GENETICS

This is a branch of science which deals with the study of heredity. It explains how characteristics are passed on from parents to offspring.

TERMS USED IN GENETIC STUDIES

1. Gene: this is the basic unit of inheritance that controls a particular characteristic of an organism. Genes are sections of DNA, located on chromosomes.
2. Alleles: these are alternative forms of a gene, which control contrasting characteristics. Each gene has two or more alleles.
3. Dominant allele: this is an allele that expresses its self whenever it's present, suppressing other alternative alleles.
4. Recessive allele: this is an allele that is suppressed by presence of other alternative alleles. It only expresses its self if present alone.
5. Locus: this is the point on a chromosome where a gene or allele is located.
6. Genotype: this is the genetic makeup of an organism. It states which alleles of genes are present.
7. Phenotype: this is the outside appearance of an organism. It's determined by the genotype and the environment.
8. Homozygous: this is a genotype consisting of two similar alleles of the same gene.
9. Heterozygous: this is a genotype consisting of two dissimilar alleles of the same gene.
10. Pure breeding line: a breed of organisms that consistently show the same phenotype from generation to generation when bred within its self.
11. F_1 generation: a generation of offspring that has descended directly from crossing two pure breeding lines.
12. F_2 generation: a generation of offspring obtained by crossing two F_1 generation individuals.
13. Test cross: a cross carried out to establish the genotype of an organism by crossing it with an individual of a homozygous recessive phenotype.
14. Back cross: a test cross carried out with a homozygous recessive individual being one of the parents.
15. Ploidy: the number of complete sets of chromosomes present in the nucleus of a cell of an organism. Diploid organisms have two sets and represented by 2n while haploid have one set and are represented by n
16. Homologous chromosomes: two similar chromosomes in the nucleus of a cell having alternative alleles of the same genes, one of which is maternal and the other paternal.

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MENDEL'S WORK ON INHERITENCE

Gregor Mendel was an Austrian monk who carried out various breeding experiments in order to find out the transmission of characteristics from one generation to another. As a result of his findings, he came to be known as the father of modern genetics.

Mendel carried out several breeding experiments using garden pea plants (*pisum sativum*). He would transfer pollen grains from one plant to the stigma of another hence carrying out cross pollination. The seeds obtained would then be planted and their characteristics analyzed when they germinate. He analysed features such as length of the plants, position of flowers, pod colour, seed shape

From his findings, Mendel made conclusions and put up two laws that are now known as Mendel's laws of inheritance.

He chose pea plants because of the following reasons;

- Peas were easy to cultivate
- They were fast growing with a short life cycle
- Their petals were closed which minimized interference
- Several varieties would easily be obtained.

MONOHYBRID INHERITENCE AND THE LAW OF SEGREGATION

In one of his experiments, Mendel crossed pure breeding tall pea plants with pure breeding short pea plants. All the resulting offspring were tall. He then obtained some of these tall offspring and crossed them with each other. The resulting offspring contained a mixture of tall and short peas.

He then concluded that the factor responsible for tall peas is dominant to that for short peas. However, reappearance of short plants in the next generation indicated that the factor for short was still present in F_1 offspring uncontaminated though not expressed. Therefore factors that control these characteristics occur in pairs since an organism is formed from two gametes (one member of a pair paternal and the other maternal) and they separate during gamete formation.

Illustration

Let T represent the factor (allele) for tallness

Let t represent the allele for shortness

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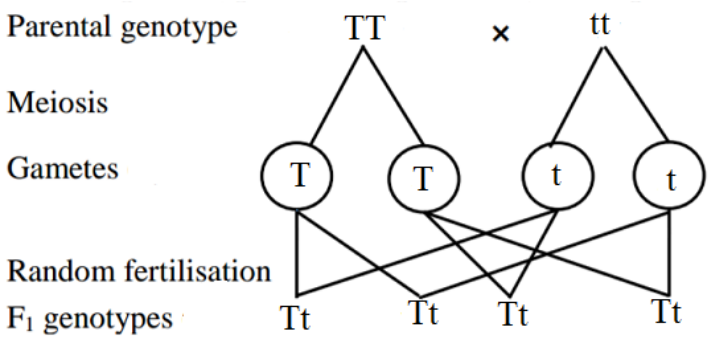


Phenotypes All tall

	T	t
T	TT Tall	Tt Tall
t	Tt tall	tt short

F_2 generation; 3 tall, 1 short

Phenotypic ratio of F_2 generation 3:1

The ratio of 3:1 is always the phenotypic ratio of monohybrid in the F_2 generation whenever two true breeding parents with contrasting characteristics are crossed.

Summary of Mendel's findings

- Since the original parent plants were true breeding and formed from two gamete, each possessed two factors responsible for length
- The F_1 offspring obtained one factor from each parent via gametes.
- The factor for tallness is dominant to that of shortness
- The factors do not blend in the F_1 generation but maintain individuality.

Mendel thus stated his first law of inheritance as follows;

'The characteristics of organisms are controlled by internal factors which occur in pairs but during gamete formation the factors separate such that only one member of a pair can be present in a single gamete'

This law is known as the law of segregation.

Example on monohybrid inheritance.

In peas, seed shape is controlled by a gene which has two contrasting features i.e. round and wrinkled.

When pure breeding round seeded plants are crossed with pure breeding wrinkled seeded plants, all the offspring have round seeds. What is the expected ratio when a heterozygous round seeded plant is crossed with a wrinkled seeded plant?

Let R represent the allele for round seeds

Let r represent the allele for wrinkled seeds

Parents heterozygous round seed X wrinkled seed

Genotype Rr rr

Gametes (R) (r) (r)

	(R)	(r)
(r)	Rr round	rr wrinkled

Phenotypic ratio 1:1

Therefore half of the offspring would have round seeds and half have wrinkled seeds.

N.B: Other characteristics which are inherited in the same way include;

- Albinism in humans, rhesus antigens, eye color in humans
- Coat color in mice
- Eye color in drosophila sp.
  etc.

TEST CROSS

Individuals who show the dominant characteristic may be of two genotypes and they can't be differentiated from their phenotype. A test cross is therefore carried out to establish the genotype of the individuals.

A test cross is a cross carried out between an individual of unknown genotype and another that shows the recessive character.

Two options are there;

a) If the unknown genotype is homozygous dominant, all offspring obtained will show the dominant characteristic.
b) If the unknown genotype is heterozygous, half of the individuals will show the dominant character and half will show the recessive character.

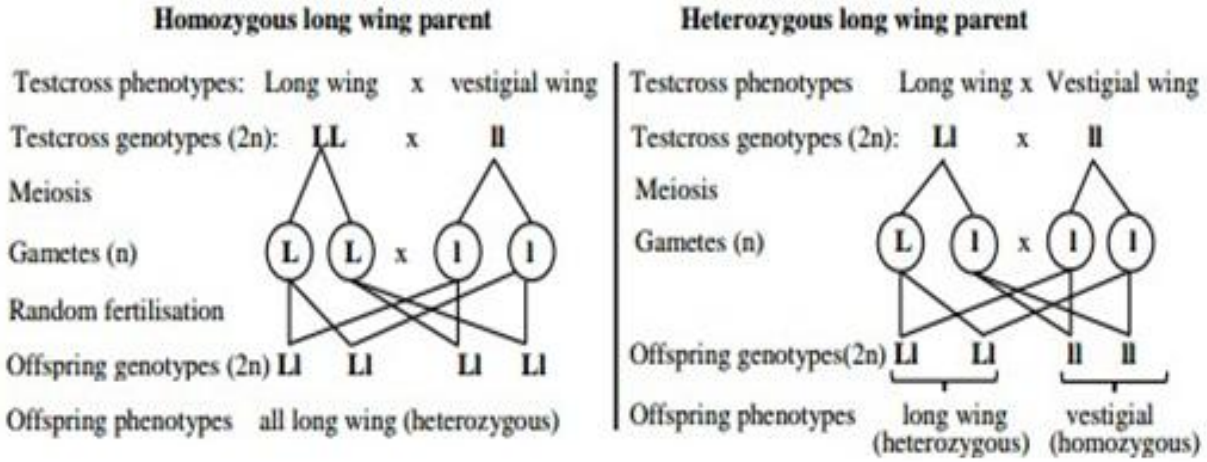
Example

In fruit flies, *Drosophila melanogaster* long wing id dominant to vestigial wing. In order to establish the genotype of a fly showing long wing, the fly of unknown genotype is crossed with another having vestigial wing.

