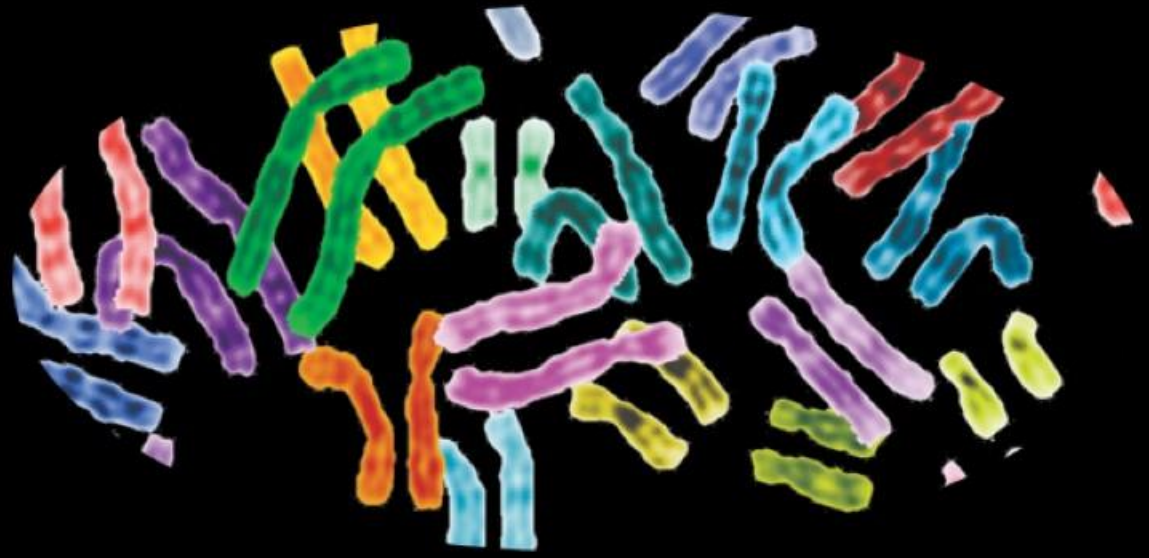

GENETIC DISORDERS

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Genetic disorders are the disorders due to change in genes or chromosomes.

GENETIC DISORDERS

Mendelian disorders

- Haemophilia
- Sickle cell anaemia
- Colour blindness
- Phenyl-ketonuria
- Thalassemia
- Cystic fibrosis

Chromosomal disorders

- Down's syndrome
- Klinefelter's syndrome
- Turner's syndrome

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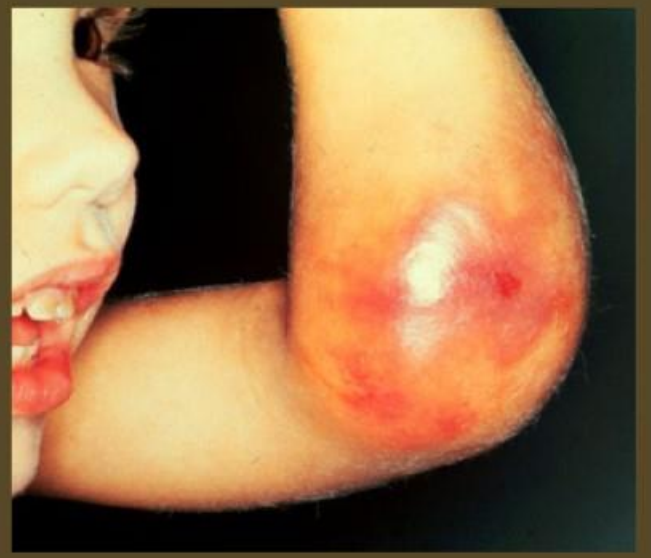
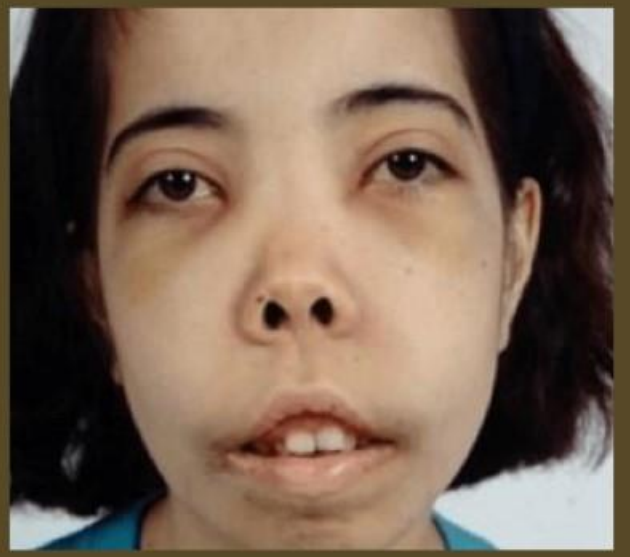
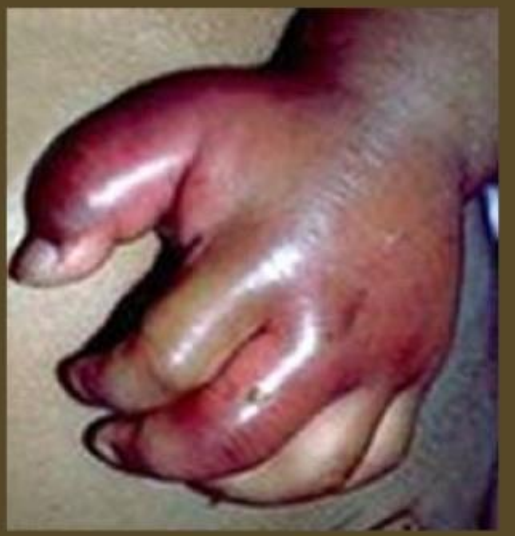
GENETIC DISORDERS

Mendelian Disorders

- The disorders caused by alteration or **mutation in the single gene.**
- E.g. Haemophilia, Colour blindness, Sickle-cell anaemia, Phenylketonuria, Thalassemia, Cystic fibrosis etc.
- The pattern of inheritance of Mendelian disorders can be traced in a family by pedigree analysis.



