Principles of Inheritance and Variation

Inheritance of One Gene

Inheritance of One Gene

Genetics

- Genetics is a branch of biology dealing with inheritance and variation of characters from parents to offspring.
- **Inheritance**

  Process by which characters are passed on from parent to progeny

- **Variation**

  Degree by which the progeny differs from its parents

Mendel's Experiments

- Gregor Johann Mendel known as the father of genetics proposed the laws of inheritance.
- He used garden pea as his sample.
- Large sampling size gave credibility to his collected data.
- Garden pea plant possessed certain completely opposite traits.

  Example – tall and dwarf plants

- He worked on the following **seven** traits of garden pea:

S. No.	Character	Dominant	Recessive
1	Stem height	Tall	Dwarf
2	Flower colour	Violet	White
3	Flower position	Axial	Terminal

4	Pod shape	Inflated	Constricted
5	Pod colour	Green	Yellow
6	Seed shape	Round	Wrinkled
7	Seed colour	Yellow	Green

- True breeding pea lines were obtained by continuous self pollination for several generations.
- Fourteen true breeding pea lines were selected as pairs, which were similar except for one character with contrasting traits.
- Artificial cross pollination (hybridisation) was performed on such varieties to obtain first hybrid generation known as the first filial progeny or F_1.

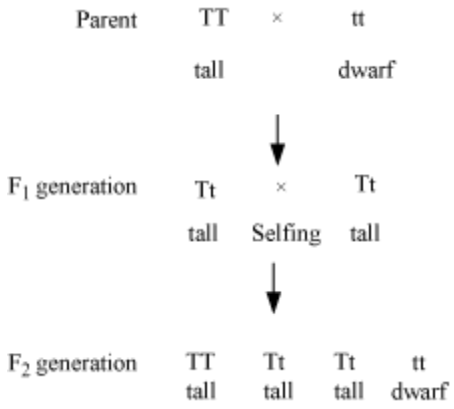
Inheritance of One Gene

- After hybridisation, the F_1 generation so obtained resembled only one of its parents (say, all tall; no dwarf).
- When 2 plants from F_1 generation were self pollinated, the second filial progeny or F_2 generation was obtained.
- Revival of unexpressed trait (dwarf) was observed in some F_2 progeny. Both traits, tall and dwarf, were expressed in F_2 in ratio 3:1.
- Mendel proposed that something is being passed unchanged from generation to generation. He called these things as 'factors' (presently called genes).
- Factors contain and carry hereditary information.
- Alleles – Slightly different form of same factor

Two alleles code for a pair of two contrasting traits. (e.g., tall and dwarf)

Monohybrid Cross

- Cross that considers only a single character (e.g., height of the part)

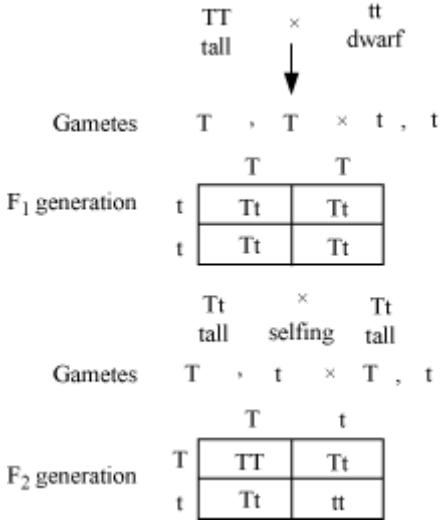


- Studying the cross:

- TT, tt, and Tt are genotypes while the traits, tall and dwarf, are phenotypes.
- T stands for tall trait while t stands for dwarf trait.
- Even if a single 'T' is present in the genotype, phenotype is 'tall'. When 'T' and 't' are present together, 'T' dominates and suppresses the expression of 't'. Therefore, T (for tallness) is dominant trait while t (for dwarfness) is recessive trait.
- TT and tt are homozygous while Tt is heterozygous.
- From the cross, it can be found that alleles of parental pair separate or segregate from each other and only one allele is transmitted to the gamete.
- Gametes of TT will have only T alleles; gametes of tt will have only t alleles, but gametes of Tt will have both T and t alleles.

- **Punnett square**

- Graphical representation to calculate the probability of all possible genotypes of offsprings in a genetic cross
- Possible gametes are written on two sides, usually at top row and left columns, and combinations are represented in boxes.



- With the help of Punnet square, genotypic ratio in F_2 generation can be found. From the above given Punnet square, it is evident that genotypic ratio TT: Tt: tt is 1:2:1.
- The ratio 1:2:1 or $\frac{1}{4}:\frac{1}{2}:\frac{1}{4}$ of TT: Tt: tt can be derived from binomial expression $(ax + by)^2$.
- Gamete-bearing genes are in equal frequency of $\frac{1}{2}$.
- Hence, the expression can be expanded as

$$\left(\frac{1}{2}\mathrm{T}+\frac{1}{2}\mathrm{t}\right)^2=\left(\frac{1}{2}\mathrm{T}+\frac{1}{2}\mathrm{t}\right)\times\left(\frac{1}{2}\mathrm{T}+\frac{1}{2}\mathrm{t}\right)$$
$$=\frac{1}{4}\mathrm{TT}+\frac{1}{2}\mathrm{Tt}+\frac{1}{4}\mathrm{tt}$$

Law of Dominance

- According to this law, characters are controlled by discrete units called factors, which occur in pairs with one member of the pair dominating over the other in a dissimilar pair.
- This law explains expression of only one of the parental character in F_1 generation and expression of both in F_2 generation.