Let L represent the allele for long wing

Let l represent the allele for vestigial wing.

If;



BACK CROSS

This is a test cross carried out when the individual with the recessive characteristic is one of the parents. It's a cross backwards within the same family line.

DIHYBRID INHERITENCE AND THE LAW OF INDEPENDENT ASSORTMENT

Dihybrid inheritance is a situation where two characteristics simultaneously inherited, with each character having two contrasting features.

For example in garden peas, inheritance of seed shape and color of pods were investigated by Mendel. Seed shape has two features i.e. round and wrinkled and pod color has two features i.e. yellow and green.

When pure breeding round seeded plants with yellow pods were crossed with pure breeding wrinkled seeded plants with green pods, all the offspring had round seeds and yellow pods. When the F_1 offspring were selfed, they gave rise to F_2 offspring with different characteristics in different ratios.

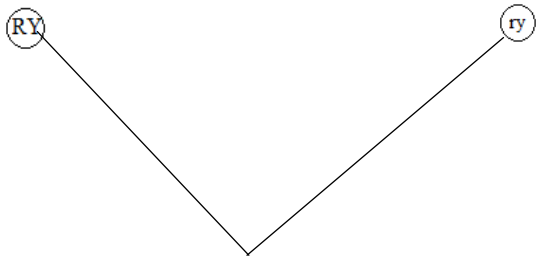
Illustration

Let R represent the allele for round seeds
Let r represent the allele for wrinkled seeds.
Let Y represent the allele for yellow pods.
Let y represent the allele for green pods.

Parents round seeds yellow pods X wrinkled seeds green pods

Genotypes RRYY rryy

Gametes



F_1 offspring RrYy

F_1 phenotype round seeds, yellow pods

Selfing F_1 offspring; RrYy X RrYy

Gametes RY Ry rY ry RY Ry rY ry

Using a punnet square;

	RY	Ry	rY	ry
RY	RRYY Round, yellow	RRYy Round, yellow	RrYY Round, yellow	RrYy Round, yellow
Ry	RRYy Round, yellow	RRyy Round, green	RrYy Round, yellow	Rryy Round, green
rY	RrYY Round, yellow	RrYy Round, yellow	rrYY wrinkled, yellow	rrYy wrinkled, yellow
ry	RrYy Round, yellow	Rryy Round, green	rrYy wrinkled, yellow	rryy wrinkled, green

Phenotypes; round yellow, round green, wrinkled yellow, wrinkled green,
9 3 3 1

Thus the phenotypic ratio in the F_2 generation is 9:3:3:1

The dominant characteristics appear in the F_2 generation in greater proportions, and the recessive characteristics in least proportions but there is appearance of new combination of characteristics i.e. round green and wrinkled yellow.
Due to this Mendel concluded that the two pairs of contrasting characteristics while combining in the F_1 generation separate and behave independently of one another in subsequent generations.

From this he derived the second law of inheritance known as the law of independent assortment. It states that;

'*During inheritance of two pairs of contrasting characteristics, any one member of a pair may combine with either of another pair'*

For example in one cross, in the F_2 generation Mendel obtained a total of 556 offspring. Of these, 315 were round and yellow, 101 wrinkled and yellow, 108 round and green and 32 wrinkled and green. This approximates to the ratio of 9:3:3:1.

The above ratio is the F_2 ratio whenever a dihybrid cross of two pure breeding lines is made.

GENETIC EXPLANATION OF MEMDEL'S FINDINGS

The internal factors referred to by Mendel are alleles which are alternative froms of genes control phenotypic characteristics. Alleles are portions of DNA on a chromosome with a particular sequence of nitrogenous bases.The alleles code for a specific polypeptide molecule and the polypeptide formed determines the phenotype e.g. melanin determines the hair and skin color.

In a diploid organism, contrasting alleles are located on homologous chromosomes and during meiosis homologous chromosomes move to different gametes hence segregation.

During metaphase I, independent assortment occurs by any member of a pair of homologous chromosomes having equal chances to go to either gamete.

GENE LINKAGE

Linked genes are genes located on the same chromosome and hence they are inherited together as a single unit.

If genes are linked, they do not separate and thus in such a cross, the ratio of 9:3:3:1 is not obtained.

Example on linkage

In fruit flies, *drosophila* the genes for body color and wing length have the following allelomorphs; grey body and black body, long wing and vestigial wing. Grey body is dominant to black body while long wing is dominant to vestigial wing.

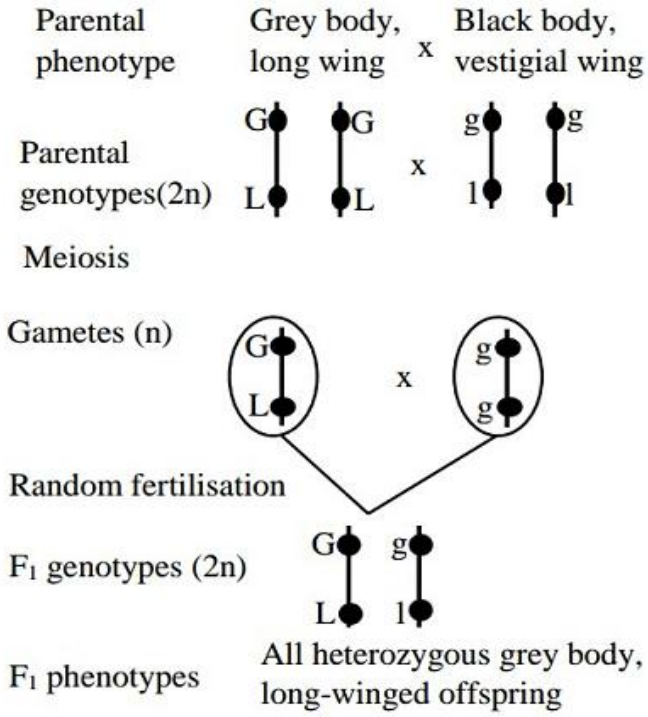
When true breeding grey bodied long winged flies are crossed with true breeding black bodied vestigial winged flies, all the F_1 offspring have grey bodies and long wings.Selfing the F_1 offspring gives rise to F_2 offspring with grey body long wing and black body vestigial wing in the ratio 3:1

