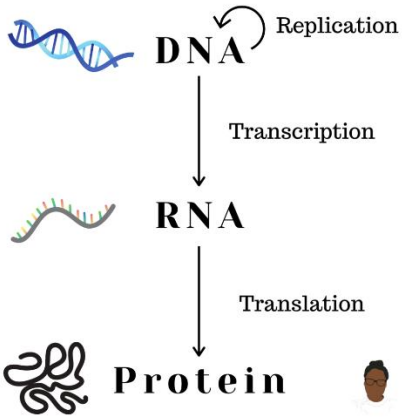
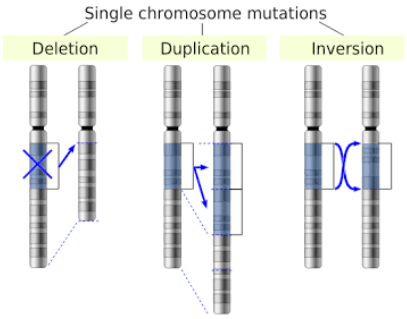
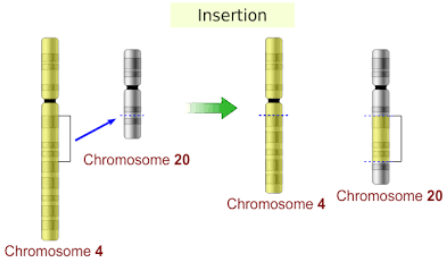
Mutation

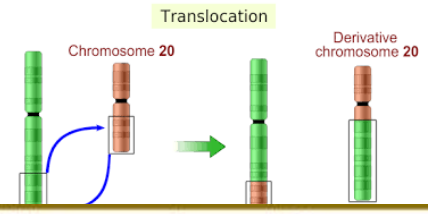






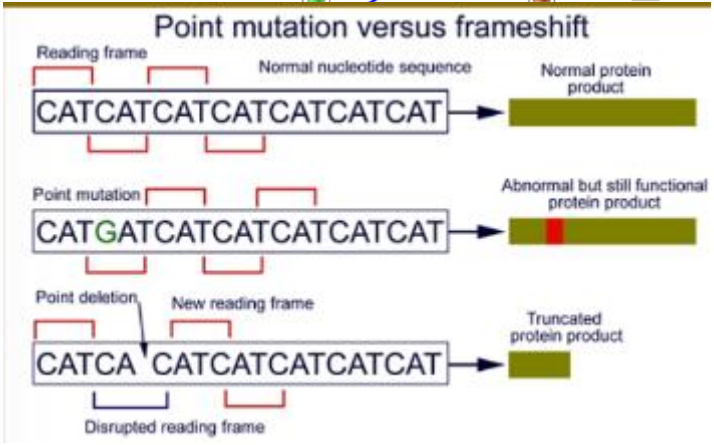
- Any changes in the sequence of DNA is called a mutation. Viable mutations get inherited from one generation to another. A mutation changes the genotype as well as the phenotype of an organism
- It is linked to various diseases, but not all mutations are harmful
- Changes like, deletion, insertion, duplication, substitution, etc. result in mutation. A mutation is the major cause of cancer.
- Mutagens are the agents that induce mutation:

a) **Physical Mutagens**: UV Radiation, Alpha, beta Gama , X- Rays etc.
b) **Chemical Mutagens:** Mustard gas, Ethyl methanesulfonate (EMS) etc.