Law of Segregation

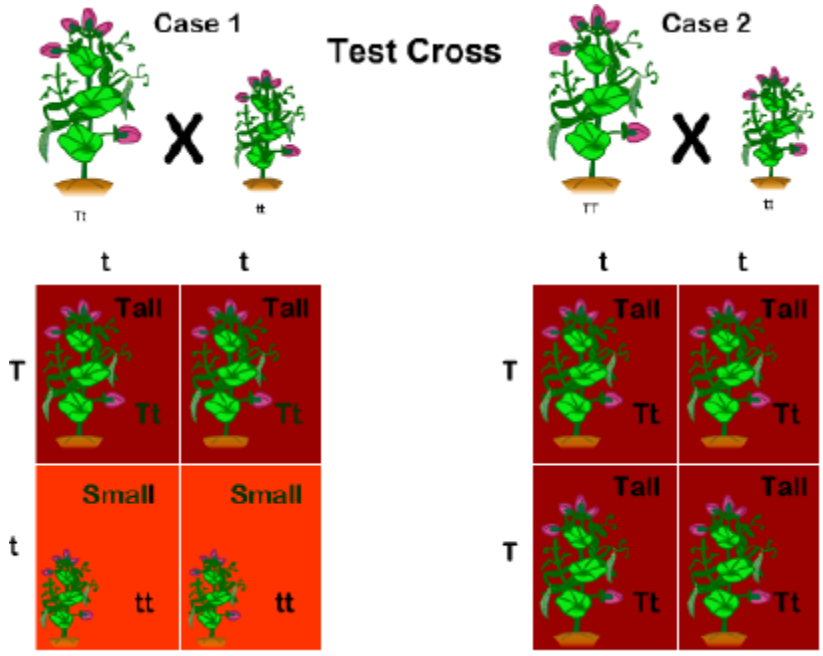
- This law states that the two alleles of a pair segregate or separate during gamete formation such that a gamete receives only one of the two factors.
- In homozygous parents, all gametes produced are similar; while in heterozygous parents, two kinds of gametes are produced in equal proportions.

Test Cross

Test Cross and Back Cross

Test Cross

- Cross between F_2 progeny and its homozygous recessive parent
- This cross determines whether the dominant character is coming from homozygous dominant genotype or heterozygous genotype. (e.g., tallness coming from TT or Tt)
- When TT is crossed with tt, we obtain all Tt (tall) individuals in the progeny. Whereas when Tt is crossed with tt, we obtain Tt (tall) and tt (dwarf) individuals in the progeny.
- Therefore, if tallness is coming from TT, then we obtain all tall progenies in test cross. We obtain both tall and dwarf varieties in test cross, if tallness is coming from Tt.



Back Cross

- When an F1 hybrid is crossed with one of the homozygous parent from which it was derived, is known as back cross.
- This test confirms the Mendel's law of segregation.
- For example, when tall pea plants (TT) is crossed with dwarf pea plants (tt), the resulting F1 generation will contain all tall pea plants (Tt).
- Then, the F1 individual instead of selfing, was crossed with one of its parent either TT or tt, we obtain all the tall individuals in the progeny.

Backcross : Tt * TT

Gametes	**T**	**T**
T	**TT** **(Tall)**	**TT** **(Tall)**

t	**Tt** **(Tall)**	**Tt** **(Tall)**

Incomplete Dominance

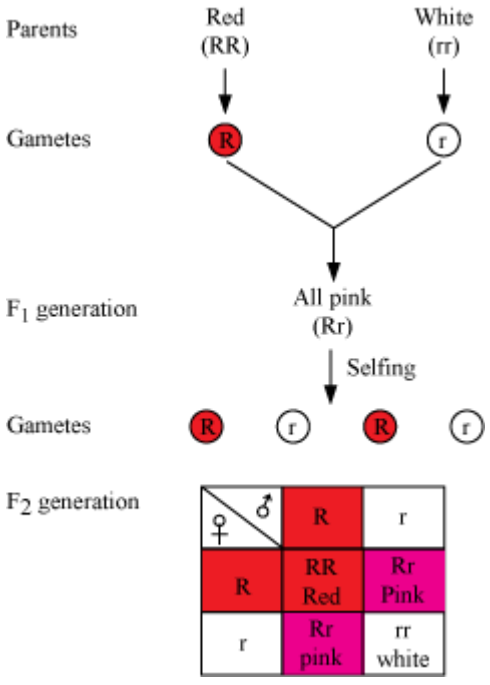
Incomplete Dominance

- In incomplete dominance, F_1 generation has a phenotype that does not resemble either of the two parents, but is a mixture of the two.

- Example – Flower colour in dog flower (snapdragon), where:

- RR – Red flowers
- rr – White flowers
- Rr – Pink flowers

- Here, genotypic ratio remains same as in Mendelian crosses, but phenotypic ratio changes since complete dominance is not shown by R (hence, incomplete dominance).



- Phenotypic Ratio – 1:2:1 that denotes Red: Pink: White
- Genotypic Ratio – 1:2:1 that denotes RR: Rr: rr

What is Dominance?

- A diploid organism produces two copies of a gene, which need not be identical and may have minor alterations.
- Suppose a normal gene produces a product P. Then, the altered version of it must produce a non-functional product P′ or no product at all.
- The altered version of the gene must not perform the functions that a normal gene performs. It must affect the phenotype.
- The original gene is said to be dominant while the modified gene is recessive.

Co-dominance

Co-dominance

- In co-dominance, the F_1 progeny resembles both the parents.
- Example: ABO blood groups in human beings
- ABO blood groups are controlled by gene *I*. Gene *I* has three alleles, I^A, I^B and *i*. A person possesses any two of the three alleles.
- I^A and I^B dominate over *i*. But with each other, I^A and I^B are co-dominant.

- I^A and I^B contain A and B types of sugar, while *i* does not contain any sugar.

Allele from Parent 1	Allele from Parent 2	Genotype of offspring	Blood type of offspring
I^A	I^A	$I^A I^A$	A
I^A	I^B	$I^A I^B$	AB
I^A	i	$I^A i$	A
I^B	I^A	$I^A I^B$	AB
I^B	I^B	$I^B I^B$	B

I^B	i	$I^B i$	B
i	i	$i\,i$	O

- Multiple alleles: When more than two alleles control a character, as in human blood groups
- Multiple alleles are used in population studies.

Pleiotropy

- When a single gene is responsible to have multiple phenotypic effect, it is known as **pleiotropy**.
- The products of gene [protein] give rise to many functional traits
- Most common example-coat colour in Mice

EXAMPLE

- In mice, allele 'Y' control two functional characters i.e. coat colour [yellow/grey] and survival.
- The yellow coat colour is dominant over gray coat colour.
- When this allele is present in homozygous recessive form [yy], the mice has coat colour grey.
- When this allele is present in homozygous dominant form, (YY), the coat colour is yellow but mice do not survive as this genotype proves lethal for mice.
- When this allele is present in heterozygous condition, mice with yellow coat colour survived.
- When a cross is made between two yellow mice, the ratio obtained is 2:1.

