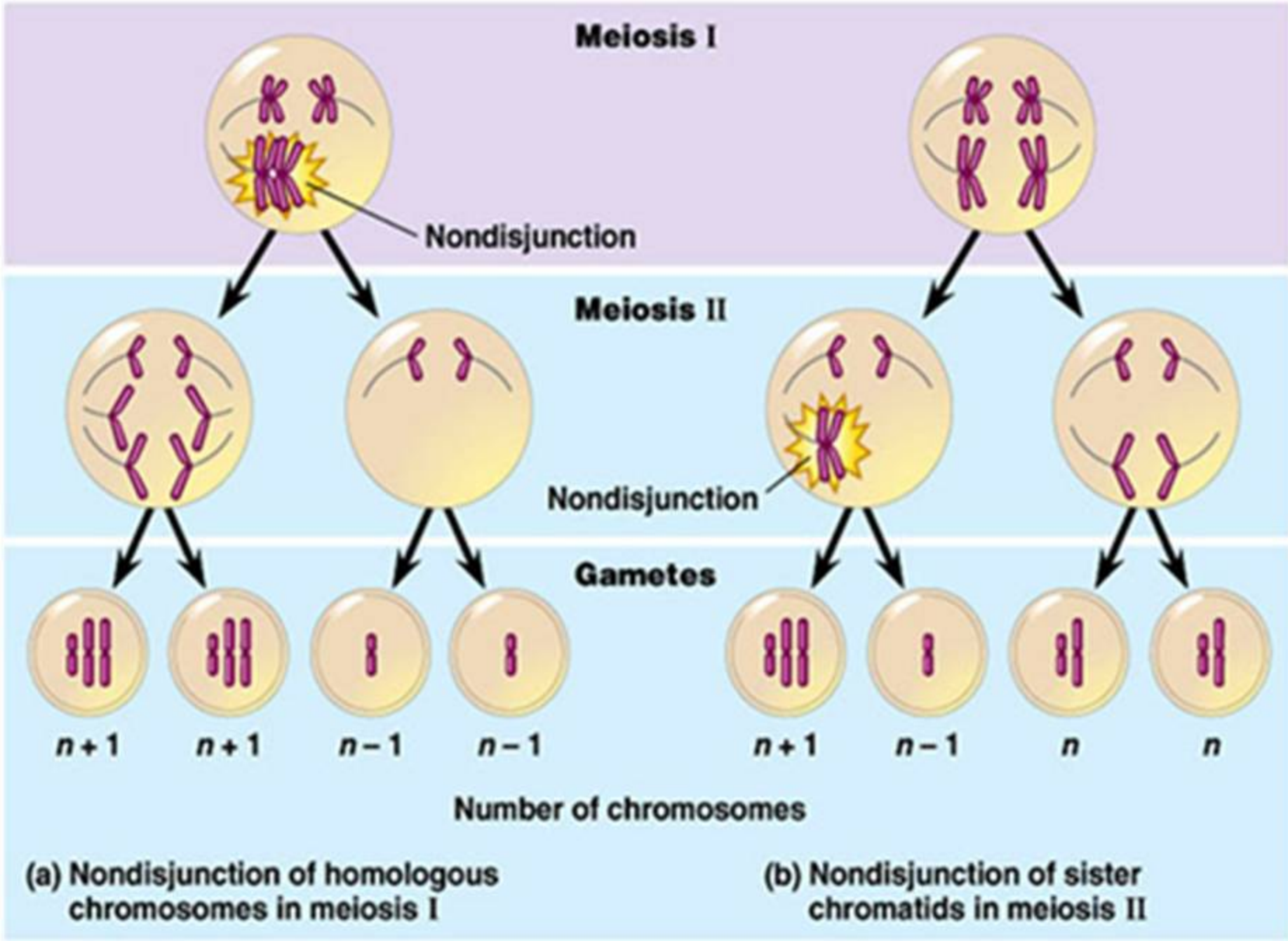


Normal meiotic division



Non- disjunction at meiosis 1

Non- disjunction at meiosis 2



Nondisjunction

- During meiosis, homogolous chromosome pair, then separate.
- One double-stranded (Replicated) chromosome migrate to each pole, and the other chromosome migrates to the other pole.
- If a homologous pair fails to separate during meiosis, however, one of the new cells will end up with and extra chromosome.

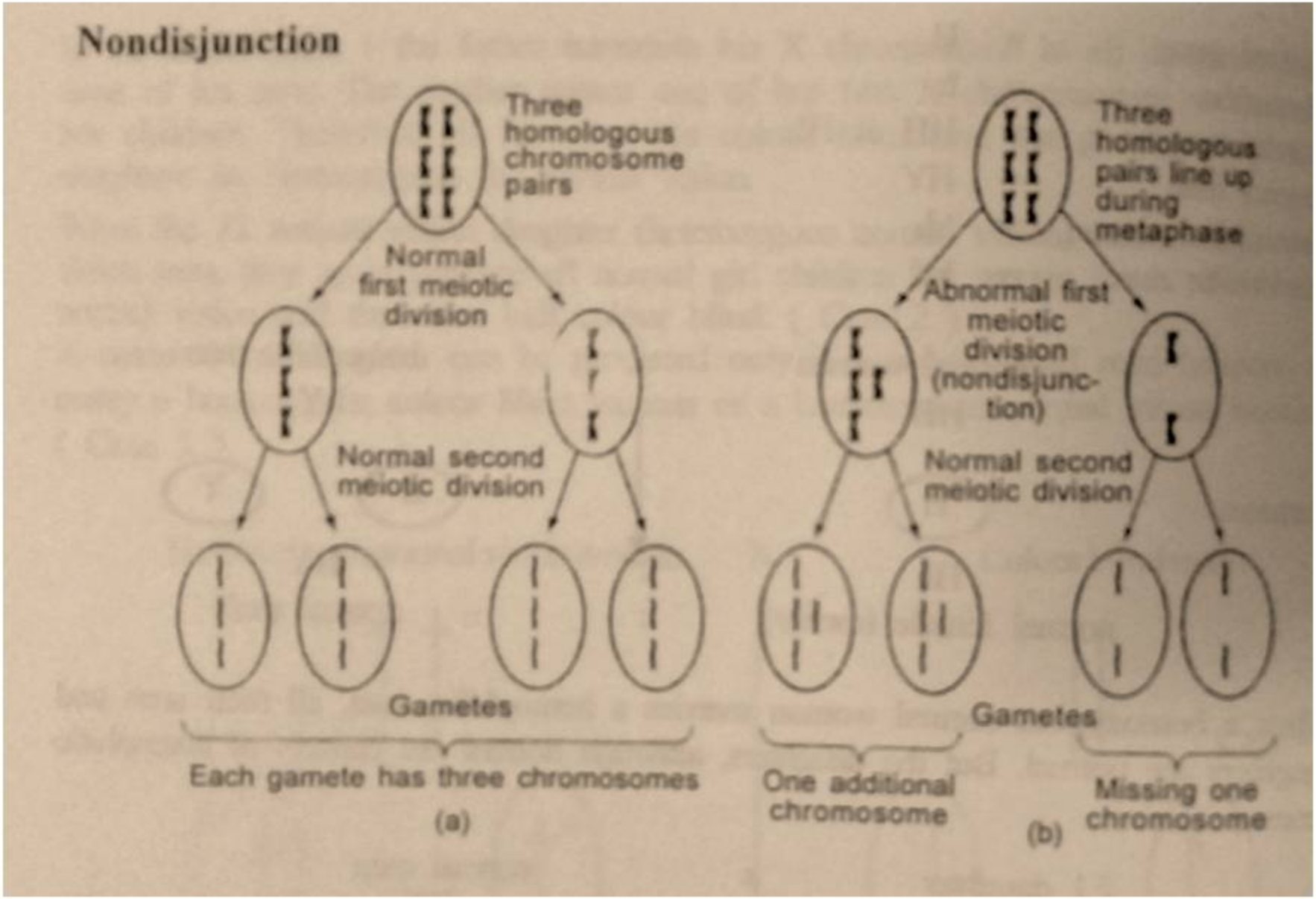
- The failure of homologous chromosome to separate is called nondisjunction.
- Abnormal chromosome numbers generally result from a failure of chromosomes to separate during gamete formation (meiosis).
- Nondisjunction can also occur in the second meiotic division.
- In the division (of Humans) the 23 double-stranded (replicated) chromosome split apart, with one chromatid going to each doughter cell.