Let G represent the allele for grey body

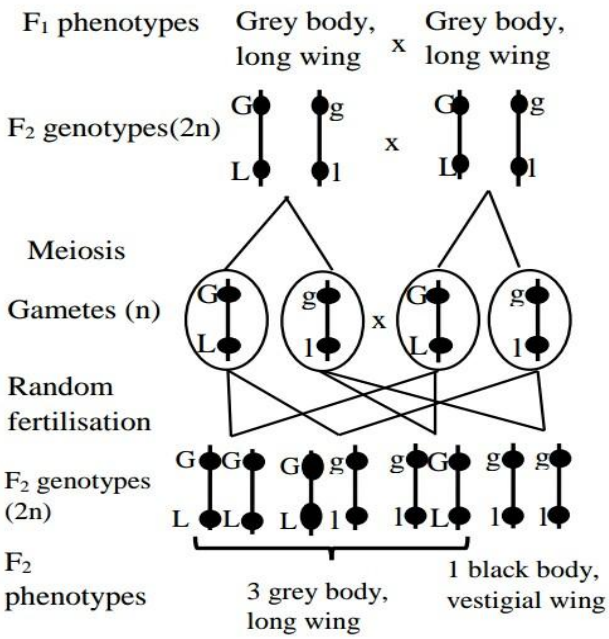
g represent the allele for black body

L represent the allele for long wing

l represent the allele for vestigial wing.



Selfing F_1 offspring,



The F_2 phenotypic ratio is 3:1 similar to that of monohybrid inheritance.

In practice however, the ratio of 3:1 is not obtained because total linkage is rare. Some other combinations of phenotypes may appear.

Crossing over and cross over values

Crossing over is the exchange of parts (containing genetic material) between non sister chromatids of homologous chromosomes. This results onto separation of linked genes so that they may not be inherited together. Crossing over takes place during prophase I of meiosis.

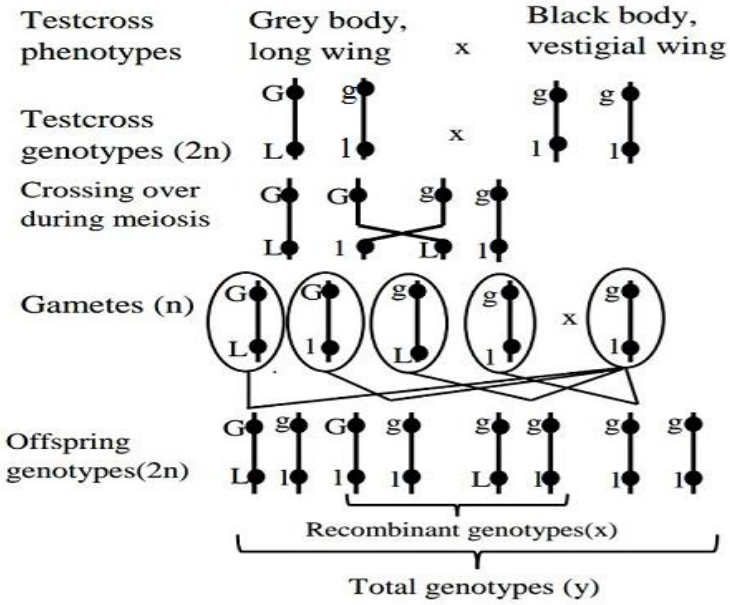
The new phenotypes formed as a result of crossing over are known as **recombinants**.

Recombinants show new combinations of characteristics which are not possessed by the parents, and their numbers are usually lower than those of the rest.

Cross over value or recombinant frequency is the percentage of the total number of offspring that are recombinants.

Example on recombination

In *drosophila* the genes for body color and wing length are linked. A cross between a true breeding long winged grey bodied fly and a true breeding vestigial winged black bodied fly produced offspring that are long winged and grey bodied. When these offspring were test crossed by crossing with a doubly homozygous recessive fly, the following results were obtained.



In case of total crossing over, phenotypic ratio = 1:1;1:1.
In practice, a number of offspring with different phenotypes were obtained as below;

Grey body long wing	965		phenotypes like those of parents
Black body vestigial wing		944	
Black body long wing	206		recombinants
Grey body vestigial wing		185	

N.B: In the above example, if the two genes were located on different chromosomes (not linked) a phenotypic ration of 1:1:1:1 would be obtained. Therefore a deviation from this ratio shows that the genes are linked. However, failure to obtain a ratio of 1:1 (appearance of phenotypes different from those of the parents) show that it's not total linkage but crossing over occurs.

<u>Calculating crossover values</u>

The following formula is used.

$$\frac{number\ of\ recombinants}{total\ number\ of\ offspring} X100\%$$

From the cross above;

C.O.V = $\frac{206+185}{965+944+206+185} x100\%$

= $\frac{391}{2300} x100\%$

= 17%

Recombinant frequencies show the extent of crossing over and this gives an indication of how close together two genes are on a chromosome. A big value of C.O.V indicates a lot of crossing

over meaning the genes are far apart. However a low C.O.V indicates less crossing over meaning the genes are close together, with less chances of separation.

Cross over values are used in gene mapping.

GENE MAPPING

This is a diagrammatic representation of the relative positions of genes on a chromosome.

The distance between two genes is indicated by their cross over values. If two genes X and Y have a C.OV. of 10% it means they are 10 units apart and if genes W and X have a C.O.V of 5% between them , it means they are 5 units apart.

Example:

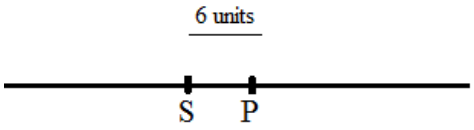
The genes P, Q, R and S have the following cross over values between them.

P-Q = 24%
S-P = 6%
R-S = 8%
R-P = 14%
Draw a diagram to represent the relative positions of the gens on the chromosome.

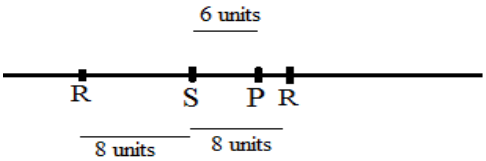
Steps:

i) Draw a straight line to represent a chromosome.

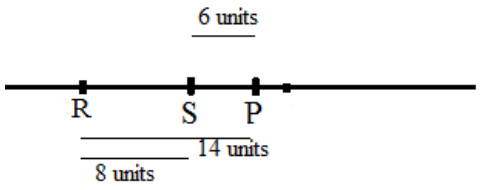
ii) Identify the genes with the smallest C.O.V and place them on the line drawn e.g. S-P



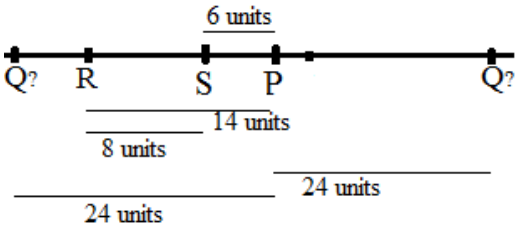
iii) Identify the second smallest C.O.V (R-S) and place the missing gene (R) on the line having the genes inserted above. This gives two possible positions of gene R, but using the C.O.V between R and P it eliminates one of the positions of R.



Then,



iv) Then the largest C.O.V is put, leaving two possible positions of one gene (Q)



SEX DETERMINATION

Sex is the state of being either male or female. This state is determined by genes located on certain chromosomes.

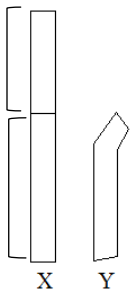
In organisms, there exists chromosomes in pairs, with each chromosome having another similar member, forming homologous chromosomes. However, there is a pair whose chromosomes are not similar. The two chromosomes are called sex chromosomes, and they have the genes that determine the sex of an organism. The rest of the chromosomes are known as autosomes and they determine the rest of the characteristics of an organism.