Parent Yellow mice × Yellow mice

Yy Yy

Gametes	Y	y
Y	YY	Yy
y	Yy	yy

- In the above cross, 1 mice with homozygous genotype (YY) did not survive. So the ratio was 2:1 i.e. two yellow-coloured mice and one grey-coloured mouse.
- These genes are also known as **lethal genes**.

Complementary and Supplementary Genes

Supplementary or Modifying Genes

- These are non- allelic genes that interact with each other to produce new trait but, when one gene is present alone, it produces its own trait.

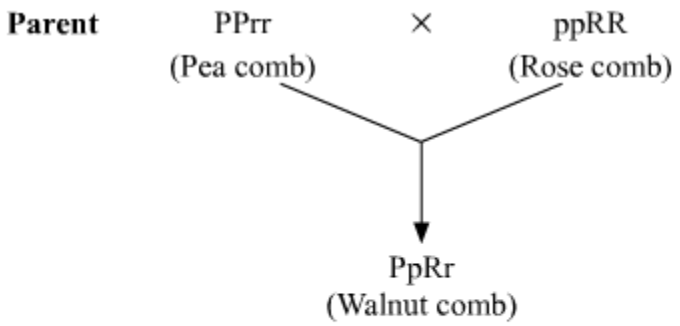
- The interaction of supplementary genes can be understood with the help of example of coat colour in mice or with the help of types of comb in chickens.

Inheritance of comb Types in Chickens (Domestic Fowls)

- In domestic fowls, three different types of comb are known; **Rose comb**, **Pea comb** and **single comb**.

- **Rose comb** and **Pea comb** are dominant over **single comb** i.e., the genotype of Rose comb is [RRpp], Pea comb rrPP whereas single comb is (rrpp)

- When a cross is made between true varieties of domestic fowl, one with Rose comb and other with Pea comb, a new type of comb i.e. **Walnut comb** was observed in offsprings.



When F_1 generation was self crossed

PpRr (walnut) × PpRr (walnut)

Gametes	PR	Pr	pR	pr
PR	Walnut PPRR	Walnut PPRr	Walnut PpRR	Walnut PpRr
Pr	Walnut PPRr	Pea PPrr	Walnut PpRr	Pea Pprr
pR	Walnut PpRR	Walnut PpRr	Rose ppRR	Rose ppRr
pr	Walnut PpRr	Pea Pprr	Rose ppRr	single pprr

Walnut	:	Rose	:	Pea	:	Single
9	:	3	:	3	:	1

- Thus, it is clear from the given cross that where both the dominant alleles 'P' & 'R' are present, walnut comb is observed. Individually, they produce pea and rose comb respectively.

Complementary Genes

- These are non allelic genes that interact with each other to produce a particular trait but none of them shows the effect when present independently.

The interaction of complementary can be understood with the help of an example of flower colour in lathyrus odoratus (sweet pea).

Inheritance of Flower Colour in *Lathyrus odoratus* (Sweet pea)

- Different varieties of sweet pea, on breeding, produce white coloured flowers with genotype PPcc and ppCC.

- When a cross is made between the two varieties (PPCC × ppcc) artificially, all red/purple coloured flowers were obtained instead of white colour, with genotype PpCc as shown in the given cross

Parent PPCC × ppcc

F_1 generation PpCc (purple)

The F_1 generation was self crossed

PpCc × PpCc

Gametes PC, Pc, pC, Pc

Gametes	PC	Pc	pC	pc
PC	Purple PPCC	Purple PPCc	Purple PpCC	Purple PpCc
Pc	Purple PPCc	White PPcc	Purple PpCc	White Ppcc
pC	Purple PpCC	Purple PpCc	White ppCC	White ppCc
pc	Purple PpCc	White Ppcc	White ppCc	White ppcc

Purple Flower : White Flower

9 : 7

- It is clear from the given cross that when both the alleles'P' & 'C' are present together in dominant form, purple coloured flowers appear and when either of the two is absent, white coloured flowers appear.
- These results were totally different from those observed by Mendel. According to Mendel, the phenotypic ratio should be 9 : 3 : 3 : 1 but it came out to be 9 (purple) : 7 (white)

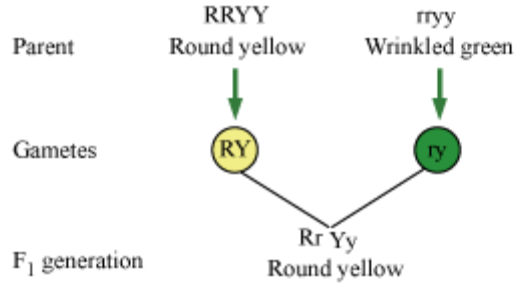
Molecular Basis

- Thus, it can be concluded that the flower colour in sweet pea is controlled by complementary genes, C and P.
- Gene C produces the raw material for formation of purple pigment, anthocyanin while gene P produces enzymes that convert the raw material into the pigment, anthocyanin.
- Thus, at least one P and C genes should be present for the appearance of purple flowers.

Inheritance of Two Genes (Dihybrid Cross) & Law of Independent Assortment

Inheritance of Two Genes (Dihybrid Cross)

- In dihybrid cross, we consider two characters. (e.g., seed colour and seed shape)
- Yellow colour and round shape is dominant over green colour and wrinkled shape.



	RY	rY	Ry	ry
RY	RRYY Round yellow	RrYY Round yellow	RRYy Round yellow	RrYy Round yellow
rY	RrYY Round yellow	rrYY Wrinkled yellow	RrYy Round yellow	rrYy Wrinkled yellow
Ry	RRYy Round yellow	RrYy Round yellow	RRyy Round green	Ryy Round green
ry	RrYy Round yellow	rrYy Wrinkled yellow	Ryy Round green	rryy Wrinkled green

- Phenotypic ratio – 9:3:3:1
  Round yellow – 9
  Round green – 3
  Wrinkled yellow – 3
  Wrinkled green –1

Law of independent Assortment

- When two pairs of traits are combined in a hybrid, one pair of character segregates independent of the other pair of character.
- In a dihybrid cross between two plants having round yellow (RRYY) and wrinkled green seeds (rryy), four types of gametes (RY, Ry, rY, ry) are produced. Each of these segregate independent of each other, each having a frequency of 25% of the total gametes produced.