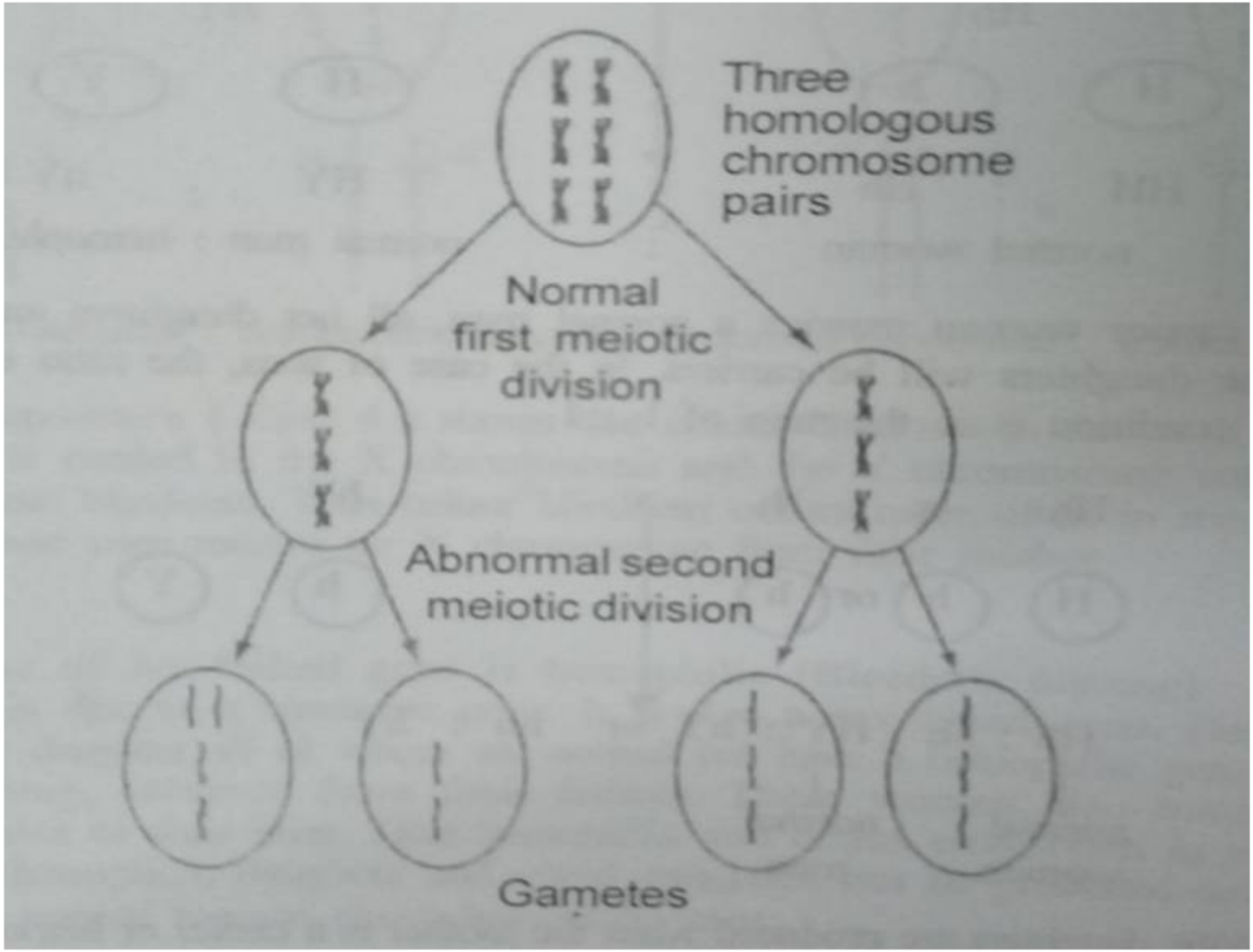
- If a chromosome fails to separate into its two chromatids, the result is the same as nondisjunction in meiosis I a daughter cell with an extra chromosome.
- When a gamete with an extra chromosome unites with a normal gamete, the resulting zygote will contain 47 chromosomes.
- The zygote may be able to divide successfully by mitosis, producing an embryo all of the cells of which have an additional chromosome.

- Thus, instead of the normal 23 chromosomes pairs, each cell in the embryo contains 22 pairs and one triplet.
- This condition is called trisomy (literally "three bodies").
- One of the most common trisomes is Down syndrome, or trisomy 21.
- Gametes with a missing chromosome can unite with normal gametes, producing individuals with 45 chromosomes, 22 chromosomes pairs and a chromosome singlet.

- This condition is called monosomy.
- Monosomy and trisomy are collectively referred to as aneuploidy.
- Aneuploidy (literally "not a true number") has profound effects on human reproduction and development.
- Surprisingly, one of every two conception is aneuploid.

- Most aneuploid embryos and fetuses die in uterus and aneuploidy is believed to be responsible for 70% of all early embryonic deaths and 30% of all fetal dealths.
- Aneuploidy is also associated with an increased miscarriage rate in older mothers.


