

Mendelian Disorder :->

- Mendelian disorders are mainly determined by alteration or mutation in the single gene.
- These disorder transmitted to the offspring in line of Mendelian genetics.
- The pattern of inheritance of such Mendelian disorders can be traced in family by the pedigree analysis.
- Most common + prevalent Mendelian disorders are Haemophilia, sickle cell anaemia, Colour blindness, Phenylketonuria, Thalassemia, Cystic fibrosis etc.

(a) X-linked recessive disorder

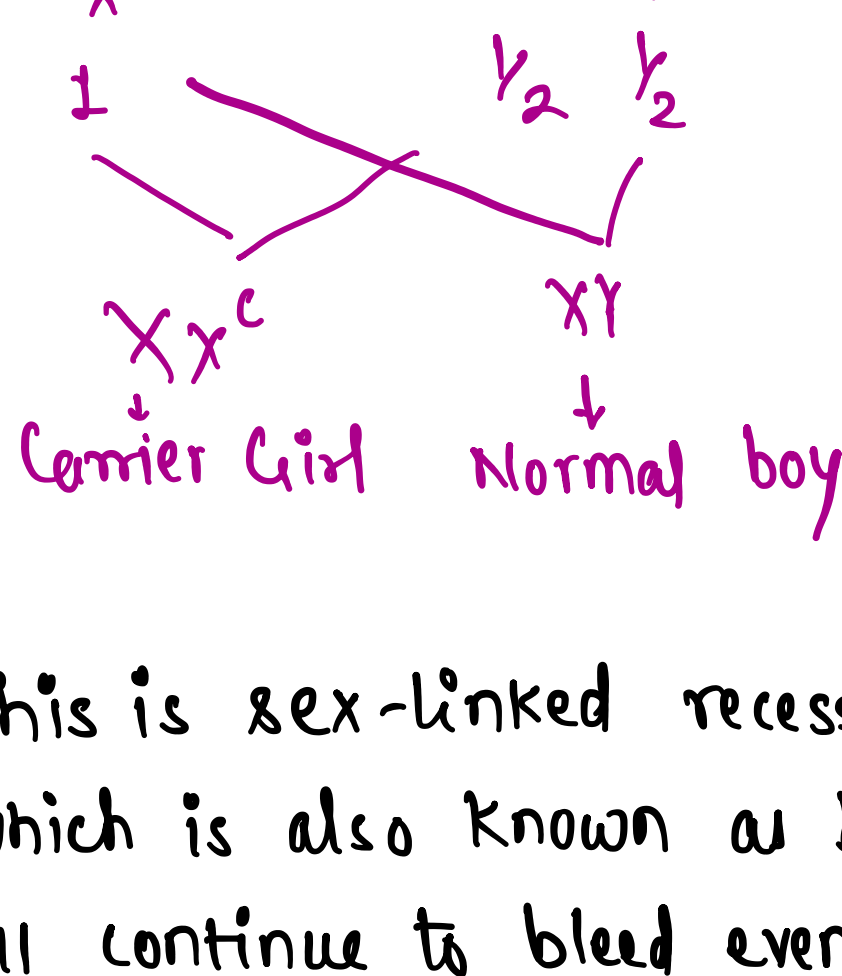
- (a) Colorblindness (b) Haemophilia

(a) Colorblindness :- It is sex-linked recessive disorder due to defect in either red or green cone of eye resulting in failure to discriminate between red & green color. It is a recessive sex-linked trait.

- This defect is due to mutation in certain genes present in the X-chromosome.
- It occurs in about 8% of males and only about 0.4% of females. This is because the genes that lead to red-green color blindness are on the X-chromosome.
- Males have only X-chromosome and females have two.
- The son of women who carries the gene has a 50% chance of being colorblind. The mother is not herself color blind because the gene is recessive that means its effect is suppressed by her matching dominant normal gene.
- A daughter will not normally be color blind, unless her mother is carrier and her father is colorblind.