Chromosomal Theory of Inheritance

Rediscovery of Mendel's Work

- Mendel's work remained unrecognised for several years because of the following reasons.
- Lack of communication and publicity
- His concept of factors (genes) as discrete units that did not blend with each other was not accepted in the light of variations occurring continuously in nature.
- Mendel's approach to explain biological phenomenon with the help of mathematics was also not accepted.
- In 1900, three scientists Hugo deVries, Correns and Von Tschermak independently rediscovered Mendel's work.

Chromosomal Theory of Inheritance

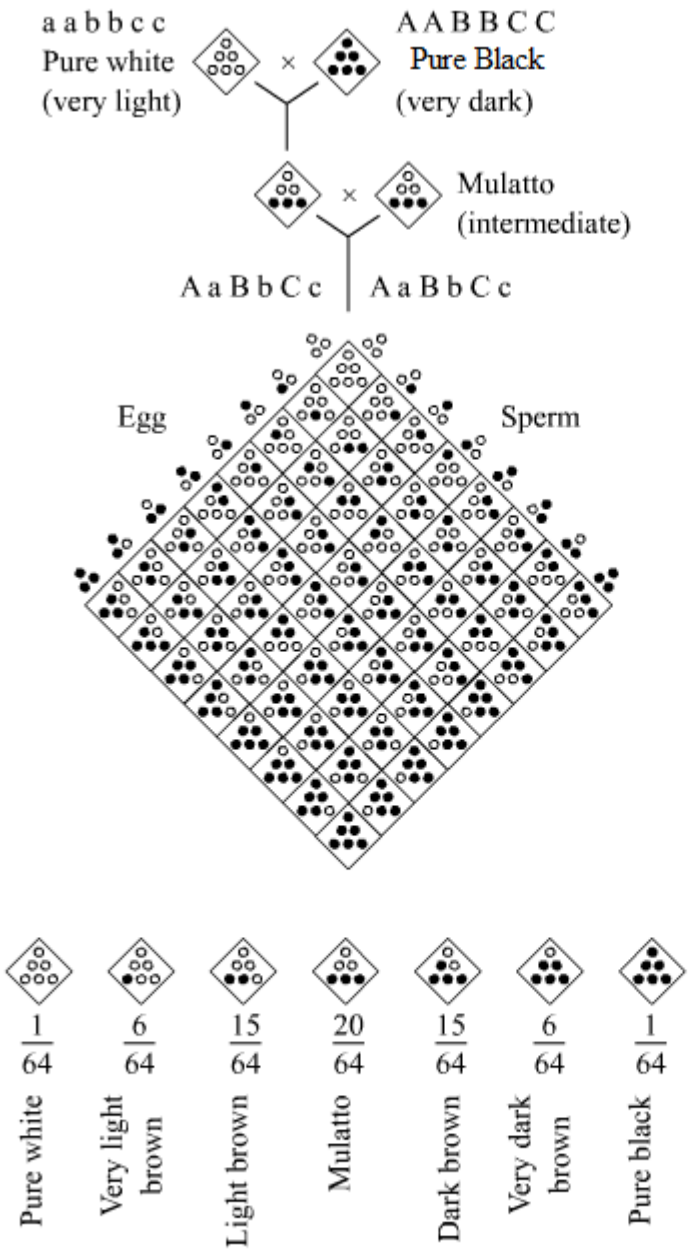
- By 1900, due to the advancement in microscopy, chromosomes were also discovered.
- Sutton and Bovery discovered that the behaviour of chromosomes was parallel to the behaviour of genes.
- Chromosomes and genes both occur in pairs—two alleles of a gene pair are located on **homologous sites of homologous chromosomes**.
- Sutton and Bovery further proposed that it is the pairing and separation of a pair of chromosomes that ultimately leads to segregation of the pair of factors they carry.
- Union of knowledge of chromosomal segregation with Mendelian principles constitutes chromosomal theory of inheritance.

Polygenic Inheritance

Polygenic Inheritance

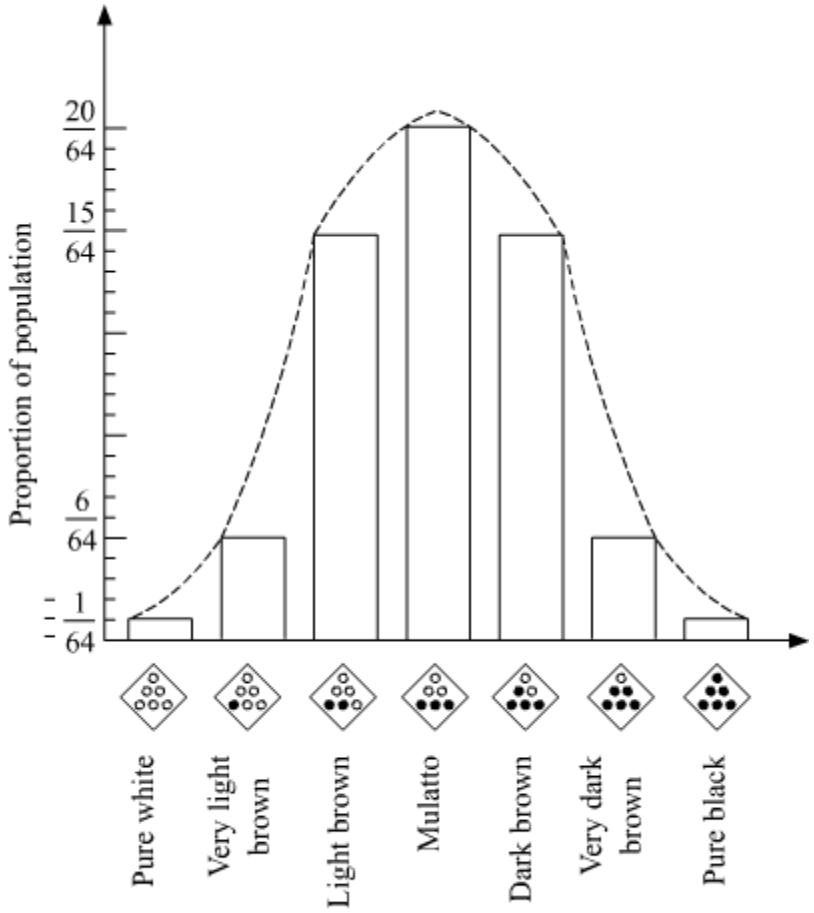
- The traits studied by Mendel in pea plant did not have any intermediate form i.e. when a pure breeding tall plant was crossed with a pure breeding dwarf plant, all the progeny were tall.
- Plants of intermediate height were not observed. Therefore, it was concluded that they were controlled by a single set of genes.
- Such type of inheritance is known as monogenic or quantitative inheritance.

