Genetic Disorders

Classification of Genetic disorders

- Single gene disorders
  - Mendelian disorders
    1) Autosomal Dominant
    2) Autosomal Recessive
    3) X linked Dominant
    4) X linked Recessive.
    5) y linked
  - Non Mendelian Disorders
    1) Mitochondrial inheritance
    2) Genomic imprinting
    3) Trinucleotide repeat disorder
    4) Germline Mosaicism
- Chromosomal disorders
  - Structural disorders
  - Numerical disorder.
- Multi factorial

Mendelian disorders

→ caused due to gene Mutation
→ Dominant or Recessive.
→ Due to Mutation in gene, the proteins or enymes which are required for Metabolic activity are not formed so it results in disturbed Metabolism or Inborn errors.

I Phenylketonuria (PKU)
→ Discovered by A. Folling
→ It is Recessive autosomal.
→ genes located on chr. 12.
→ Enzyme phenylalanine hydroxylase is not formed due to Mutation in gene
Phenylalanine —Phenyl A. hydroxylase→ Tyrosine

Phenyl alanine

↓ Enzyme absent

X

Phenyl alanine and its derivative are collected.

→ High level of Phenyl alanine in blood and tissue fluid it is accumulated in Brain, Muscles and cartilage of legs.

→ Phenylalanine also excreted through kidney and affects kidney functions.

→ $\frac{1}{10,000}$ persons

→ effect can be reduced by using less protein diet.

II Cystic Fibrosis

→ Gene mutation occur in gene located on chromosome no 7.

→ Due to Mutation an abnormal Glycoprotein is formed which interfere with salt Metabolism Due to which there is formation of large quantity of Mucus.

→ Mucus is highly viscous block passages in the lungs, liver, Pancreas and various Secretory organs

→ When oxygen and enzymes donot reach at appropiate organs then organs development and metabolic activities are

Affected

→ It is caused due to recessive Mutation.

III ALKAPTOURIA

→ Recessive Mutation

→ Discovered by A. Garrod. Father of Physiological Genetics.

→ Accumulation of Homogentisic acid. in body

→ Reason
Normal condition
Homogentisic acid
↓ Homogentistic acid oxidase.
Maleyl acetoacid acid

Mutation

Homogentistic acid

↓ ✕

✕

→ Homogentistic acid is commonly called Alkapton.

→ Alkapton is excreted through Urine. It puts pressure on Kidneys. When Urine comes in contact to air light

Alkapton $\xrightarrow{\text{light}}$ ~~oxidised~~ Black

→ So Urine appear Black

→ Also called Black Urine Disorder.

Sickle cell Anaemia

→ Sickle cell Anaemia is a genetic disorder it occur due to Mutation of gene on chromosome 11.

→ This gene is responsible for formation of β- chain of Haemoglobin.

→ The sixth amino acid in β- chain of Normal haemoglobin is glutamic acid but in Sickle celled haemoglobin ad the Substitution mutation occur and due to it at 6th position valine is present in place of glutamic acid.

→ Due to change in haemoglobin the RBC shape changes from Biconcave to sickle shaped.

→ Due to change in RBC shape the oxygen carrying capacity of RBC decreases. and they do not reach carry oxygen to the organs properly.

Normal Hb DNA

6th codon.

GAG

CTC

↓

GUC

Normal shaped RBC

mRNA

Sickle cell Hb DNA

GAG

CTC

↓

GUG

m-RNA

Valine

sickled shaped RBC

Normal condition (Homozygous) $Hb^A\ Hb^A$

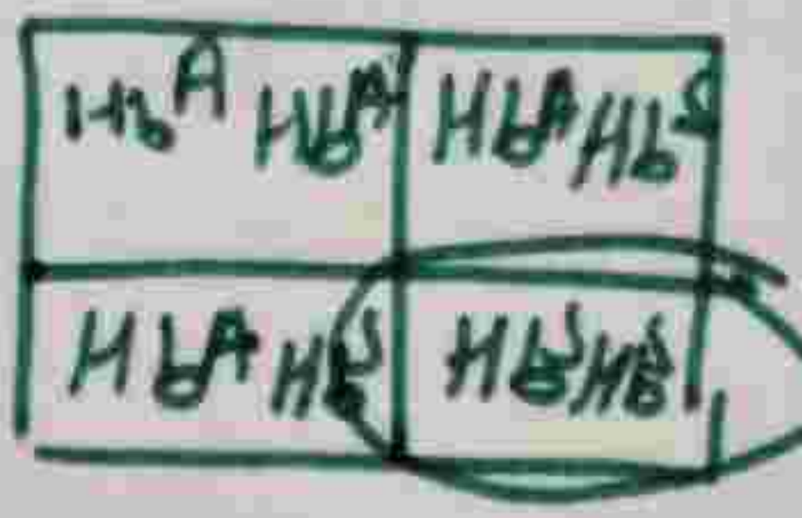
Carrier (Heterozygous) $Hb^A\ Hb^S$

Sickle celled anaemic $Hb^S\ Hb^S$ (Lethal gene)

The individual has short life span i.e 20 years because oxygen can not reach organs.

How sickle celled disease keeps maintained in population

$Hb^A\ Hb^S \times Hb^S \times Hb^A\ Hb^S$



→ $Hb^A\ Hb^S$ also shows codominance ie they have 50% Normal RBC and 50% sickle shaped RBC.

These persons are safe from Malaria caused by Plasmodium falciparum.