• Example

Normal women X Color blind Man



(b) Haemophilia :- This is sex-linked recessive disease (Royal disease) which is also known as bleeders disease as the patient will continue to bleed even from a minor cut since he or she does not possess the natural phenomenon of blood clotting due to absence of single protein that is a part of the cascade of proteins involved in the clotting of blood.

Haemophilia A - absence of factor VIII (Antihemophilic globulin)

Haemophilia B - absence of factor IX (Thromboplastin factor)

Due to this, in an affected individual a simple cut will result in non-stop bleeding.

- The heterozygous female (carrier) for haemophilia may transmit the disease to sons.
- The possibility of a female becoming a haemophilic is extremely rare because mother of such a female has to be at least carrier and the father should be haemophilic [unviable in the later stage of life]
- The family pedigree of Queen Victoria shows a number of haemophilic descents as she was a carrier of the disease.

✱✱ The Haemophilic girl babies are still born because the double recessive gene of haemophilia is fatal.

✱✱ X-linked recessive disorders show criss-cross inheritance.

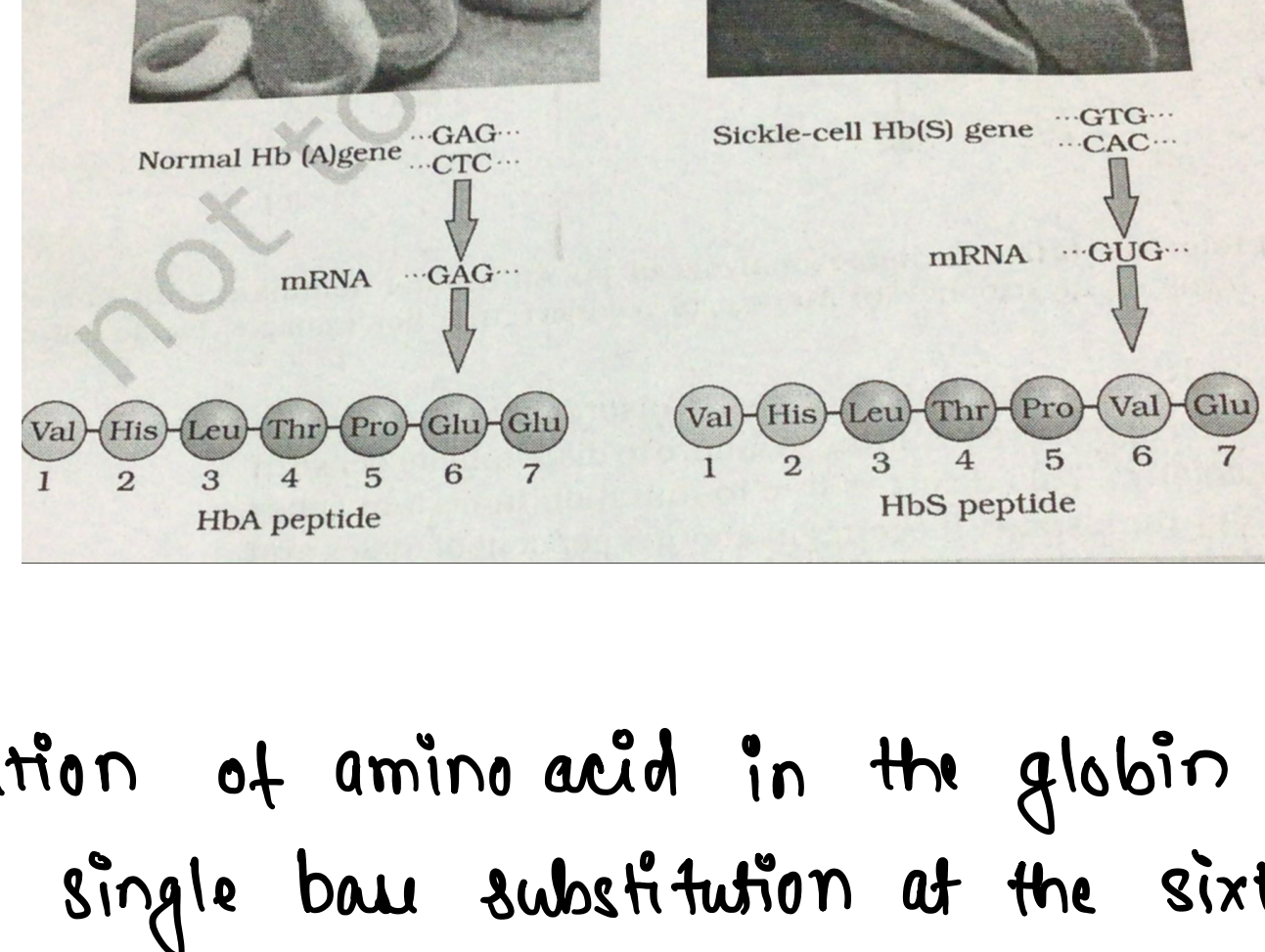
(a) Autosomal recessive disorder :->

- (a) Sickle cell anaemia (b) Thalassemia (c) Phenylketonuria

(a) Sickle cell anaemia :- This is autosomal recessive trait that can be transmitted from

parents to the offspring when both the partners are carrier for the gene (or heterozygous).

- The defect is caused by the substitution of glutamic acid (glu) by valine (val) at the sixth position of the beta globin chain of the haemoglobin molecule.



- The substitution of amino acid in the globin protein results due to the single base substitution at the sixth codon of the beta globin gene from GAG to GUG. This will change 1st structure of beta chain into change 2nd → 3rd → 4th structure. because of this mutant haemoglobin molecule undergoes polymerisation under low oxygen tension causing change in the shape of the RBC from biconcave disc to elongated sickle like structure.

• Hb^AHb^S → now called co-dominant

• Hb^SHb^S → die in childhood (before reproductive age) due to acute anaemia.

• It is also example of disruptive selection

Hb^AHb^S → It has survival value in Malaria infested area.

• sickle cell erythrocyte cannot pass through narrow capillaries. They have tendency to clot and degenerate. It results in anaemia.