In humans, there are 22 pairs of autosomes, and 1 pair of sex chromosomes. The members forming the 23rd pair are the X and Y chromosome. The X chromosome is big while Y is smaller.

Illustration showing chromatids of the sex chromosomes

Non homologous portion

Homologous portion



In humans individuals with a genotype XX are phenotypically female while individuals with XY genotype are phenotypically male.
Inheritance of sex occur in the normal mendelian fashion. i.e;

Parents female X male

Genotypes XX XY

Gametes all X X , Y

Fertilization using punnet square;

	X	Y
X	XX female	XY Male

Phenotypic ratio 1:1

This shows that there is an equal chance of producing a male or a female.

It has been proved that presence of the Y chromosome determines maleness. That's why individuals whose genotype is XXY are males. This is because the Y chromosome contains genes that cause undifferentiated gonads in embryonic development to differentiate into tests. In absence of the Y chromosome, the genitalia develop into ovaries.

In birds, moths and butterflies, the sex genotypes are reversed, with XX being male and XY being female. In grasshoppers, the Y chromosome is empty hence the male genotype is XO while that of female is XX.

SEX LINKED GENES

These are genes whose alleles are located on the sex chromosomes. The characteristics that result are known as sex linked characteristics.

Sex linked alleles are located on the X chromosome because it's big and giving space where such genes can be located. The Y chromosome carries no other alleles except those that cause differentiation of testes.

Sex linked characteristics appear more in males because of having one X chromosome hence no possibility of being heterozygous. However females can be heterozygous hence recessive alleles may not expressed in females. Individuals who are heterozygous for recessive alleles are known as *carriers.* Males pass on their sex linked alleles to their daughters while females pass on sex linked alleles to both their sons and daughters.

Examples of sex linked traits in humans

- Hemophilia (bleeder's disease)
- Red-green colour blindness
- Premature balding
- Porcupine hairs

Example

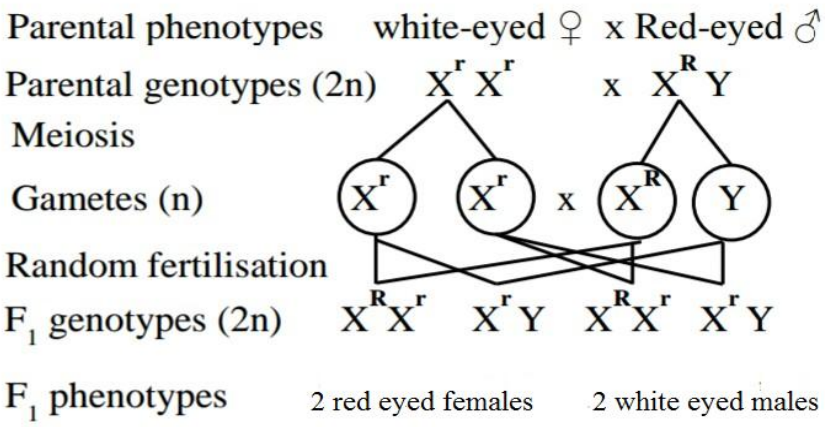
In drosophila, the gene for eye colour is sex linked. Red eyes is dominant to white eyes.

Determine the results of

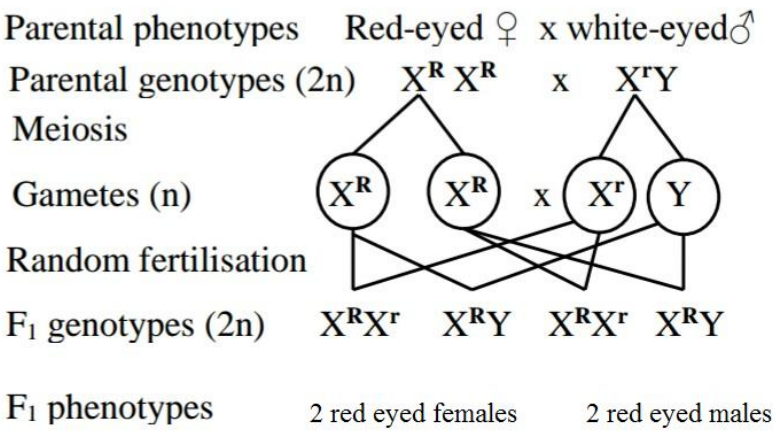
a) A cross between a white eyes female and a red eyed male.
b) A reciprocal cross of the above test.

Let the allele for red eyes be R and that for white eyes be r.

a)



b)



Inheritance of hemophilia in humans

This condition is controlled by a recessive allele carried on the X chromosome. This allele prevents the formation of blood clotting factor VIII, hence failure of blood to clot. The individual usually bleeds to death in case of serious injuries.

However this condition cannot be completely eliminated due to heterozygous individuals appearing normal.

If we let the normal allele be represented by H and the hemophiliac allele be represented by h, the following genotypes are possible.

Genotype	**phenotype**
X^HX^H	normal female
X^HX^h	normal female (carrier female)
X^hX^h	hemophiliac female
X^HY	normal male
X^hY	hemophiliac male

Questions;

a) Using suitable genetic symbols, explain how two parents who both appear normal can give birth to a hemophilic boy.

b) Explain why there are more colour blind individuals than hemophiliacs yet the two conditions are sex linked and transmitted in the same way.

SEX LIMITED CHARACTERISTICS

These are characteristics in organisms that are limited to only one sex, regardless of whether the allele is present in the opposite sex. The common example of sex limited traits are the secondary sex characteristics. Those that occur in males do not occur in females and vice-versa.

CO-DOMINANCE AND INCOMPLETE DOMINANCE

Incomplete dominance is where one allele of a gene is not fully dominant over the other so that the heterozygous organisms show a feature that's intermediate between the dominant and recessive characteristic.
For example in snapdragon plants, when true breeding red flowered plants are crossed with true breeding white flowered plants, all the offspring have pink flowers. This indicates that the allele for red flowers is partially dominant.

Co-dominance is where neither of the two alleles of a gene is dominant over the other such that both alleles express themselves in unaffected states in the heterozygous state.
For example in cattle, when true breeding black coated cows are crossed with true breeding white coated cows, the offspring has a roan coat (mixture of black and white spots).

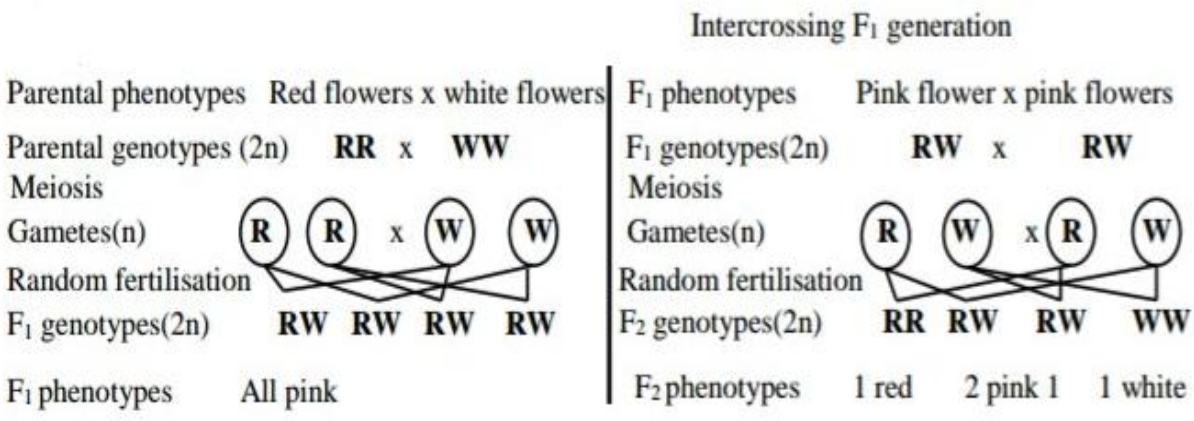
In both of above cases, when F_1 offspring are crossed to obtain the F_2 generation, a phenotypic ratio of 1:2:1 is obtained, indicating that alleles maintain their individuality in the heterozygous state.