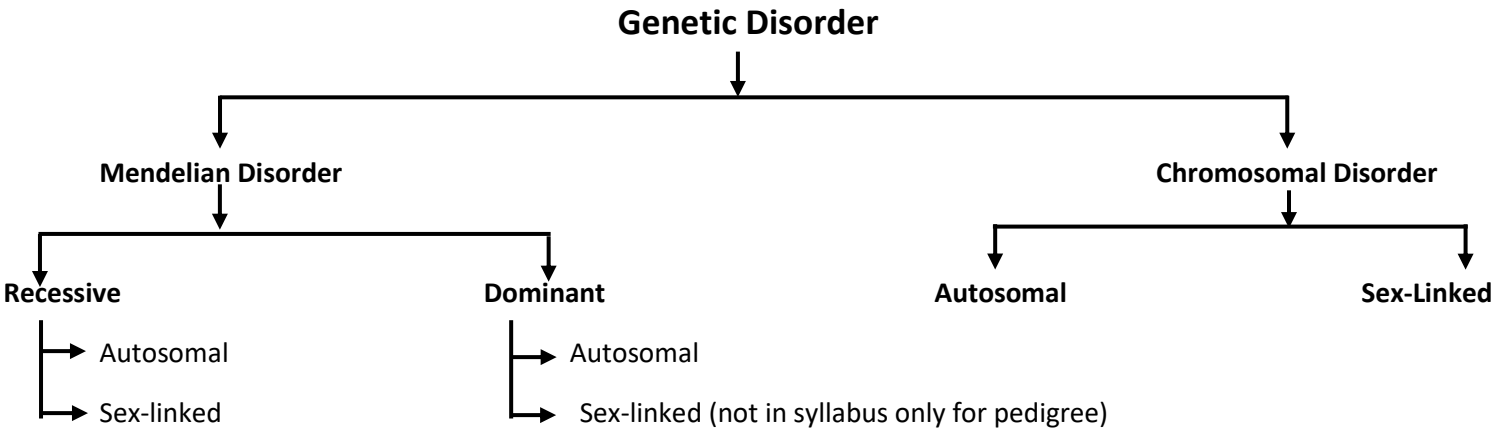
- There are two types of genetic mutation:

1. **Point mutation:** A **substitution** in the single base pair of DNA, e.g. in the **sickle cell anaemia**.
2. **Frameshift mutation:** It results from the **insertion or deletion** of one or more pairs of bases in DNA. it changes the reading frame of triplet codons, that code for certain amino acids of the protein.



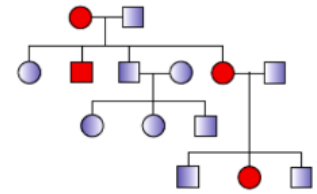
Genetic Disorders

There are many disorders in the human being that are inherited and caused due to mutation in the gene or alteration in chromosomes.

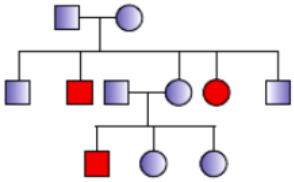


Pedigree Analysis helps in determining the risk of getting a genetic disorder in the offsprings by studying the inheritance pattern of a particular trait present in various generations of an individual.

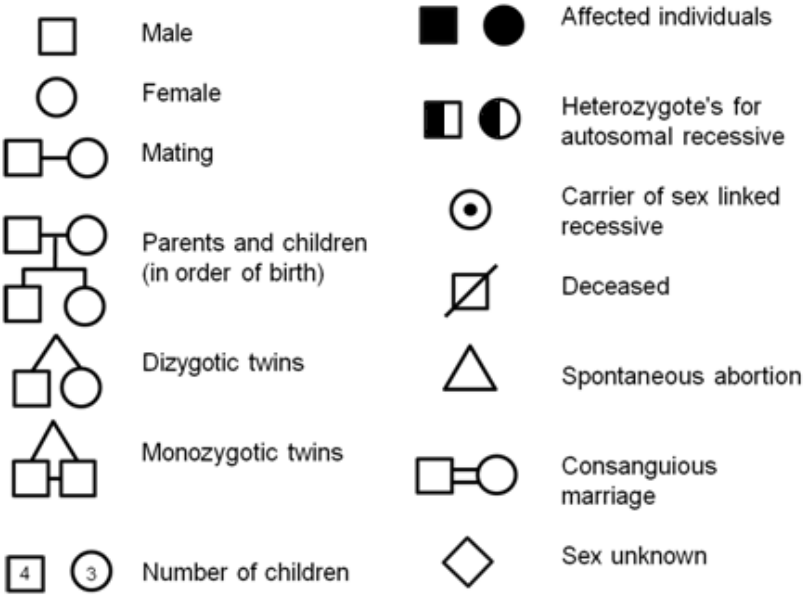
Help to understand family history and weather trait is dominant or recessive



Pedigree analysis of Autosomal dominant trait (E.g. Myotonic dystrophy)