Nondisjunction
Three homologous chromosome pairs
Normal first meiotic division
Normal second meiotic division
Gametes
Each gamete has three chromosomes
(a)
Three homologous pairs line up during metaphase
Abnormal first meiotic division (nondisjunction)
Normal second meiotic division
Gametes
One additional chromosome
Missing one chromosome
(b)


Three homologous chromosome pairs
Normal first meiotic division
Abnormal second meiotic division
Gametes

Primary Nondisjunction

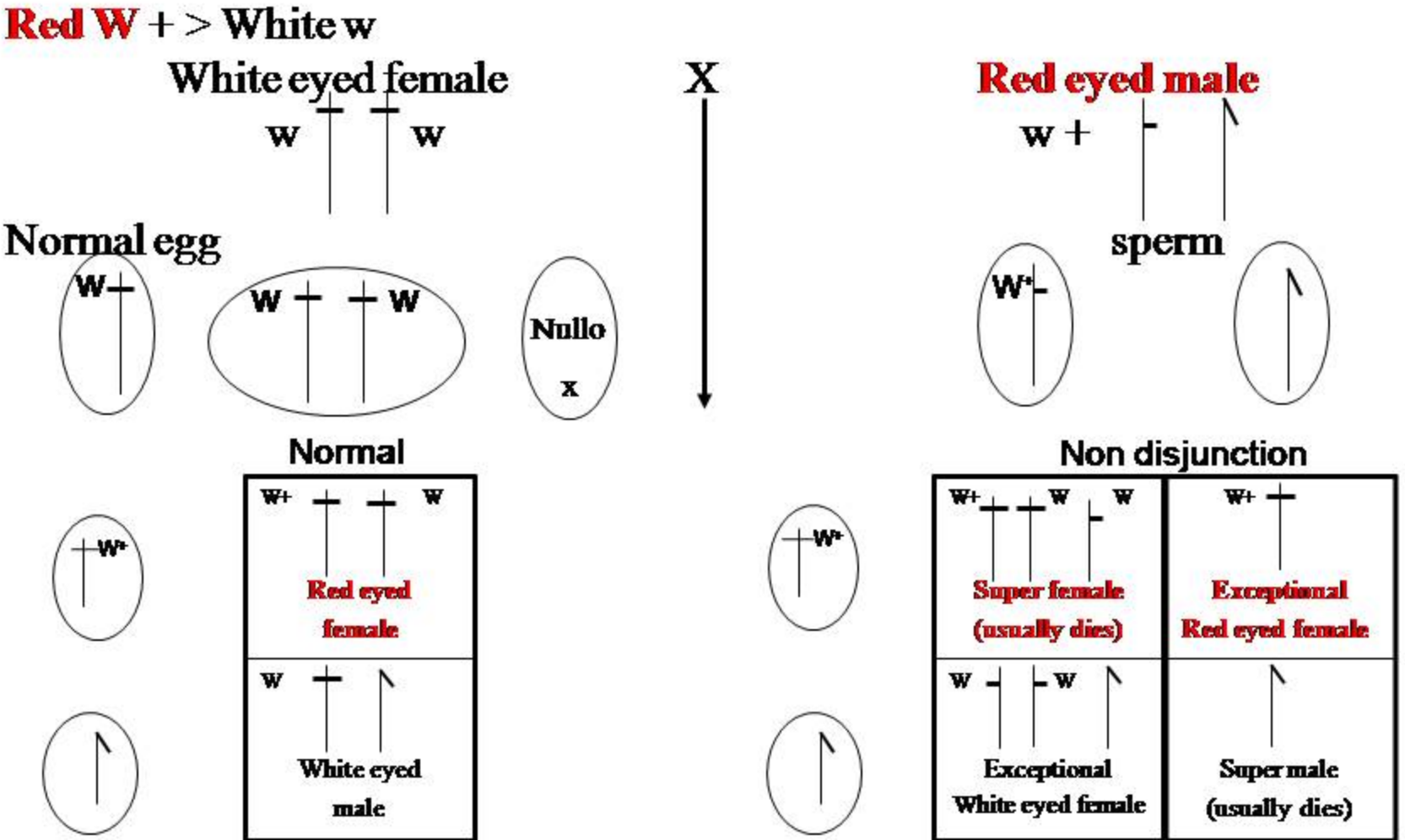
- The determination of sex chromosome was discovered since 1900.
- But there was still puzzled that Y chromosome was important for the identification of male.
- This difficulty was proved cytologically by Bridges with Drosophila as follows :
- This result was explained by Bridges as follows.

- The two maternal chromosomes fail to disjoin at the meiotic division as they should normally do.
- Therefore the white eyed female produces two special types of eggs which are called as non - disjunctional gametes.
- One type contains two X chromosomes and the other one no X chronosome as shown in the above figure.
- These eggs will be fertilized by normal sperms of red eyed male producing two type of females and males. Of the two females the super female consists of three X chromosomes but it usually dies.