Example on incomplete dominance

In snapdragon plants, the allele for red flowers is partially dominant to that of white flowers. If true breeding red flowered plants are crossed with true breeding white flowered ones, determine the phenotypes in the F_1 and F_2 generation.

Let R represent the allele for red flowers

W represent the allele for white flowers. (Different capital letters are used in this case)

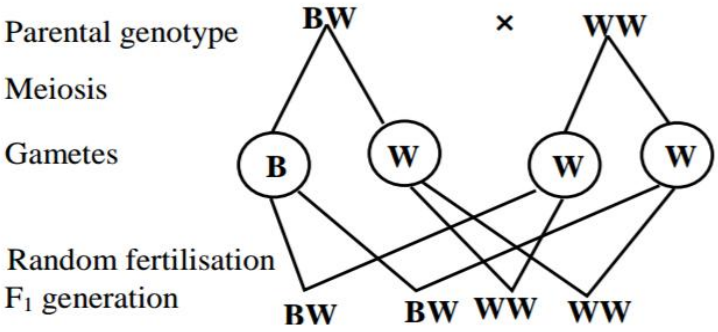


Example on co-dominance

In cattle, when true breeding black coated cows are crossed with true breeding white coated cows, the offspring has a roan coat. Find the results of a cross between a roan cow and a white coated bull.

Let B represent the allele for black coat. W represent the allele for white coat.

Parents roan coat white coat



Phenotypes; 2 roan cattle and 2 white cattle.

Phenotypic ratio 1: 1

PARTIAL DOMINANCE

This is where an allele is partially dominant over the other with offspring failing to resemble either parents, but are closer to one of the parents. This shows that some alleles show a varying degree of dominance with a wide range of intermediate offspring.

MULTIPLE ALLELES

This is where a characteristic is controlled by a gene which has 3 or more alleles. However, the three alleles cannot occupy the same locus at the same time i.e. only two alleles can be present in one individual.

For example the ABO blood group system is controlled by a gene with 3 alleles i.e.

I^A for antigen A

I^B for antigen B

I^O for no antigen.

The alleles I^A and I^B are co-dominant and are both dominant to I^O

Therefore the following phenotypes and genotypes are possible.

Genotype	Phenotype (blood group and antigen present)
I^AI^A, $I^A I^O$	Blood group A, and antigen A
I^BI^B, $I^B I^O$	Blood group B, and antigen B
$I^A I^B$	Blood group AB and both antigens present.
I^OI^O	Blood group O, and no antigen

Example: (s)

Determine the phenotypes of the children when;

a) A man heterozygous for blood group A marries a woman heterozygous for blood group B.
b) A man of blood group O is married to a woman of blood group AB

Solution

a) Parents heterozygous group A X heterozygous group B
Genotypes $I^A I^O$ $I^B I^O$

Gametes

Fertilization

Offspring $I^A I^B$ $I^A I^O$ $I^B I^O$ I^OI^O

Phenotypes group AB group A group B group O

b) Parents blood group O X blood group AB
Genotypes I^OI^O $I^A I^B$

Gametes

Offspring $I^A I^O$ $I^B I^O$

Phenotypes group A group B

N.B: determination of the blood groups of the children can be used to predict the blood group of the parents. This has been specifically used as a guide in confirmation of the paternity of children.

DOMINANT SERIES

This is where a gene having more than 2 alleles expresses dominance in form of a series.E.g in rabbits, coat color is determined by a gene having 4 alleles;

The allele for full colour (Agouti), C^F is dominant to all other alleles

Chinchilla (grey), C^{CH} is dominant to Himalayan (white and black) and albino.

Himalayan (white and black), C^H is dominant to albino, C^A

The possible phenotypes are therefore;

C^FC^F, C^FC^{CH}, C^FC^H, C^FC^A	Agouti (full color)
$C^{CH}C^{CH}$, $C^{CH}C^H$, $C^{CH}C^A$	Chinchilla
C^HC^H, C^HC^A	Himalayan
C^AC^A	Albino

PLEIOTROPY

This is where a single gene affects an organism in more than one way. Most genes have this property for example most hereditary diseases in humans have more than one symptom.

LETHAL GENES

These are genes whose certain combinations of alleles leads to death of an individual possessing them.E.g. in certain subspecies of mice, when yellow mouse is crossed with an agouti mouse, 2 yellow and 1 agouti mouse are produced. This shows that one of the offspring (homozygous dominant) dies in embryo stage.

The phenotypic ratio of 2:1 is indicative of lethal alleles or genes.

GENE INTERACTIONS

Certain phenotypes of organisms are produced/ affected by an interaction of two or more genes located at different loci on a chromosome.

The common gene interactions are;

a) EPISTASIS

This is where a gene at one locus suppresses the action of another gene at a different locus. The gene which surpresses is called the epistatic gene while the one suppressed is called the hypostatic gene.

Example

In mice, the gene for coat colour has 2 alleles i.e. black and brown. Black coat (B) is dominant to brown (b)

However another gene determines whether a pigment will be deposited in the hair. If a dominant allele of this gene (C) is present, the colour (black or brown) is deposited. If only the recessive alleles are present (c) no pigment is deposited and the mouse is white.

The results of crossing two mice that are heterozygous for both genes (black coloured) is as follows;

Parents CcBb X CcBb

Gametes CB, Cb, cB, cb CB, Cb, cB, cb

	CB	Cb	cB	cb
CB	CCBB Black	CCBb Black	CcBB Black	CcBb Black
Cb	CCBb Black	CCbb Brown	CcBb Black	Ccbb Brown
cB	CcBB Black	CcBb Black	ccBB white	ccBb white
cb	CcBb Black	Ccbb Brown	ccBb white	ccbb white

Phenotypic ratio black: brown: white

9 : 3 : 4

The phenotypic ratio of 9:3:3:1 is modified to 9:3:4 (3+1)

Whenever the dominant allele (C) is present, a colour (black or brown) is deposited. If the recessive allele (c) is present, no colour appears.
Therefore, the gene C/c surpresses the second gene and is therefore epistatic to B/b.

b) COMPLEMENTARY GENES

Some characteristics of organisms are determined by a combination of more than one gene located at different loci in such a way that for one the genes to exert its effects, even the other must be present. Such genes therefore form a gene complex.

Example

In the inheritance of comb shape in domestic fowl, 2 genes interact and this gives rise to four different phenotypes i.e. pea, rose, walnut, single.