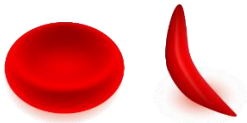
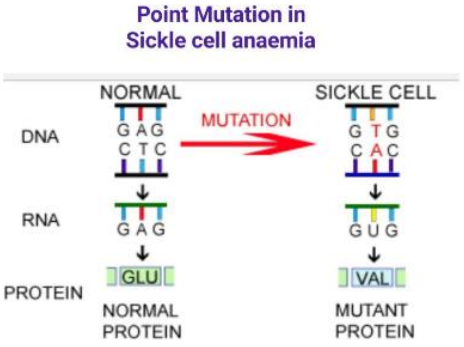
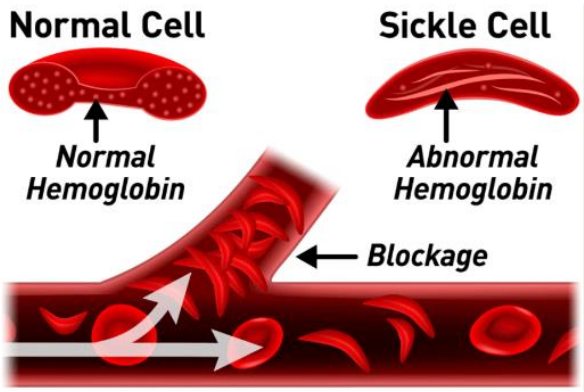


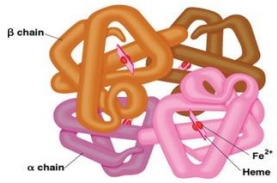
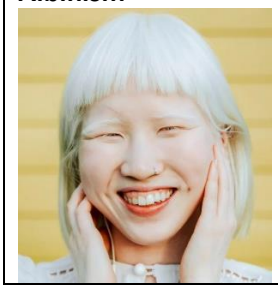
Pedigree analysis of Autosomal recessive trait (E.g. Sickle-cell anaemia)



Autosomal Recessive Disease

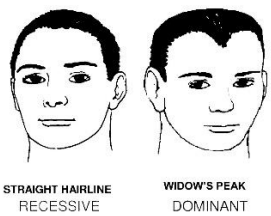
(Disease transfer from parents to offspring if at least both parents are carrier of disease)

Phenylketonuria (PKU)	Inborn error of metabolism in which individual lack enzyme phenylalanine hydroxylase that convert phenylalanine to tyrosine. Results in accumulation of phenylalanine that converts to phenylpyruvic acid & ketone derivatives that causes Mental Retardation if reaches brain and extra are excreted by urine because of poor absorption of kidney.
Cystic fibrosis	Genetic disorder affecting the lungs, pancreas, and other organs, causing production of thick sticky mucus that plug to duct & pathway. Frequent lung infections, digestive problems, poor growth, salty-tasting skin.
Sickle cell anaemia 	Sequence for Normal Hemoglobin AUG GUG CAC CUG ACU CCU GAG GAG AAG UCU GCC GUU ACU START Val His Leu Thr Pro Glu Glu Lys Ser Ala Val Thr Sequence for Sickle Cell Hemoglobin AUG GUG CAC CUG ACU CCU GUG GAG AAG UCU GCC GUU ACU START Val His Leu Thr Pro Val Glu Lys Ser Ala Val Thr  ➢ Qualitative Disorder of haemoglobin. ➢ Disease is controlled by a single pair of allele-Heterozygous Hb^A Hb^S (Carrier) present on chromosome no. 11. ➢ Only Homozygous Hb^S Hb^S are Affected. ➢ Defect caused by a single point mutation in the beta-globin chain of haemoglobin. ➢ Glutamic Acid (GLU) replased by Valine (VAL) at 6th position of beta-globin chain. ➢ Under low oxygen condition mutant haemoglobin undergo polymerisation causing change in RBC shape to Sickle shape (less life span) leading to Anaemia and other complications. 