• It is also an example of pleiotropy because gene which cause this disease alter the type of haemoglobin and also change in the form of RBCs.

• It is also an example of point mutation.

• It is qualitative defect of Haemoglobin because of synthesis of incorrectly functioning globin.

(b) Thalassemia :- It was discovered by Cooley. It is also an autosomal-linked recessive blood

disease transmitted from parents to the offspring when both the partners are unaffected carrier for the gene (or heterozygous).

- The defect could be due to either mutation or deletion which ultimately results in reduced rate of synthesis of one of the globin chains (α and β chains) that make up haemoglobin. This causes the formation of abnormal haemoglobin molecule resulting into anaemia which is characteristic of the disease.

• Thalassemia can be classified according to which chain of the haemoglobin molecule is affected.

α-Thalassemia :- * In this case production of α-globin chain is affected.

* α-Thalassemia is controlled by two closely linked genes HBA1 and HBA2 on chromosome 16 of each parent and it is observed due to mutation or deletion of one or more of the four genes. The more gene affected, the less α-globin molecules produced.

β-Thalassemia :- * In this case production of β globin (Cooley's anaemia) chain is affected.

* β-Thalassemia is controlled by a single gene HBB on chromosome 11 of each parent and occur due to mutation of one or both the genes.

• Thalassemia is quantitative disorder of globin.

(c) Phenylketonuria :- * This is an inborn error of metabolism is also inherited as the autosomal recessive trait.

* The affected individual lacks an enzyme that converts the amino acid phenylalanine into tyrosine. As a result of this phenylalanine is accumulated and converted into phenylpyruvic acid and other derivatives.

MR * Accumulation of phenylpyruvic acid and other derivatives in brain results in mental retardation.

* These are also excreted through urine because of its poor absorption by kidney. Therefore disease is known as phenylketonuria

* These individuals lack enzyme phenylalanine hydroxylase.

* Gene for this enzyme is present on chromosome 12.

* The presence of mutated gene in homozygous condition manifests itself through phenotypic expression characterized by Mental retardation and reduction in hair and skin pigmentation. Therefore it is example of pleiotropy