Pea shaped and rose shaped combs appear by presence of their respective dominant alleles controlling them, but with absence of another dominant allele.
Walnut shaped comb appears due to presence of at least two dissimilar dominant allele.
Single shaped comb appears due to presence of only recessive alleles of both genes.
If we let P and p represent gene for pea comb
R and r represent gene for rose comb

The possible genotypes and their phenotypes are therefore;

Phenotypes	**Possible genotypes**
Pea comb	PPrr, Pprr
Rose comb	ppRR, ppRr
Walnut comb	PPRR, PpRR, PPRr, PpRr
Single comb	Pprr

Qn; determine the phenotypes of offspring produced by crossing a heterozygous pea comb shaped fowl with a doubly heterozygous walnut comb shaped fowl.

c) DUPLICATE GENE INTERACTION

This is a condition determined by 2 genes but the characteristic is only expressed by absence of dominant alleles for both genes.

If the two genes are A and B, the genotype that shows the characteristic is the double homozygous recessive genotype. i.e. aabb
This gives a phenotypic ratio of 15:1 if two doubly heterozygous organisms are crossed.

d) POLYGENIC INHERITENCE

This is where a character is determined by more than two genes located on different loci. The many genes each have a dominant and a recessive character, and it gives rise to many possible genotypes.

Such genes have a cumulative effect on the phenotype, with an organism having only dominant alleles lying at one extreme and an organism with only recessive characteristics lying at the other extreme. Intermediates are usually very many and form a continuum (gradual difference in appearance).

Polygenic inheritance gives rise to continuous variation with organisms showing a gradual difference in characteristics from one extreme to another.

Examples of characteristics in humans inherited in this way include;

- Skin color in humans
- Pattern of finger prints
- Intelligence
- Body height
  etc.

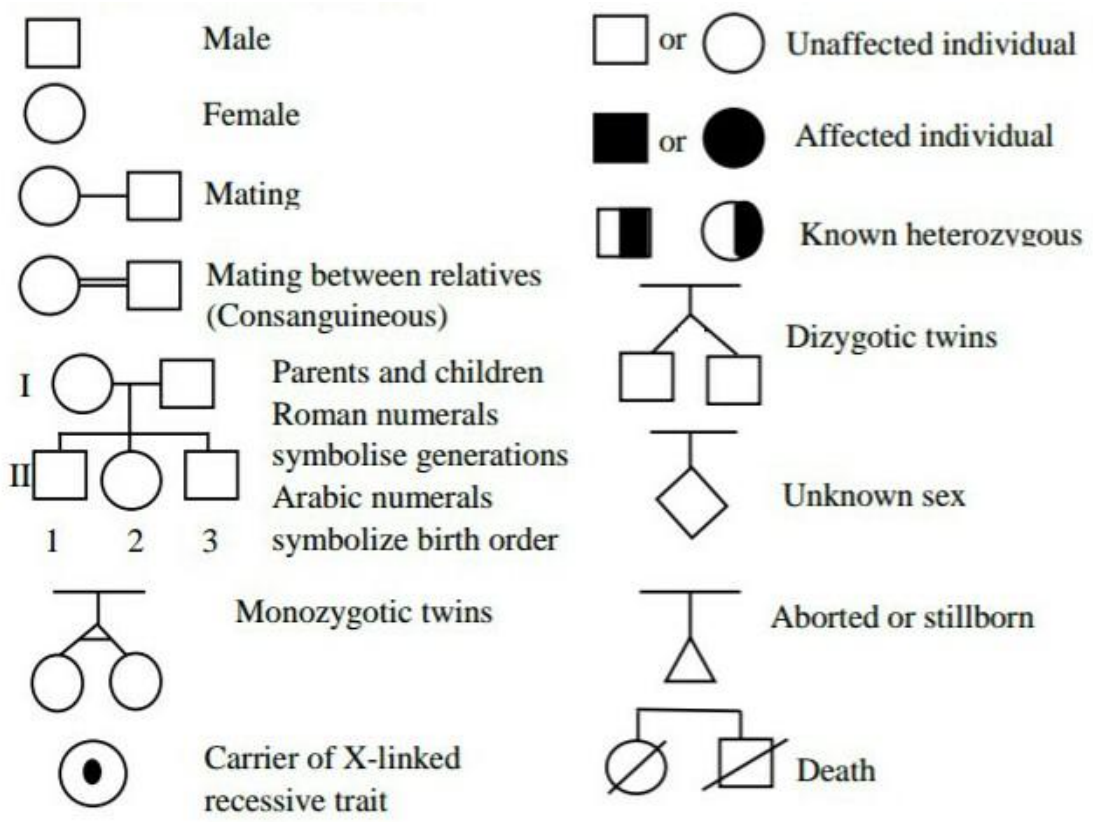
PEDIGREE ANALYSIS

This is the study of inheritance of characteristics along family lines for many generations i.e. from ancestors to parents and then to offspring of various generations.

Pedigree studies enable study and identification of traits (both useful and useless) in a family of organisms. Such studies are important in agriculture, research and human genetic analysis. During the study, phenotypes of organisms are observed and then analyzed in order to determine their genotypes. This provides useful information in selection of organisms for breeding, and avoidance of inheritable diseases of humans.

Pedigree diagrams are illustrations showing mating between organisms and the resulting offspring for various generations.

Symbols used in pedigree studies

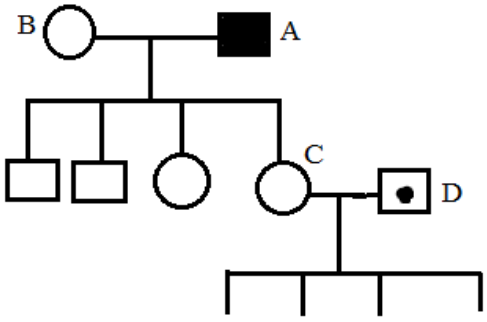


During pedigree analysis, one of the most important steps would be to establish the type of inheritance that is under consideration. The possible inheritance types are;

Autosomal dominant, autosomal recessive, x-linked dominant, x-linked recessive

Example on pedigree analysis

Cystic fibrosis is controlled by an autosomal allele. The illustration below shows its inheritance in a given family.



Given that individual A is affected by cystic fibrosis and individual D is a carrier,

Write down the

a) Possible genotype of individual B.
b) Phenotype of offspring between A and B
c) Determine the phenotypic ratio of a cross between individual C and D.

MUTATIONS

A mutation is a sudden change in the amount, structure or arrangement of the genetic material of an organism. This leads to a change in the phenotype of an organism since the genotype determines the phenotype.

Mutations that occur in the gametes or gamete producing cells are transmitted to the next generations while those that occur in the somatic cells are not transmitted.

CAUSES OF MUTATIONS

Mutations are caused by presence of certain chemicals or radiations. These are called mutagens. The common mutagens are;

- Electromagnetic radiations such as x-rays, gamma rays, ultra violet radiations
- High energy particles such as alpha and beta particles
- Chemical substances such as caffeine and formaldehyde
- Poisonous substances such as mustard gas, cholchicine, nitrous acid
- Some food preservatives and pesticides.

TYPES OF MUTATIONS

Mutations are grouped into two;

a) Chromosomal mutations

These are mutations that result into change in structure or number of whole chromosomes.They have profound effects on organisms since they change a large amount of DNA (many genes). Chromosomal mutations include;

Changes in chromosome number

i) Euploidy: this is a mutation which causes an addition or removal of a complete set of chromosomes (n) from an organisms. The resulting DNA amount in an organisms thus remains a multiple of the original haploid DNA quantity causing polyploidy. This makes the final organism triploid (3n), tetraploid (4n), etc
e.g. if the original organism had 20 chromosomes, after mutation it may have 40, 60, 80 chromosomes, and so on.
Polyploidy is important in plants because the resulting plants usually have good characteristics such as big fruits. However polyploid animals usually die in embryo stage.

ii) Aneuploidy: this is a mutation that results into addition of one or more chromosomes but not whole sets. The resulting organism has a DNA amount that is not a multiple of the original DNA quantity. E.g. if the original organism had 20 chromosomes, after mutation it may have 21, 22, etc.