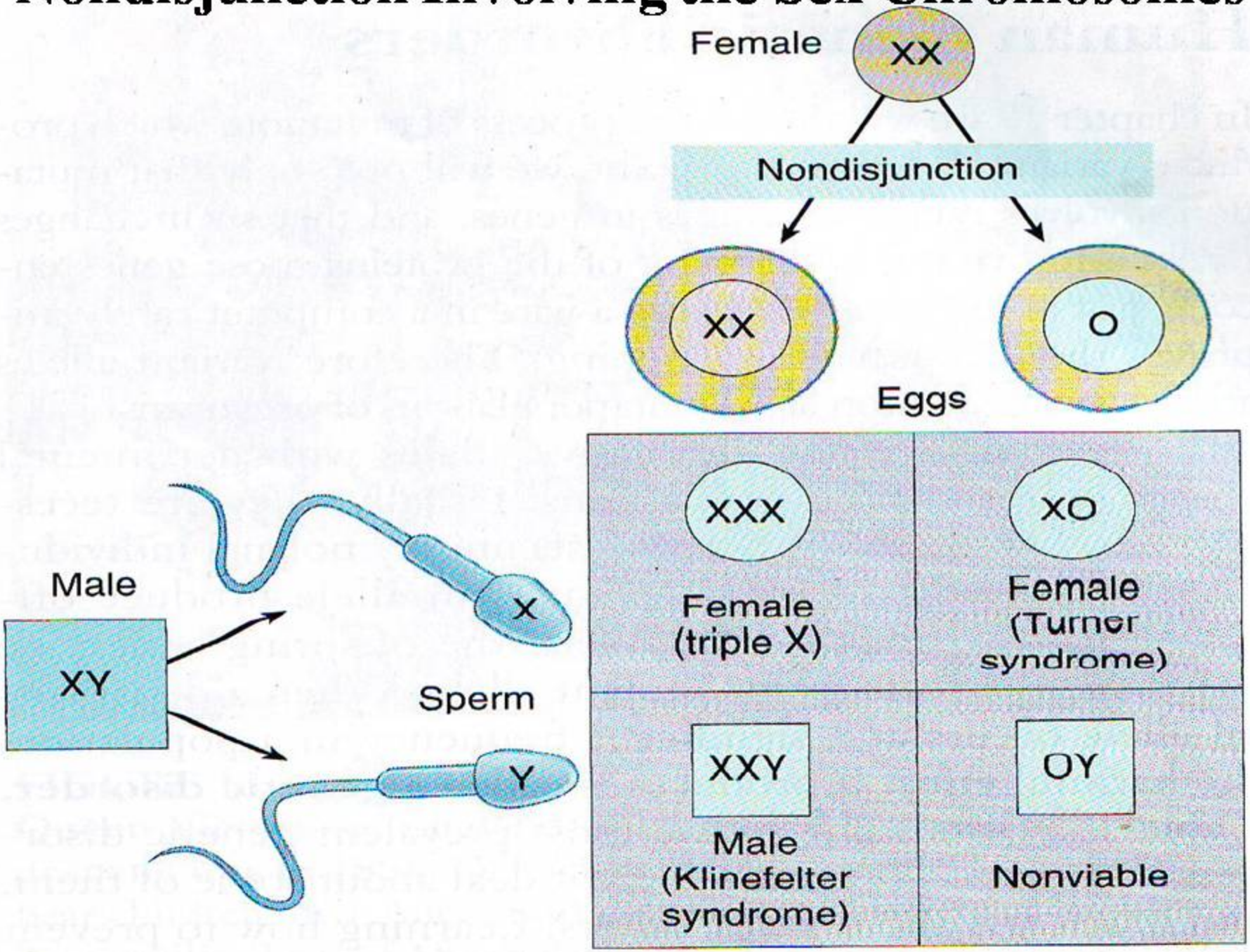
- The other exceptional one consists of two X chromosomes and one Y chromosome which is normally present only in males.
- But it is fertile and female in appearance.
- In the case of two types of male offsprings one type (super male) consists of only Y chromosome but it usually dies.
- The other one (exceptional male) consists of only one X chromosome but it is also feritle

Primary Nondisjunction

The determination of sex chromosome was discovered since 1900. But there was still puzzled that Y chromosome was important for the identification of male. This difficulty was proved cytologically by Bridges with Drosophila as follows:



Nondisjunction Involving the Sex Chromosomes



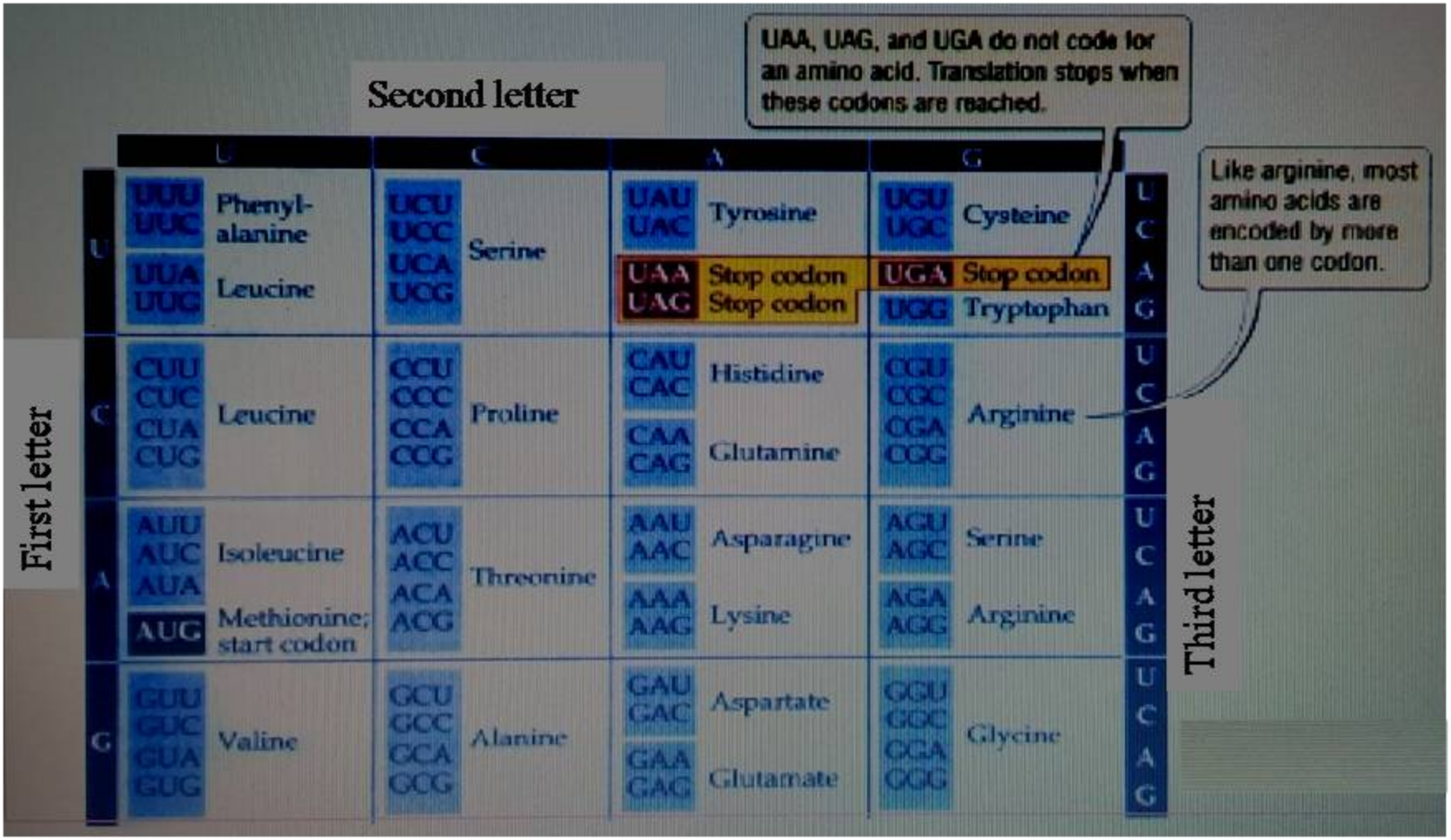
The Genetic Code

- Since there are four different bases in DNA and RNA, and 20 different amino acids in proteins, the bases cannot serve as a one to one code for amino acids.
- If a sequence of two bases codes for an amino acid, there would be $4^2 = 16$ possible combinations of bases.
- This isn't enough either.

- Three bases per amino acid, however, gives $4^3 = 64$ possible combinations, which is more than enough.
- Biologists hypothesized that the genetic code must be triplet : Three bases specify one amino acid.
- In 1961, Francis Crick and three coworkers demonstrated that this hypotheis is correct.