Thalassemia  	➢ Blood disorder causing abnormal (less) haemoglobin production. ➢ Caused due to either mutation or deletion of gene result in reduce rate of synthesis of on of the globin chain forming abnormal haemoglobin. ➢ Anaemia, fatigue, weakness, organ damage. ➢ Quantitative Disorder of haemoglobin. ➢ **Alpha-thalassemia** –Controlled by two closely linked gene HBA1 and HBA2 present on the chromosome 16 of each parent. • Caused due to mutation or deletion of one or more of the four gene. • Its severity depends on number of affected alpha globin genes (more gene affected less goblin molecule produce). • Causes moderate to severe anaemia, jaundice, and an enlarged spleen. • *Hydrops fetalis* is the most severe form and often leads to stillbirth or death shortly after birth. ➢ **Beta-thalassemia** – Controlled by a single gene pair HBB on chromosome no. 11 of each parent. • Occur due to mutation of one or both gene. • *In major cases* -profound anemia, frequent blood transfusions, bone deformities, enlarged spleen etc. Individuals require lifelong supportive care, including regular blood transfusions, iron chelation therapy, and possible stem cell transplantation.
Albinism 	➢ Mutations of certain genes that affect the amount of melanin (controls skin, eye and hair colour) decreased or absent in body ➢ Result in extremely pale skin, eyes and hair.

Autosomal Dominant Disorder

- A single parent carrying the disease may transmit the disease to offspring.
- Normal children do not carry defective gene and there is no carrier.

Myotonic dystrophy	• Characterized by progressive muscle wasting or weakness. • Prolonged muscle contractions ex: a person may have difficulty releasing their grip on a doorknob or handle.
Huntington's disease	The disorder causes nerve cells in parts of the brain to gradually break down and die. Affects the areas of brain that help to control voluntary movement. • Muscle rigidity or muscle contracture (dystonia) • Slow or unusual eye movements. • Impaired gait, posture and balance. • Difficulty with speech or swallowing.
Widow's peak  	V-shaped hairline at the center of the forehead. Can have both genetic and environmental factors.
Polydactyly	Presence of extra finger on hands or toe on feet.
Dwarfism	A genetic abnormality result in short skeleton.

Sex-Linked Recessive Disorder (Criss-Cross Disease)

- Disease transfer from Mother to Son and from Father to Daughter.
- A daughter will be affected only if the father is affected and mother is carrier.
- There is a 50 percent probability of a carrier female to transfer the disease to sons

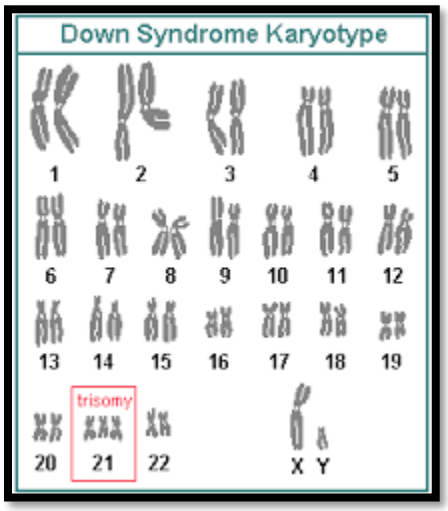
Haemophilia	X-Linked disease- in which a single protein part of cascade (group) of protein involved in blood clotting gets affected result in prolonged bleeding (both internal & external) difficulty in forming clot. ➢ Heterozygous **Female X^HX – Carrier**. ➢ **Male X^HY- Affected** ➢ Possibility of **Female** getting **affected (X^HX^H)** is extreamly low and unviable as mother needs to be at least carrier and father affected. 1. Haemophilia A (Caused by Factor VIII Deficiency): Most common (80% of all cases). 2. Haemophilia B (caused by Factor IX Deficiency): very rare known as Christmas disease and Royal Haemophilia (Found in Queen Victoria family) 3. Haemophilia C: (Caused by Factor XI Deficiency)
Colour blindness	➢ Due to mutation in X-chromosome there is defect in Red or Green Cones of eye. ➢ Results - inability to distinguish red and green colours. ➢ Found in 8% male & 0.4% female. ➢ Heterozygous **Female X^CX – Carrier**. ➢ **Male X^CY- Affected** ➢ Possibility of **Daughter** getting **affected (X^HX^H)** is low as mother needs to be at least carrier and father affected.