- In polygenic inheritance, wide spectrum of phenotypes is observed between two extremes, for a particular trait. Such traits can be measured in terms of quantity; hence, are also known as quantitative inheritance.
- The expression of quantitative traits is controlled by more than one pair of genes and the environment also contributes towards such type of inheritance.
- The most common example of polygenic inheritance is observed in the inheritance of skin colour in human
- It was first studied by C.B. Davenport (1913).
- In humans, the skin colour varies from very dark, to dark, to light or very light. Skin colour is decided mainly by the quantity of the pigment, melanin. More the secretion of this pigment, more dark will be the colour of skin.
- There are three pair of genes Aa, Bb & Cc that control the skin colour. Each dominant allele contributes to dark colour incompletely but when three dominant are present together, the skin colour is very dark [AABBCC]
- When the genes are present in recessive form, the skin shade is very light (aabbcc)
- The cross made between a very dark (AABBCC) and very light (aabbcc) leads to intermediate colour of offsprings called **mulatto** (AaBbCc)
- The cross can be represented as follows;



A cross showing polygenic (quantitative) inheritance of human skin colour. Each dominant gene is represented by a shaded circle and each recessive gene by an unshaded circle

- From the given cross, it can be concluded that the skin colour of F_2 generation varies in accordance with the number of polygenes they inherit.
- The frequency distribution of human skin colour can be represented by bell shaped curve, as shown below



Frequency distribution of human skin colour in a population

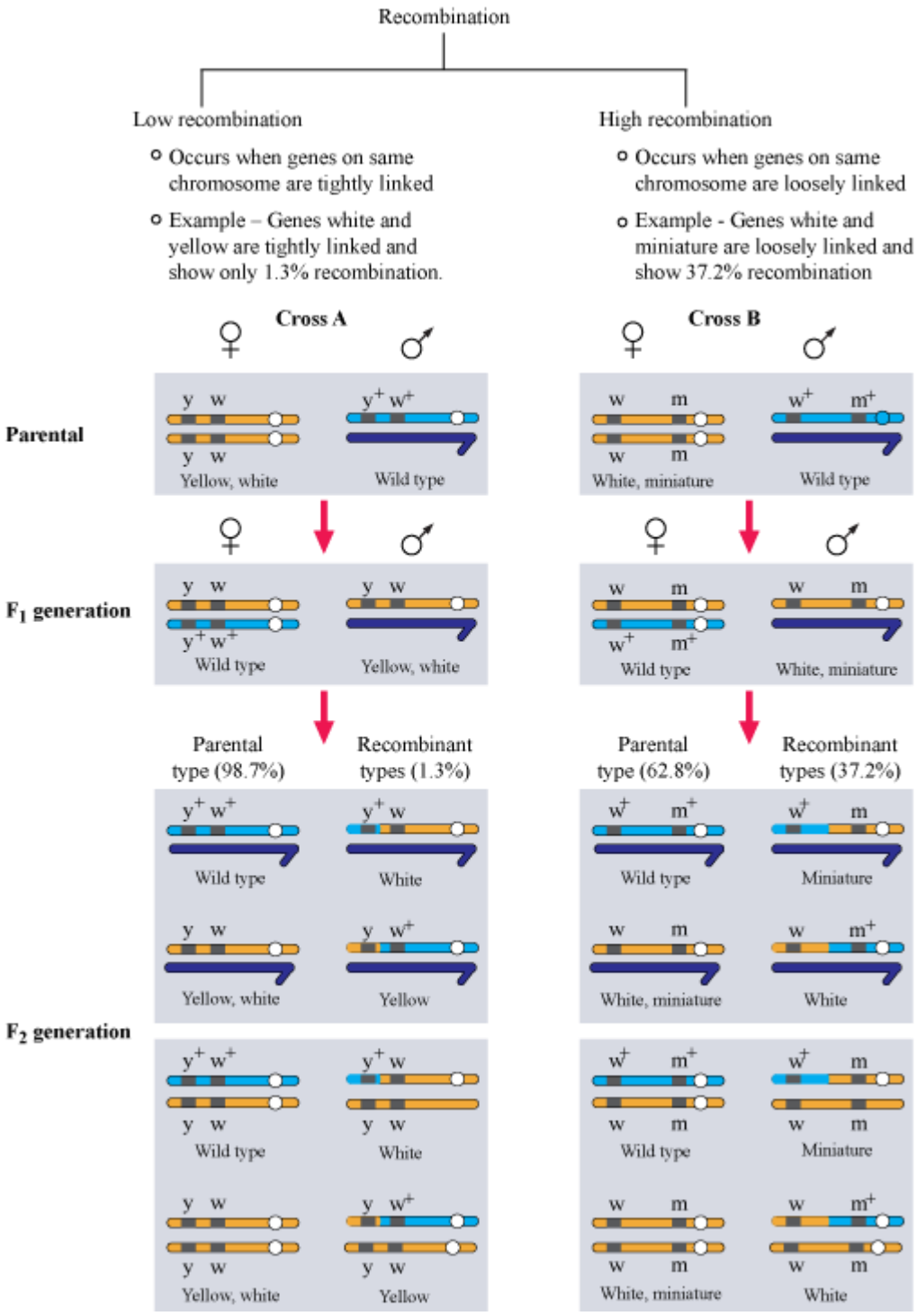
- From the curve, it is clear that the number of intermediate types increase with the increase in number of polygenes but the number of parental type remains the same.
- In other words, the heterozygous parents having a skin colour like that of a **mulatto** can produce offsprings with skin colours that are darker or lighter than themselves.