The Genetic Code

First letter	Second letter: U	Second letter: C	Second letter: A	Second letter: G	Third letter
U	UUU, UUC: Phe UUA, UUG: Leu	UCU, UCC, UCA, UCG: Ser	UAU, UAC: Tyr UAA: Stop UAG: Stop	UGU, UGC: Cys UGA: Stop UGG: Trp	U C A G
C	CUU, CUC, CUA, CUG: Leu	CCU, CCC, CCA, CCG: Pro	CAU, CAC: His CAA, CAG: Gln	CGU, CGC, CGA, CGG: Arg	U C A G
A	AUU, AUC, AUA: Ile AUG: Met	ACU, ACC, ACA, ACG: Thr	AAU, AAC: Asn AAA, AAG: Lys	AGU, AGC: Ser AGA, AGG: Arg	U C A G
G	GUU, GUC, GUA, GUG: Val	GCU, GCC, GCA, GCG: Ala	GAU, GAC: Asp GAA, GAG: Glu	GGU, GGC, GGA, GGG: Gly	U C A G


UAA, UAG, and UGA do not code for an amino acid. Translation stops when these codons are reached.
Like arginine, most amino acids are encoded by more than one codon.
Second letter
First letter
Third letter
U
C
A
G
UUU UUC Phenyl-alanine
UUA UUG Leucine
UCU UCC UCA UCG Serine
UAU UAC Tyrosine
UAA Stop codon
UAG Stop codon
UGU UGC Cysteine
UGA Stop codon
UGG Tryptophan
CUU CUC CUA CUG Leucine
CCU CCC CCA CCG Proline
CAU CAC Histidine
CAA CAG Glutamine
CGU CGC CGA CGG Arginine
AUU AUC AUA Isoleucine
AUG Methionine; start codon
ACU ACC ACA ACG Threonine
AAU AAC Asparagine
AAA AAG Lysine
AGU AGC Serine
AGA AGG Arginine
GUU GUC GUA GUG Valine
GCU GCC GCA GCG Alanine
GAU GAC Aspartate
GAA GAG Glutamate
GGU GGC GGA GGG Glycine

Mutation

- A mutation is an inheritable change in a cell.
- The nature of the DNA, or its quantity is changed.

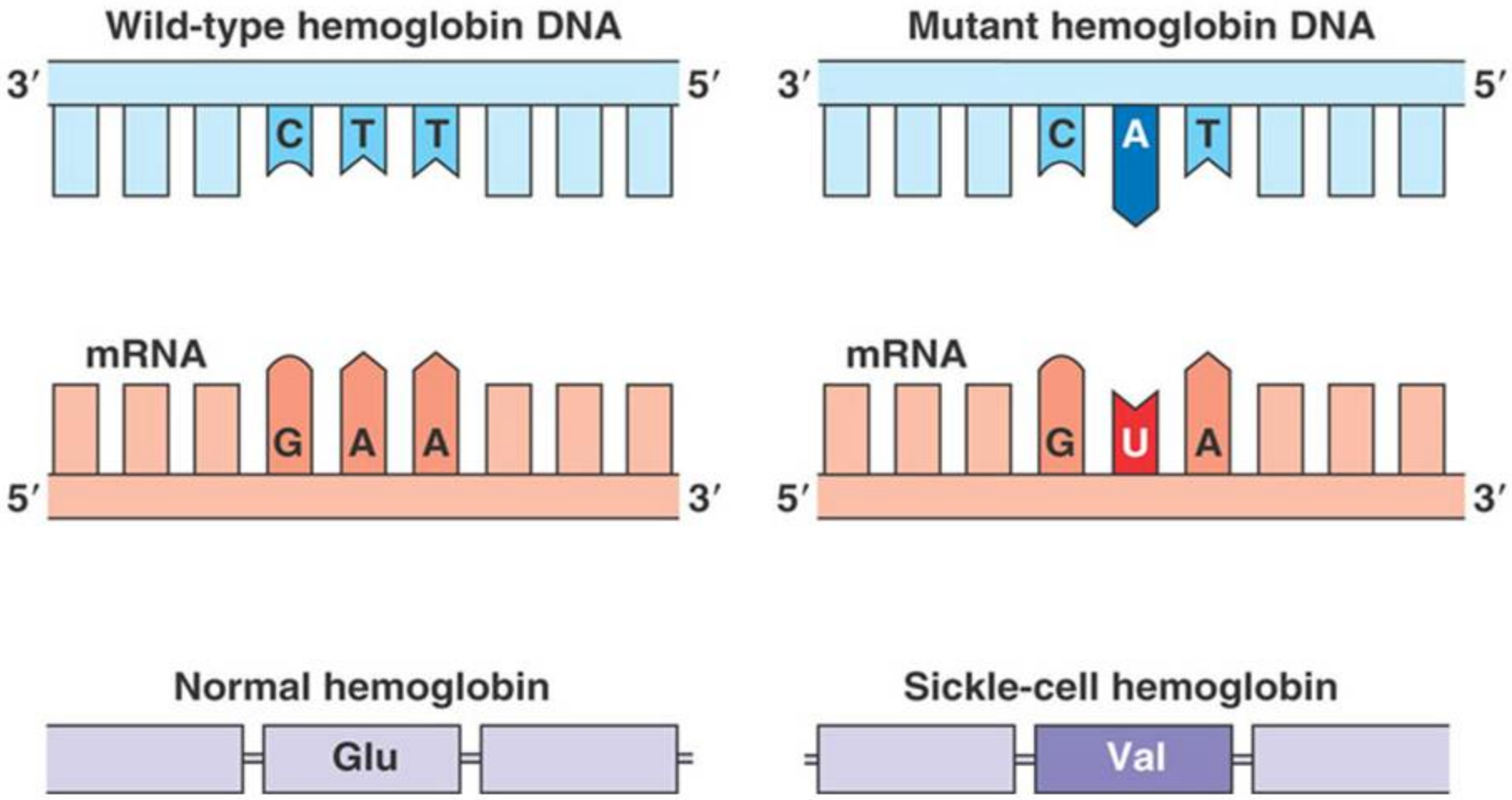
1. Point Mutation

- A point mutation is caused by the substitution, insertion, or deletion of a single base pair, Depending on the nucleotide that is replaced, the effect may or may not be expressed.
- Sickle-cell anemia is caused by mutation of a single base.

Mutation

A mutation is an inheritable change in a cell. The nature of the DNA, or its quantity is changed.