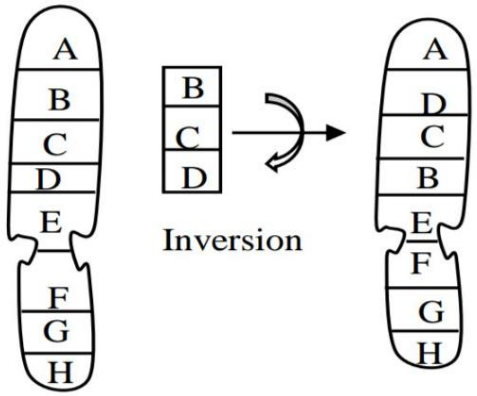
Changes in chromosome number results from chromosome non disjunction during anaphase I.

Changes in chromosome structure

i) Inversion: this is where a portion of a chromosome breaks off, rotates through 180^{o} and then rejoins the chromosome. This changes the loci of some genes which affects the phenotype.

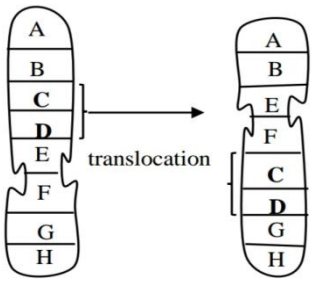
Illustration

Before After



ii) Translocation: this involves a region of a chromosome breaking off and then rejoins the chromosome at another portion or another chromosome.

Before after



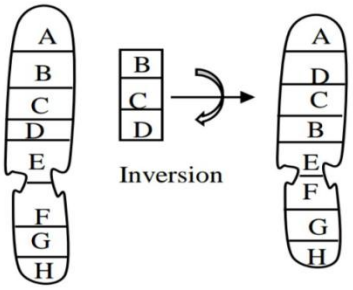
b) Gene mutations/ point mutations

These are mutations which affect only one gene on a chromosome by changing the sequence of nitrogenous bases on DNA.

They include;

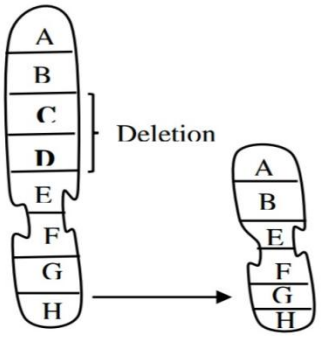
i) Inversion: this is where a portion of DNA breaks off, rotates through 180^{o} and then rejoins the chromosome. This changes the sequence of bases which affects the gene.

Before after



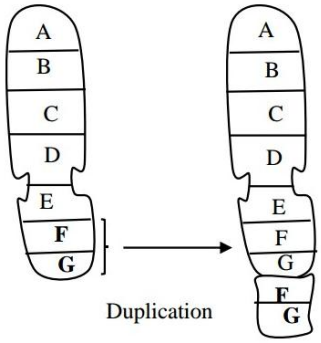
ii) Deletion; this is a mutation which results into some nitrogenous bases being removed from DNA.

Before after



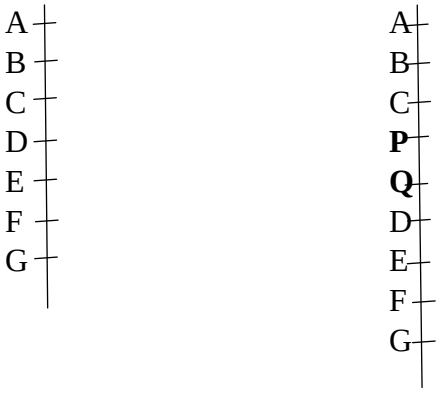
iii) Duplication: this mutation results into repeating of a portion of nitrogenous bases. This changes the overall sequence of a gene.

Before after



iv) Insertion: this is a mutation resulting into addition of one or more DNA bases into the existing DNA.

Before After



v) Substitution: this is where a base on a DNA portion is removed and is replaced by another. This type of mutation only affects one codon.

N.B: Some point mutations do not affect any of the genes of an organism and they are thus called silent mutations. Those that change the reading frame of DNA in terms of codons are called frame shift mutations.

EFFECTS OF MUTATIONS

Some mutations result into formation of good characteristics in organisms. These make organisms more adapted to their environment. However some mutations result into bad traits appearing in a population which may even lead to death of the organism.

In all the above cases, mutations result into variations coming into a population and it's the only source of new genes.

EXAMPLES OF GENETIC DEFECTS IN HUMANS

a) Sickle cell anemia

This is a genetic condition where the red blood cells of an individual change their shape to a sickle shape at low oxygen concentration. This affects their ability to transport oxygen to body tissues. The sickle shaped cells also clog blood capillaries preventing passage of blood.

Sickle-cell anaemia is a recessive character caused by a point substitution mutation in which glutamic acid in normal haemoglobin is replaced by valine. Normal haemoglobin **(Hb^A)** contains an amino acid glutamic acid at position 6 of the β-chain. The amino acid is **polar and hydrophilic** which make normal haemoglobin soluble in water. It is coded for by the DNA triplet CTT and its complementary mRNA codon is GAA. A substitution mutation leads to replacement of T with A making the DNA triplet CAT and its complementary mRNA codon GUA. This tiplet codes for valine which is non-polar and hydrophobic hence reduces the solubility of haemoglobin especially at low oxygen tensions. This abnormal haemoglobin crystallizes into rigid rod-like fibres which distort the normal biconcave shape of RBCs into a crescent/sickle shape. Such abnormal haemoglobin is called **Hb^S,** It has a very low oxygen-carrying capacity leading to symptoms of anaemia and the disease is known as **sickle-cell anaemia.**

Being a recessive character, for a person to be a sufferer they must possess two copies of the faulty gene (homozygous recessive, i.e. Hb^SHb^S or ss). Heterozygotes (carriers, i.e. Hb^AHb^S or Ss) have one copy of the responsive gene whose effects are masked by the other dominant gene. They don't suffer from the disease symptoms except at exceptionally low oxygen tensions; this is known as **sickle-cell trait**.

It is therefore advisable to avoid exposure of such people to low oxygen environments like crowded places, high altitudes and flying in unpressurised aircrafts.

Question; if two people suffering from sickle cell trait are married, what is the probability that they will produce an anaemic child?

<u>Complications due to sickle cell anaemia</u>

1. Anaemia: this is occurs because the sickle cells are destroyed which lowers the amount of oxygen to be carried leading to acute anaemia. This leads to;
    - Fatigue (weakness)
    - Poor physical development
    - Dilation of the heart which may lead to heart failure
2. Interference with circulation of blood because sickle cells get jammed in tiny capillaries and small arteries. This leads to;
    - Heart damage which leads to heart failure
    - Lung damage which leads to pneumonia

- Kidney damage which leads to kidney failure
- Liver damage

3. Enlargement of the spleen because the sickle cells collect in the spleen for destruction

The effects above make the homozygous sufferers to often die before reproductive age.