Linkage and Recombination

Linkage and Recombination

- Thomas Hunt Morgan discovered the basis of variations that sexual reproduction produced.
- He worked on fruit flies, *Drosophila melanogaster*. He chose *Drosophila* because of the following reasons:
- They were suitable to grow on synthetic medium in laboratory.

- Their life cycle is complete in two weeks.
- Single mating produces many progeny flies.
- Clear differentiation of sexes – Easily distinguishable male and female
- Hereditary variations clearly visible with low power microscopes
- Morgan's experiment
- Dihybrid cross was carried out on fruit flies. Yellow bodied, white eyed females were crossed with brown bodied, red eyed males.
- F_1 progeny was obtained, which were inter-crossed.
- F_2 progeny was obtained and F_2 ratio was observed.
- F_2 ratio was observed to be significantly different from 9:3:3:1 as observed in Mendelian dihybrid cross.
- Explanation of deviation from Mendelian ratio:
- Genes involved are located on X chromosome.
- When two genes are located on the same chromosome, the proportions of parental gene combinations were much higher than those of non-parental.
- Linkage – Physical association of genes on a chromosome
- Recombination – Non-parental gene combination



- Alfred Sturtevant utilised the knowledge of frequency of gene recombination as a measure of physical distance between two genes and to map their position on chromosomes.
- In this way, genetic maps were prepared, which are extensively used today for genome sequencing projects as in human genome project.

Sex Determination

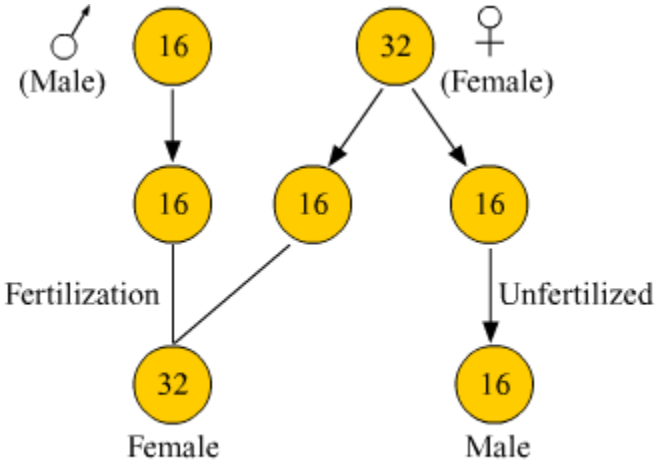
Sex Determination

- Henking discovered the genetic/chromosomal basis of sex determination by working on insects. He observed specific nuclear structures during spermatogenesis in insects. He named these structures as X bodies.
- He observed that after spermatogenesis, 50% of the sperm obtained these structures, while 50% did not.
- Later on, it was found that the X body observed by Henking was actually a chromosome and thus, this chromosome was named X chromosome.
- Chromosomes involved in sex determination are called sex chromosomes, while the other chromosomes are called autosomes.
- XO type of sex determination
- Other than autosomes, at least one X chromosome is present in all insects.
- Some sperms contain X chromosomes, while some do not.
- Eggs fertilised by sperms having X chromosomes become females. So, females have two X chromosomes.
- Eggs fertilised by sperms not having X chromosomes become males. So, males have only one X chromosome.
- Example of organisms with XO type of sex determination − Insects
- XY type of sex determination
- Males have X chromosome and its counterpart Y chromosome, which is distinctly smaller. Hence, males are XY.
- Females have a pair of X chromosomes. Hence, females are XX.
- Example of organisms with XY type of sex determination − Humans and *Drosophila*
- Male heterogamety − XO and XY types of sex determination are examples of male heterogamety.
- In XO type, some gametes have X chromosomes, while some gametes are without X chromosomes.
- In XY type, some gametes have X chromosomes, while some gametes have Y chromosomes.

- Female heterogamety – ZW type of sex determination is an example of female heterogamety.
- In ZW type, the female has one Z and one W chromosome, while the male has a pair of Z chromosomes.

Sex Determination in honeybees -

- Honey bees show a special mechanism of sex determination called the haplo-diploidy.
- In honeybees, the sex of the offspring is determined by the fertilization or non-fertilization of eggs, rather than the presence or absence of sex chromosomes.
- The unfertilized honey bee eggs normally develop into male progeny and are haploid in nature (have just one set of chromosomes).
- The fertilized honey bee eggs, differentiate into queens and worker bees and are diploid in nature (have two sets of chromosomes).



Sex determination in honeybees

What is Sex Linked Inheritance?

Genes carried by sex chromosome are said to be sex linked. The appearence of a trait because of the presence of an allele either on X chromosome or Y chromosome is called Sex-linked Inheritance.

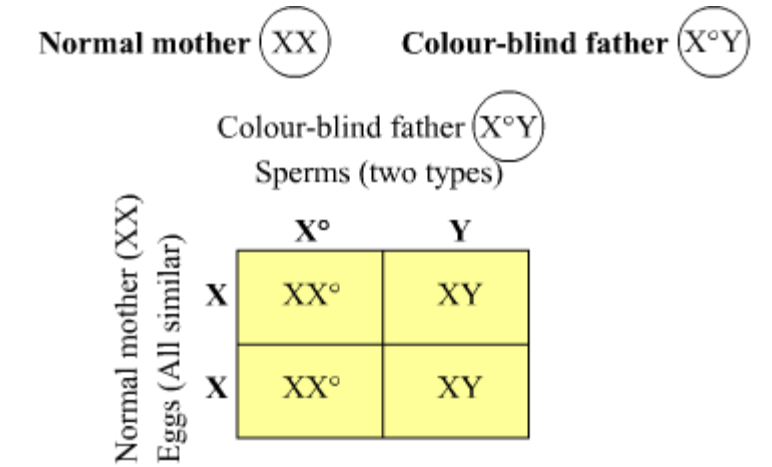
Diseases observed in X-linked Inheritance

Any disease that is determined by the sex chromosomes, or that occurs due to defects in a gene on the sex chromosomes, is said to be sex linked. These diseases can descend to the offsprings from the parents through gametes. The diseases that occur due to any defective gene present on X chromosomes are known as X-linked diseases. Most of these diseases are recessive in nature, that means, in the case of females, the defective allele should be present on both of the X chromosomes.