1. Point Mutation

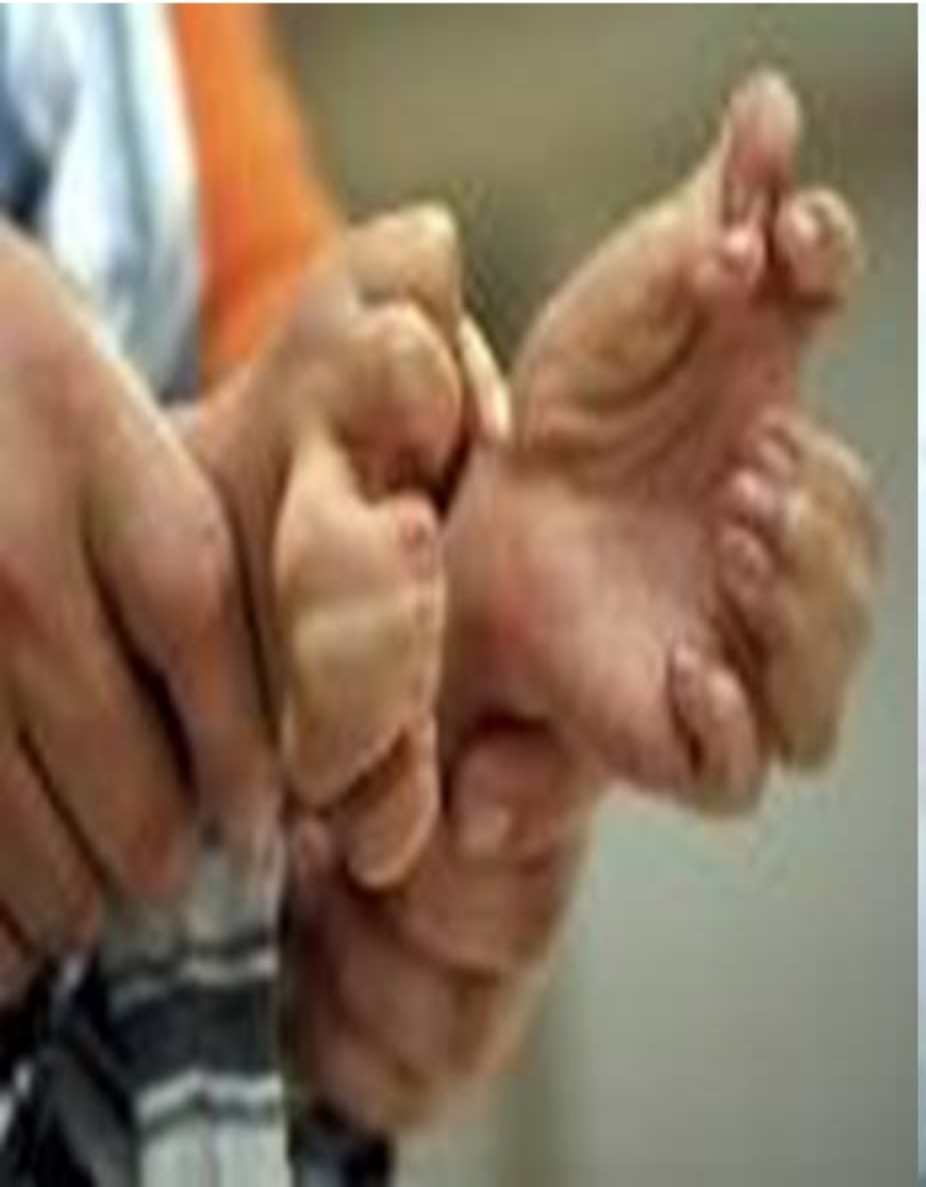


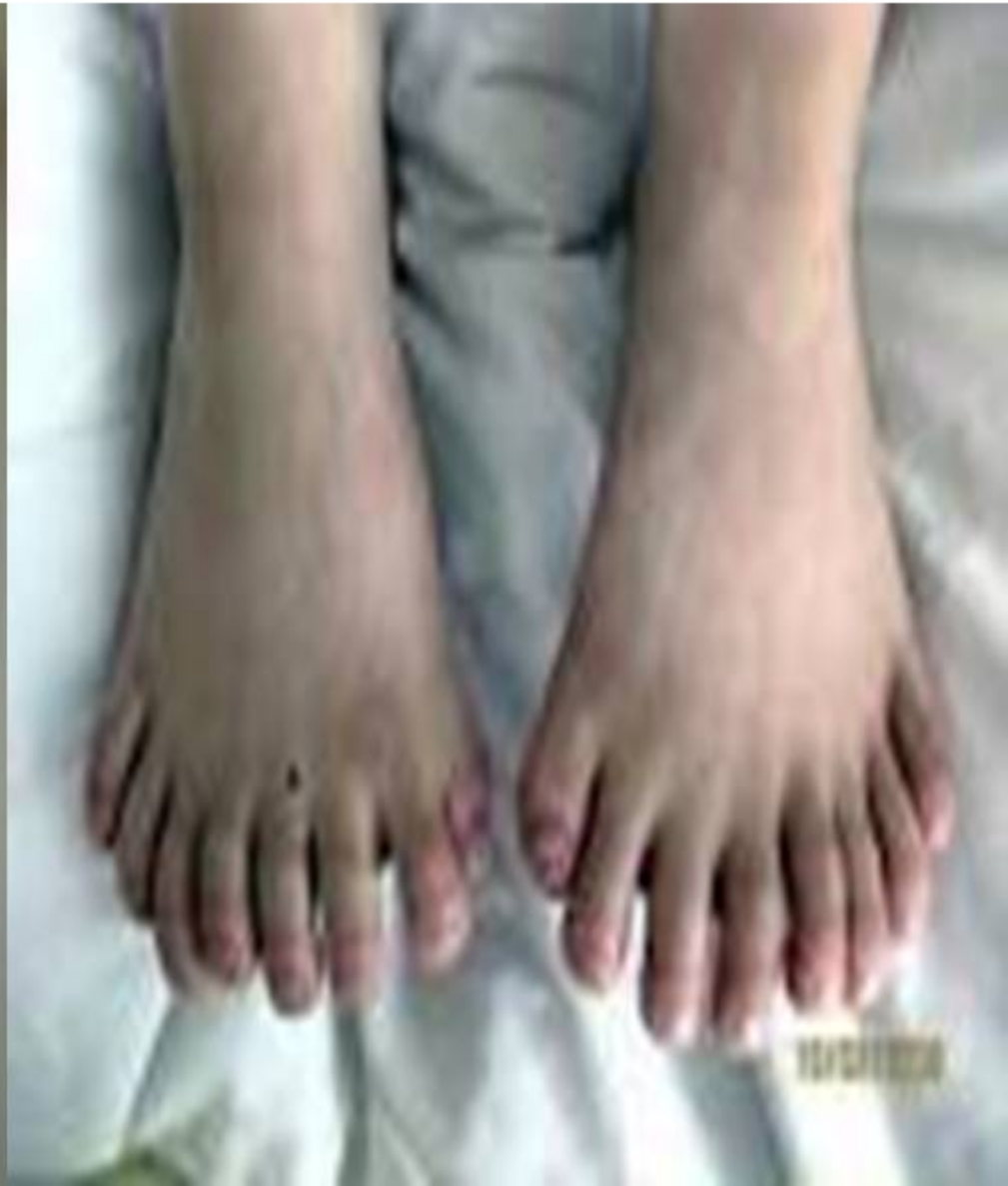
2. Gene Mutaion

- Insertions or deletions of a series of bases into or from the DNA sequence can have drastic effects on a gene.
- A mutation in a gene can alter the sequence of amino acids in the gene's protein product, and this, can disable or otherwise alter the function of the protein.