NB: Despite the above complications suffered by sufferers of sickle cell anaemia, the heterozygotes tend to have an advantage of showing increased resistance to the plasmodium parasite that causes malaria much more than both the sufferers and the normal. This resistance is as a result of:

The consistent change in oxygen levels between normal and sickle cells makes it difficult for the parasite to adapt. In such cases, the immune system of the body eliminates the parasites before the disease is established rendering resistance to the heterozygotes

This is referred to as the **heterozygous advantage** which increases chances of survival for heterozygotes especially in the tropics where malaria is one of the leading causes of death

b) Inheritance of albinism

Albinism is a recessive character which results into failure of formation of body colour pigments.

Albinos have the following characteristics as a result;

- Light-coloured skin
- White hair
- Pink eyes

Question; man with normal skin marries a carrier for albino skin. What is the probability that some of their children will be albinos?

c) Inheritance of cystic fibrosis

This is a recessive character caused by a mutation resulting into accumulation of abnormally **thick and sticky mucus** that blocks the pancreatic duct, bile duct and air passages.
The mutation occurs on an autosomal chromosome 7 affecting the gene that codes for **a chloride channel protein** in epithelial cells. This results into total absence or malfunctioning of this channel protein hence interfering with chloride ion flow. Chloride ions accumulate in the cells and attract sodium ions towards the opposite charge; this increases the ion concentration, hence osmotic potential of the cells which prevents **osmotic outflow** of water. As a result, the mucus secreted is dry, thick and sticky; blocking small tracts of some body organs. This is known as cystic fibrosis.

In the pancreas, fibrous patches called cysts develop (hence the name) and complications include digestive problems due to poor release of pancreatic enzymes, poor absorption of digestive products, chronic lung diseases, reduced fertility etc.

d) Phenyl ketonuria

This is a genetic condition where the body of an individual cant breakdown the amino acid phenylalanine. This amino acid therefore builds up in the body hence affecting body functioning.

This condition is caused by an autosomal mutation on chromosome 12. Sufferers of the condition can't synthesize the enzyme phenylalanine dehydroxylase, hence cant convert phenylalanine to other amino acids especially tyrosine.

Symptoms of phenyl ketonuria

- Severe mental retardation
- Poor hand and walking posture
- Lighter skin pigmentation
- Convulsions due to abnormal brain activity
- Very dry skin

e) Huntingiton's chorea (huntingiton's disease)

This is an inherited condition that leads to deterioration and eventual death of brain cells. It's controlled by an autosomal dominant allele on chromosome number 4.

Symptoms of huntingiton's disease

- Uncontrollable motor movements
- Mental retardation
- Mood changes
- Memory loss

f) Down's syndrome (trisomy 21)

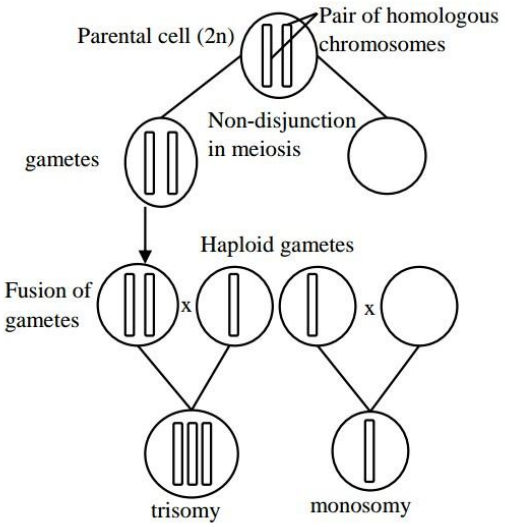
This is a genetic condition caused by presence of a third copy of chromosome 21 in an individual. It's named after Langdon Down who first described it.

Downs syndrome results from non-disjunction of chromosome 21 during anaphase of meiosis, hence one of the gametes gets an extra copy.

Symptoms of Down's syndrome

- Eyelids slant upwards
- Flat rounded face
- Severe mental retardation
- Short stature and small skull
- Increased risk of infections, heart failure, intestinal problems
-

Illustration



g) Klinefelter's syndrome

This is a genetic disorder caused by presence of one or two extra X chromosomes in males. This makes the genotype to be XXY or XXXY instead of the normal XY. The individual therefore has 47 chromosomes instead of 46.

This condition also results from non-disjunction during spermatogenesis of oogenesis, producing a gamete with extra sex chromosome.

Symptoms of Klinefelter's syndrome

- Infertility due to spermatogenesis not taking place, though erection and ejaculation may occur
- Usually taller than average
- Breast development may occur
- Smaller testis
- High pitched sound than normal
- Higher levels of FSH
- Possible sighs of obesity
- Learning difficulties

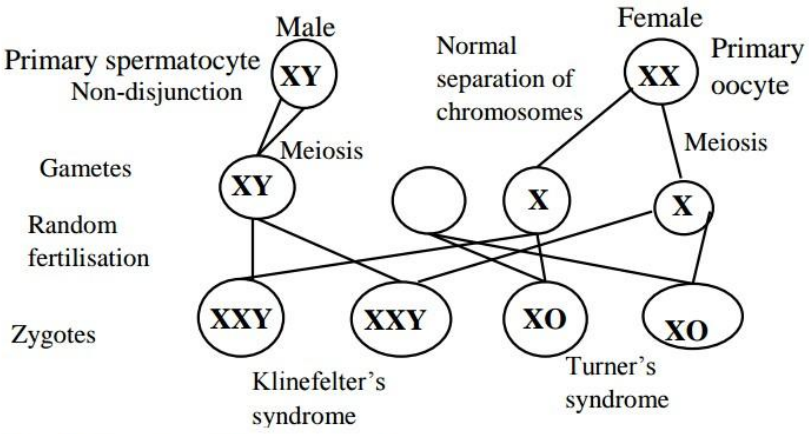
h) Turners syndrome

This sis a genetic condition caused by absence of the second X chromosome in females, thus individuals have the genotype XO. Such individuals can be described as incompletely developed females. It also results from non-disjunction in both males and females during gametogenesis.One of the gametes gets no X chromosome and it fuses with another having an X chromosome, XO is formed.

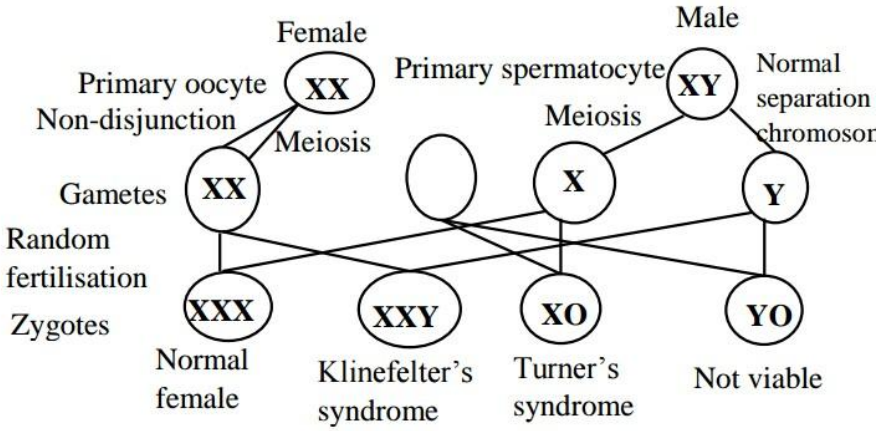
Symptoms of Turner's syndrome

- Infertility due to ovaries being absent
- Short stature
- Small uterus
- Puffy fingers

Illustration for turner and Klinefelter's syndrome



Non-disjunction of Father's sex hormones



Non-disjunction of the mother's sex chromosomes