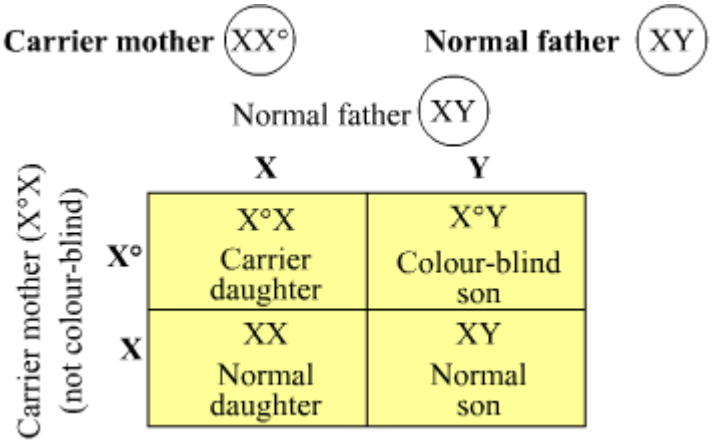
These disorders are more commonly observed in males as they have only a single X chromosome. A single recessive gene on that X chromosome will cause the disease. Most commonly observed diseases are:

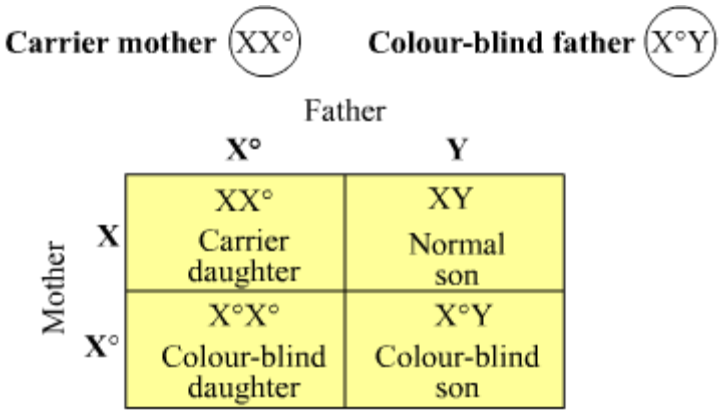
- Haemophilia - It is a genetic disorder under which the sufferer (recessive X bearing male and homozygous recessive female) is at a risk of excessive blood loss leading to death as blood fails to clot.
- Colour blindness - It is also a genetic disorder in which the sufferer is unable to identify or distinguish between various colours.

The following example will explain the sex-linked inheritance of colour-blindness in humans more clearly.



XX° : Daughters - heterozygous dominant, normal vision
XY : Normal sons





Criss-Cross Inheritance

The transfer of a gene from mother to son or father to daughter is known as criss-cross inheritance. For example, as in X-chromosome linkage.

Mutation

Mutation

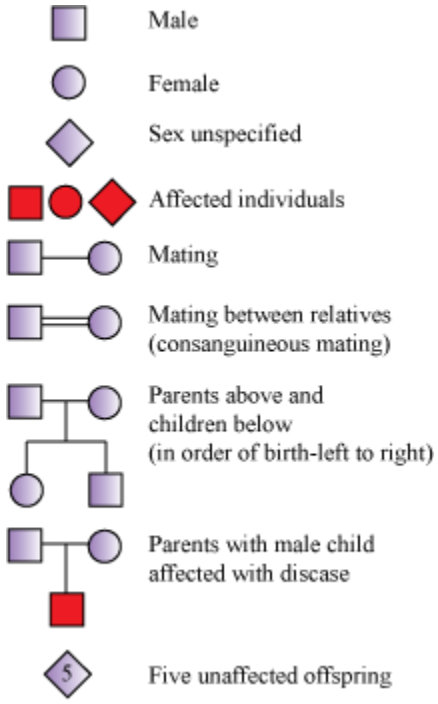
- Alteration of DNA sequence resulting in changes in genotype and phenotype of organisms
- DNA helix runs in a chromatid, hence any change (insertion or deletion) in the DNA sequence affects the chromosome.
- Point Mutation – Mutation arising due to change in single base pair of DNA as in sickle cell anaemia
- Frameshift Mutation – Mutations arising due to deletion or insertion in DNA sequence
- Mutagens – Chemical or physical agents that lead to mutations
  Example – UV radiations

Effects of Mutations on Genetic Code

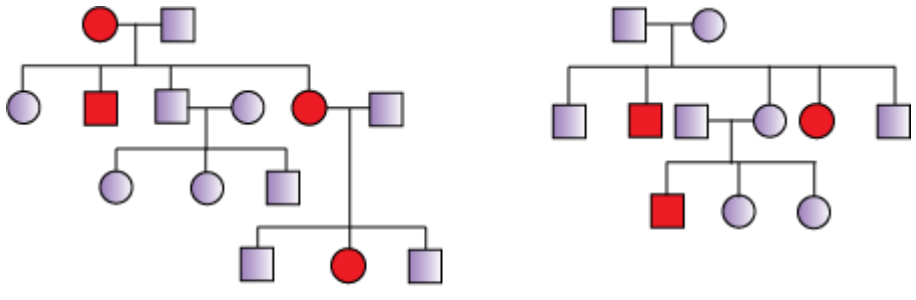
- Mutations include insertions, deletions, and rearrangements.
- Mutation results in changed phenotype and diseases such as sickle cell anaemia. (Change Glu → Val in gene coding for beta globin chain of haemoglobin) Such mutations are called **point mutations**.
- Insertion or deletion of a single base pair disturbs the entire reading frame in mRNA. Such mutations are called **frameshift mutations**.
- Frameshift mutations hold the proof of the fact that codon is triplet because if we insert three or multiple of three bases followed by the deletion of same number of bases, then the reading frame will remain unaltered.