2. Gene Mutation

GENE MUTATION



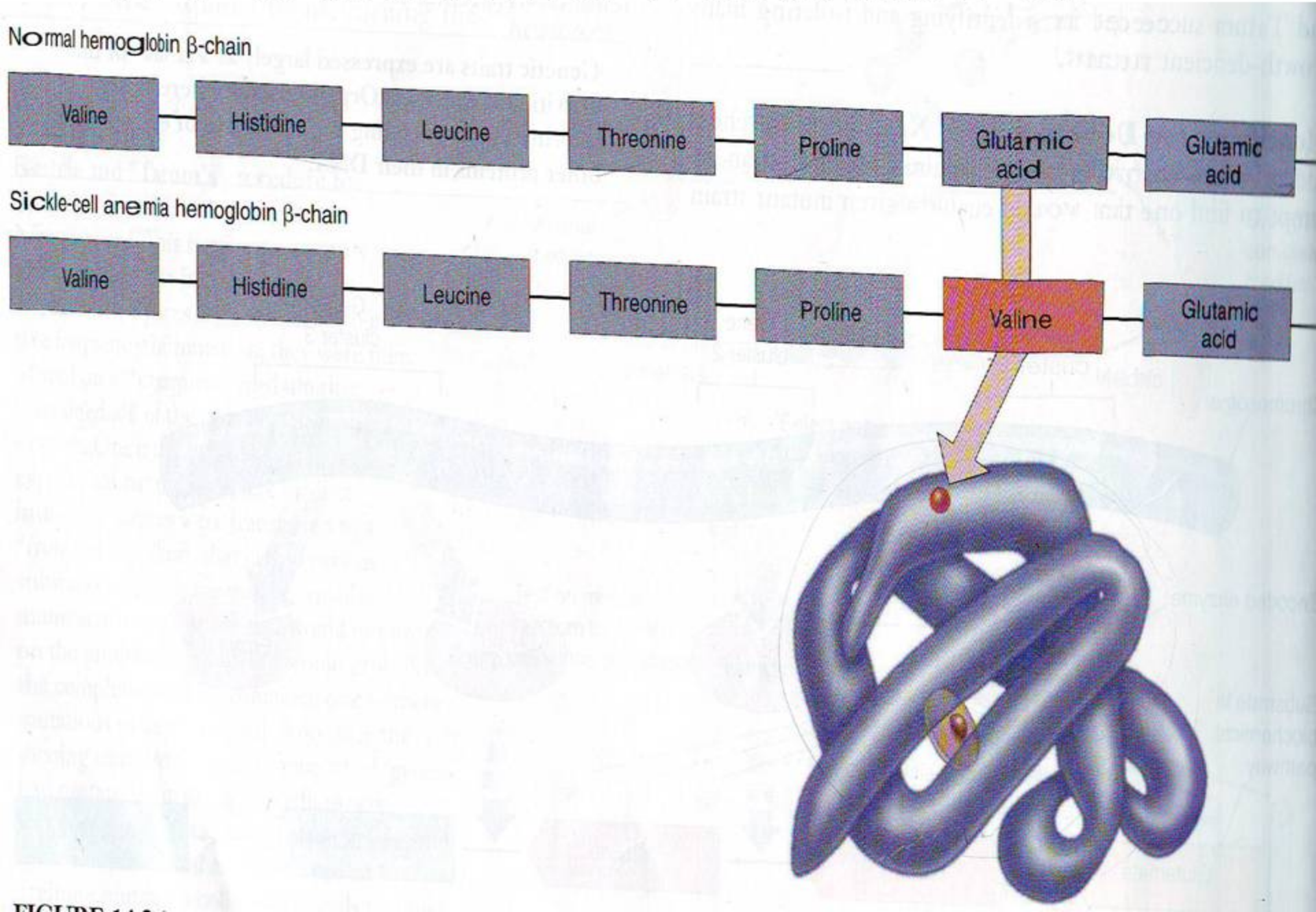


3. Chromosome Mutations

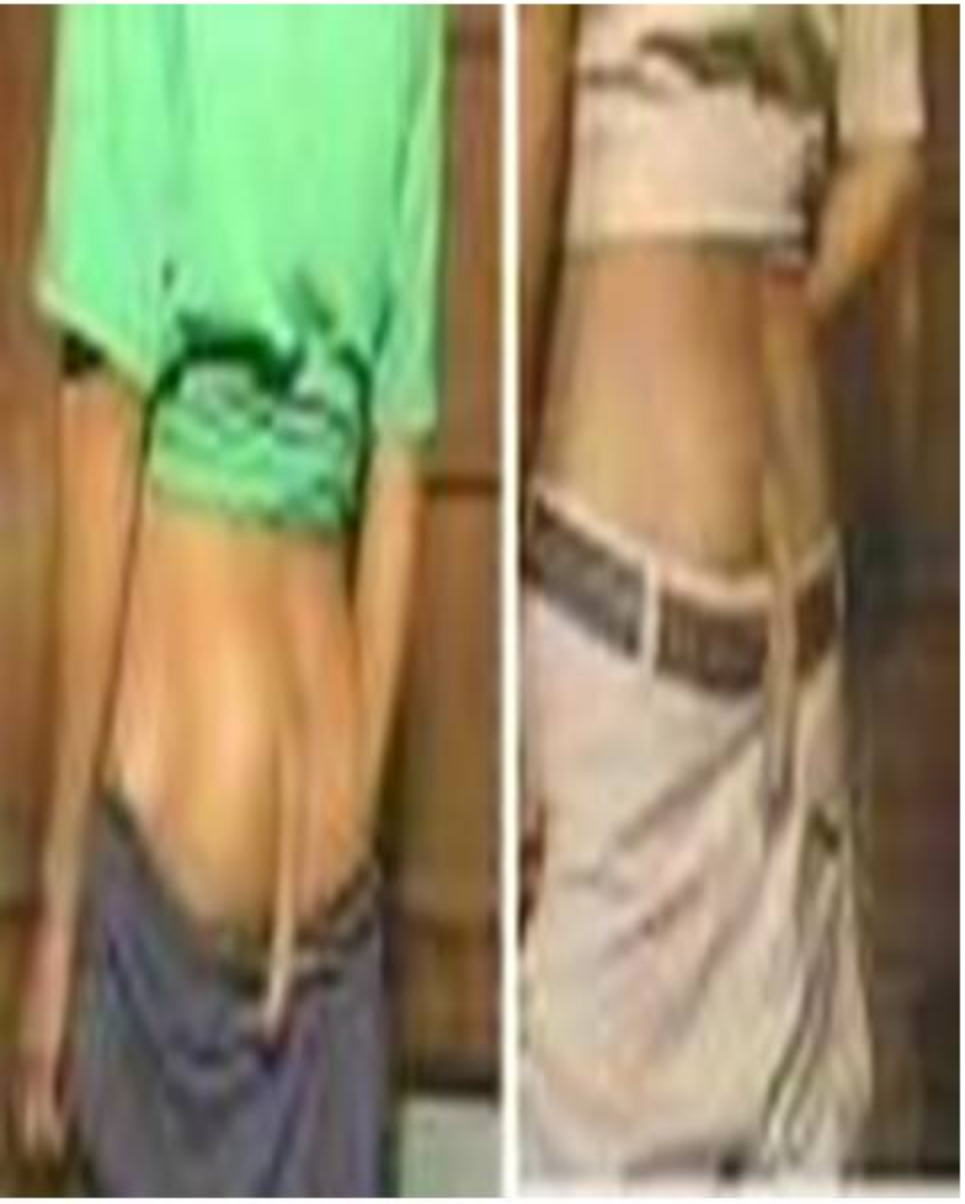
a. Parts of a chromosome may be lost during crossing over and at other times.