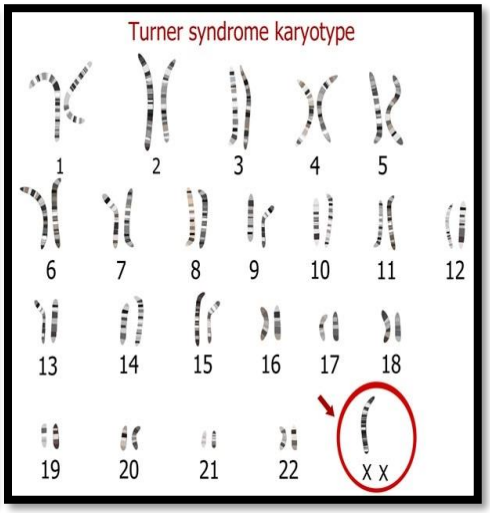
Chromosomal Disorders-

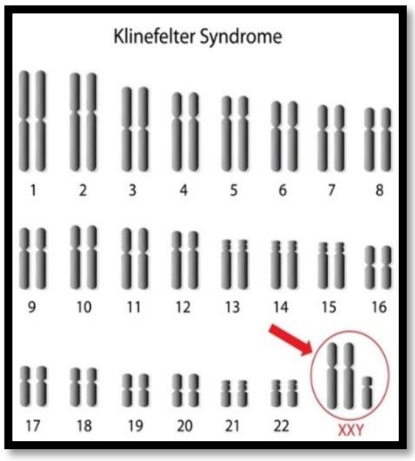
These are disorders due to excess, absence or abnormal arrangement of chromosomes

- Chromosomal disorders are of two types:
  (i) Aneuploidy- Gain or loss of one or more chromosomes. It is due to failure of segregation of chromatids during anaphase of meiosis

- **Nullisomy (2n-2):** A chromosome pair is lost from diploid set.
- **Monosomy (2n-1):** A chromosome is lost from diploid set.
- **Trisomy (2n+1):** A chromosome is added to diploid set.
- **Tetrasomy (2n+2):** 2 chromosomes are added to diploid set.







(ii) Polyploidy- It is very very rare in animals but often found in **plants**. This happens due to an increase in the full set of chromosomes. Failure of cytokinesis results in polyploidy. . e.g. '3n (triploid)', '6n (hexaploid)' etc.

Disorder	Genotypic Effect	Phenotypic Effect
Down's syndrome (Mangolism)	**Defect in :** Autosomes (Recessive disease)	• First describe by **Langdon Down-1866** • Short height with a small round head Flat from back • Big, wrinkled & Furrowed tongue with partially open mouth

	Genotype: Trisomy of 21st chromosome **No. of Chromosomes :** 47	• Broad palm with palm crease • Many loops on finger tips • Physical, psychomotor and mental development is retarded • Congenital Heart Disease • Shorter life span
Klinefelter's syndrome	**Defect in :** Sex Chromosomes **Genotype:** Trisomy of 23st chromosome- XXY **No. of Chromosomes :** 47	• Individual have overall masculine development with some feminine characteristics. • Have tall height • Development of breasts (gynecomastia) • Sterile (cannot reproduce) • Small testicles, high-pitched voice and less body hairs • Mental retardation
Turner's syndrome	**Defect in :** Sex Chromosomes **Genotype:** Monosomy of 23st chromosome- XO **No. of Chromosomes :** 45	• Only viable monosomy in humans • Sterile females (cannot reproduce) • Short height • Breasts and ovaries are underdeveloped • Lack of secondary sexual character • Thin and less pubic hairs
Triple X syndrome	**Defect in :** Sex Chromosomes **Genotype:** Trisomy of 23st chromosome- XXX **No. of Chromosomes :** 47	• Super females • Fertile Females (Can Reproduce) • Mild development delays and menstrual irregularities
XYY syndrome	**Defect in** : Sex Chromosomes **Genotype**: Trisomy of 23st chromosome- XYY **No. of Chromosomes :** 47	• Fertile Males with an unusual height • Severe acne • Below normal intelligence

Que: Differentiate between Autosomal traits and Sex-linked traits.