Pedigree Analysis

- Pedigree analysis is the analysis of inheritance of traits in several generations of a family.
- A particular trait under study is represented in a family tree.
- By using pedigree analysis, inheritance of a specific trait, abnormality or disease, can be traced.
- DNA is believed to be the carrier of genetic information, which passes unaltered from generation to generation. Mutations occasionally alter the genetic material and genetic diseases are believed to be associated with these alterations only.
- Standard symbols in pedigree analysis are as follows:



- Pedigree chart is represented as follows:



(a) (b)

Chart (a) represents inheritance of an autosomal dominant trait as in muscular dystrophy.
Chart (b) represents inheritance of an autosomal recessive trait as in sickle cell anaemia.

Genetic Disorders

Genetic Disorders

- Include Mendelian disorders and chromosomal disorders

Mendelian Disorders

- Characterized by mutation in a single gene
- Their mode of inheritance follows the principles of Mendelian genetics.

- Mendelian disorders can be

- autosomal dominant (muscular dystrophy)
- autosomal recessive (sickle cell anaemia)
- sex linked (haemophilia)

- Haemophilia

- Sex-linked recessive disease
- Transmission − From unaffected female (carrier) to male progeny
- Females act as carriers of disease, but rarely suffer from haemophilia since for a female to become haemophilic, the mother should be carrier and father should be haemophilic.
- In this disease, protein involved in blood clotting is affected. Therefore, even a simple cut results in uncontrolled bleeding.

- Sickle cell anaemia

- Autosomal recessive disease
- Transmission − From parent to offspring when both parents are carriers of disease
- Pair of alleles Hb^A and Hb^S controls the expression of this disease.
  Hb^A and Hb^A – Normal
  Hb^A and Hb^S – Carrier of disease
  Hb^S and Hb^S – Diseased
- Cause of the disease − Change in gene causes the replacement of GAG by GUG leading to the substitution of Glu by Val at sixth position of beta globin chain of haemoglobin.
- The mutant haemoglobin so formed polymerises at low oxygen tension, resulting in change in shape of RBC to sickle-like.
-
- Albinism
- Autosomal recessive disease
- Transmission occurs from parent to offspring when both or either of the parent is carrier of the disease.
- In this disease, a pigment called melanin is absent which imparts colour to our eyes, skin and hair. Due to this, the skin becomes pale, hair become white and eyes appear pink due to the absence of melanin.

- Phenylketonuria

- Autosomal recessive disease
- Phenylalanine $\xrightarrow{\text{Enzyme}}$ Tyrosine
  The enzyme responsible for this conversion gets mutated.
- Phenylalanine accumulates. Then, phenylalanine gets converted to phenyl pyruvic acid. Phenyl pyruvic acid gets accumulates in brain which causes mental retardation.
- Phenylpyruvic acid also gets excreted through urine since kidneys poorly reabsorb it.
- Thalassemia
- An autosomal recessive blood disorder.
- Pair of alleles Hb^A and Hb^T controls the expression of this disease.

  Hb^A and Hb^A : Normal

  Hb^A and Hb^T : Carrier

  Hb^T and Hb^T : Diseased

  If father and mother both are the carriers (Hb^A Hb^T) of beta thalassemia.

Parents :	Hb^A Hb^T (Father)	×	Hb^A Hb^T (Mother)	
Offsprings :	Hb^A Hb^A Normal child	Hb^A Hb^T Carrier child with thalassemia trait	Hb^A Hb^T Carrier child with thalassemia trait	Hb^T Hb^T Child with severe thalassemia

  The resulting offspring will be 1 normal, 2 carriers and 1 diseased child. Thus the couple has 25% of chance for the child to inherit the two thalassemia genes.

  This disease affects the ability of body of making healthy haemoglobin and red blood cells which leads to anaemia.

  Haemoglobin is made up of four protein chains :

- **Two alpha globin** : Four genes are involved in the production of alpha globin protein chains.

- **Two beta globin** : Two genes are involved in the production of beta globin protein chains.

  There are two types of thalassemia :

- **Alpha thalassemia** : It occurs when one or two of the four genes involved in the production of alpha globin is missing or mutated.

- **Beta thalassemia** : It occurs when one or both the genes involved in the production of beta globin is missing or mutated.

  Both alpha and beta thalassemia are of the two forms :

  Thalassemia major : When an individual receive the altered or mutated gene from both the parents, it results in the development of thalassemia major.

  Thalassemia minor : When an individual receive the altered or mutated gene only from one of the two parents, it results in the development of thalassemia minor.

  Symptoms of thalassemia

  (i) Thalassemia minor results only in mild anaemia, characterized by low haemoglobin level.

  (ii) Thalassemia major also known as Cooley's anaemia. In thuis disease affected infants are normal but as they reaches 6 to 9 months, they develop severe anaemia, skeletal deformities, jaundice, fatigue etc.

Chromosomal Disorders

- Total number of chromosomes in humans = 46 (23 pairs)
- Total 23 pairs = Autosomes (22 pairs) + Sex chromosomes (1 pair)
- Monosomy − Lack of any one pair of chromosomes
- Trisomy − Inclusion of an additional copy of chromosomes
- Aneuploidy − Loss or gain of chromosomes due to failure of segregation of chromatids during cell division
- **Down's Syndrome**
- Cause: Presence of an additional copy of chromosome 21 (Trisomy of 21)
- Affected individual has short stature, small, round head, furrowed tongue, partially opened mouth, palm crease, congenital heart disease and mental retardation.

- **Klinefelter Syndrome**

- Cause: Additional copy of X chromosome, i.e., 47 chromosomes (XXY)
- Affected individual has an overall masculine development with gynaecomastia; individual is sterile

- **Turner's Syndrome**

- Cause: Absence of one X chromosome, i.e., 45 chromosomes (XO).

- Affected females are sterile; have rudimentary ovaries; secondary sexual characters are absent.

- **Cri-du-chat syndrome**
- Cause: Deletion on the short arm of chromosome number 5.
- Affected infants produce high-pitched cry that resembles the sound of cat, low birth weight, small head size and retarded growth.