- Sometimes these "Lost Parts" may rejoin the chromosome, but may attach backwards or at the wrong end.
- Also they may attach to the wrong chromosome.
- All these can result in abnormal information in the genetic code.

3.Chromosome Mutations



CHROMOSOME MUTATION



b. Changes in chromosome number may also occur.

- Gametes with an extra or missing chromosome may be formed.
- Individuals with an extra or missing chromosome are abnormal.
- When there is an extra chromosome, the condition is known as **trisomy; if a chromosome is missing it is called monosomy**

- Whole sets of chromosomes may be affected, meiosis may go completely wrong and produce diploid (2n) gametes.
- Fertilization of this diploid gamete with a normal haploid (n) gamete would result in a triploid (3n) individual.
- Many apple varieties are triploid.

- Cells with more than 2 sets of chromosomes (polyploids) are larger than diploid (2n) ones.
- So man encourages and selects for these mutations to give bigger crops.
- e.g. wheat in 6 n.

- Man also "mutates" cells by genetic engineering. Mutations occur constantly in populations.
- New strains of viruses, e.g. flu catch human defences unprepared.
- New strains of bacteria, e.g. syphilis, are resistant to antibiotics.
- Mutant pest insects, e.g. mosquito are surviving insecticides.

Causes of Mutation

- Cosmic rays, ultra-violet rays, radioactive emissions and certain chemicals e.g.mustard gas, and chemicals in cigarette smoke are mutagens or mutagenic agents.
- Regardless of their causes mutations can be copied.
- If they occur in a body (or somatic) cell of an organism, they are not important to the species as a whole.
- But mutations in the sex cells may affect an entire population of organisms because the information can be passed from one generation to the next.

- Some mutations can go unnoticed or may be helpful while some are harmful.
- If it is not expressed, it is masked by a dominant gene.
- In this way a harmful allele may spread through a population slowly.
- If a gene pair has two recessive harmful alleles or one harmful dominant for the trait, defects or death could result.
- A mutation which causes death is said to be lethal.
- Non-lethal mutations become a "storehouse of variety" for a population.

Genome Biology

- A revolution is taking place in the field of genetics, one that, in its impact on society, may rival the computer revolution. This is due to a shift from the study of single genes to the study of whole genomes.
- A genome is all the DNA of an organism, including the genes.
- Thus the human genome consists of all the DNA in our 46 chromosomes.
- Genome biologists have two major goals.

1. determining the DNA sequence of entire genomes and
2. understanding the expression and function of large numbers of genes. Genome biology has the potential to revolutionize the diagnosis and treatment of human disease.

DNA Cloning

- A gene is cloned if geneticists have isolated the gene and can make many copies of it.
- Once a gene is cloned, the gene can be sequenced, transferred to other cells or organisms, and used in DNA hybridization experiments.

Clones

- In 1958 F.C. Steward and his coworkers managed to clone a single, mature plant cell from a carrot to give rise to an entire new plant.
- In 1996 a group of scientists working in Scotland used a single cell taken from the udder of a sheep to produce a now famous lamb called Dolly.

Genetic Engineering

- Genetic engineering is the transfer of a gene from one species to another.
- It is a three step process in which a DNA sequence (often a gene) is isolated, modified, and inserted back into the same species or into a different species.
- Genetic engineering works because all organisms share a similar, often identical genetic code.

Fig. A Clone and Her Offspring Dolly the sheep (left) is the first mammal to have been cloned from a mature cell. She has produced a lamb, Bonnie (right), by normal reproduction.

NATURAL SELECTION

- Natural selection is the process that results in adaptation of a population to the biotic and abiotic enviroment.

Type of selection

- Most of the traits on which natural selection acts are polygenic and controlled by more than one pair of alleles located at different gene loci.
- Three types of natural selection have been describe for any particular trait.
- They are directional selection, disruptive selection and stabilizing selection.

1. **Directional selection** favours the survival of one extreme of a phenotypic distribution that is better adapted to an environmental condition.

   For example, in a dimly lit forest directional selection would favour mice with darker fur, because they would be better camoflaged and less susceptible to predation.

   The resistance to antibiotic by bacteria and insecticide by insects are examples of directional selection.

The indiscriminate use of antibiotics and pesticides result in wide distribution of bacteria and insects that are resistant these chemicals.

When an antibiotic is administered some bacteria may survive because they are genetically resistance to the antibiotic.

These are the bacteria that are likely to pass on their gene to the next generation.

As a result, the number of resistant bacteria keeps increasing.

2. **Disruptive selection** favours the survival of two (or more) different phenotypic classes of individuals.

   For example, disruptive selection favours the survival of mice with dark fur and light fur that occupy a heterogenous enviroment.

   Disruptive selection is likely to occur in species that occupy diverse environment so that some members of species will survive in each type of environment.

Therefore, these two distinctly different phenotypes are found in the population.

In this instance natural selection has resulted in obvious polymorphism.

3. **Stabilizing selection** favours the survival of individuals with intermediate phenotypes.

   For example, mice with moderately colored fur may survive better in an environment that has an intermediate level of light, such as tall grassland.