Autosomal traits	**Sex-linked traits**
1.Traits based on chromosomes pairs no. 1 to 22 (autosomal chromosomes).	**1. Traits based on sex chromosomes pair no. 23 (sex-chromosomes).**
2. The inheritance of autosomal traits follows Mendelian principles.	**2.The inheritance of sex-linked traits follow the criss-cross inheritance and do not follow Mendelian principles.**
3. The inheritance of autosomal traits are equal for both male and female because they both have the same number of autosomes.	**3. The inheritance of sex-linked traits mainly affects males because they only have one X chromosome whereas females have two X chromosomes, hence are least affected.**
4. The autosomal traits are classified as autosomal dominant traits and autosomal recessive traits.	**4. The sex-linked traits are classified as Sex-linked dominant traits and sex-linked recessive traits.**
5.Mostly all the alleles are involved	**5.Only alleles of X-chromosome are involved.**

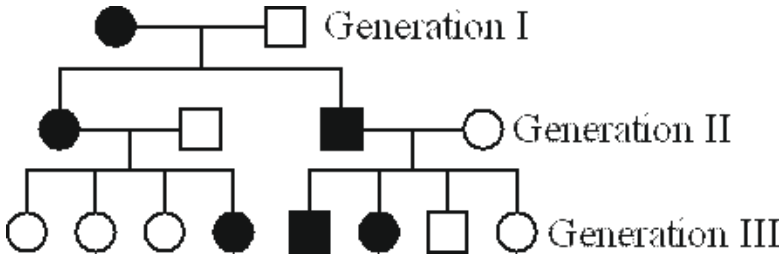
Que: What is Sickel Cell Anaemia? Why does sickle-cell anaemia persist in the human population when it is believed that the harmful alleles get eliminated from the population after a certain time?

Ans. Sickle cell anaemia is an autosomal recessive disease. Under low oxygen condition mutant haemoglobin undergo polymerisation causing change in RBC shape to Sickle shape, inhibiting the oxygen-carrying capacity of the blood as abnormal haemoglobin clump together & causes the RBCs to become rigid, hard & sickle shaped which gets accumulated together and causes difficulty to move in blood vessels and less life span of RBCs.

Despite this, it protects the carrier from malaria. Individuals with heterozygotes Hb^AHb^S survive more than the homozygotes Hb^SHb^S because they are not exposed to the same severity of risks.

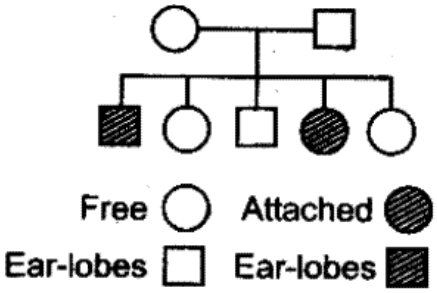
Q1) A pedigree is shown below for a disease that is autosomal dominant. The genetic made up of the first generation is

1. **AA, Aa**
2. **Aa, aa**
3. **Aa, AA**
4. **Aa, Aa.**



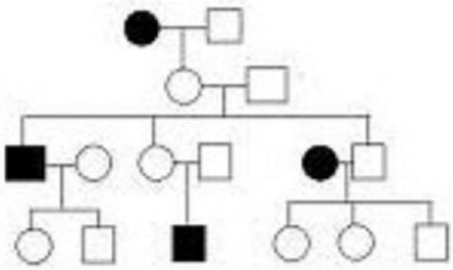
Q2) Given below is a pedigree chart of a family with five children. It shows the inheritance of attached earlobes as opposed to the free ones. Which one of the following conclusions drawn is correct?

1. **The parents are homozygous recessive**
2. **The trait is Y-linked**
3. **The parents are homozygous dominant**
4. **The parents are heterozygous**



Q4) What does the below pedigree conclude?

1. Autosomal dominant
2. Autosomal recessive
3. X-linked dominant
4. X-linked recessive



Q5) Given below is a pedigree chart showing the inheritance of a certain sex-linked trait in humans

The trait traced in the above pedigree chart is

(a) Dominant X-linked

(b) Recessive X-linked

(c) Dominant Y-linked

(d) Recessive Y-linked

(X LINKED DOMINANT)