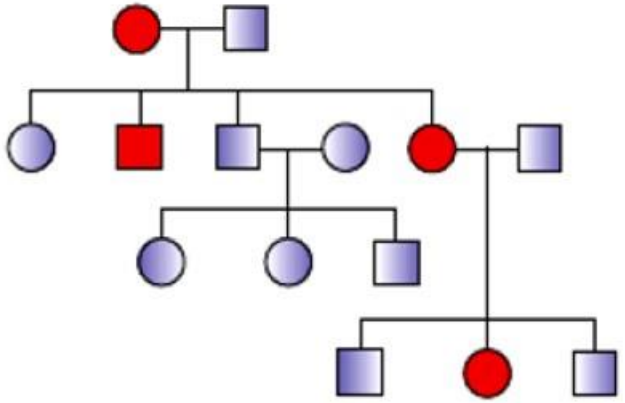




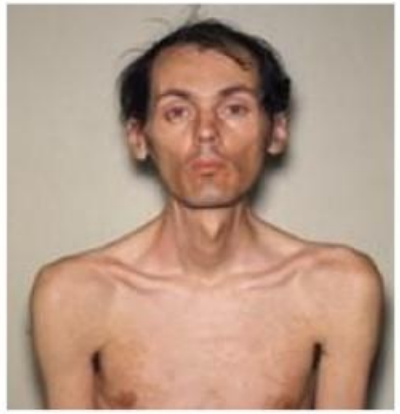
GENETIC DISORDERS

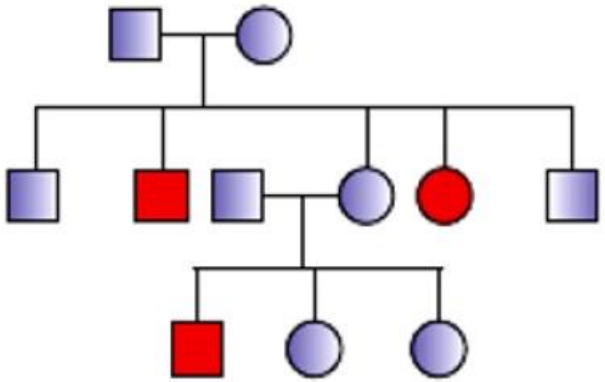
Mendelian Disorders

- Mendelian disorders may be **dominant or recessive.**
- Pedigree analysis helps to understand whether the trait is dominant or recessive.

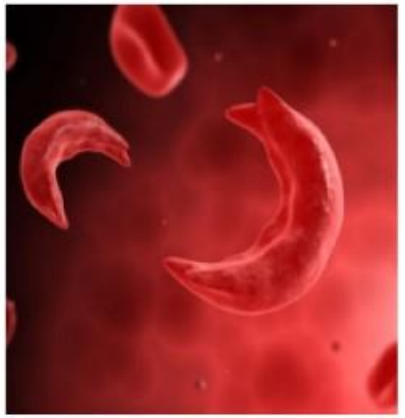


Pedigree analysis of Autosomal dominant trait (E.g. Myotonic dystrophy)





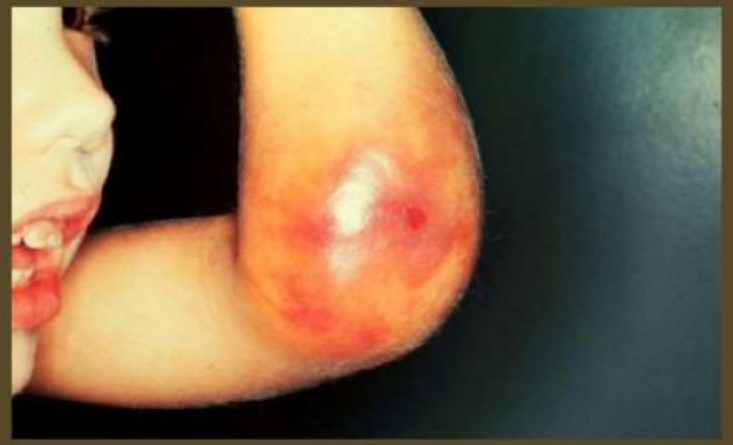
Pedigree analysis of Autosomal recessive trait (E.g. Sickle-cell anaemia)



GENETIC DISORDERS

Mendelian Disorders

Haemophilia (Royal Disease)



- **Sex linked (X-linked) recessive** disease.
- In this, a protein involved in the blood clotting is affected.
- A simple cut results in non-stop bleeding.
- It is controlled by a pair of allele, **H & h.**
- H is normal allele and h is responsible for haemophilia.

X^HX^H	Normal female
X^HX^h	Heterozygous female (carrier). She may transmit the disease to sons.
X^hX^h	Hemophilic female
X^HY	Normal male
X^hY	Hemophilic male

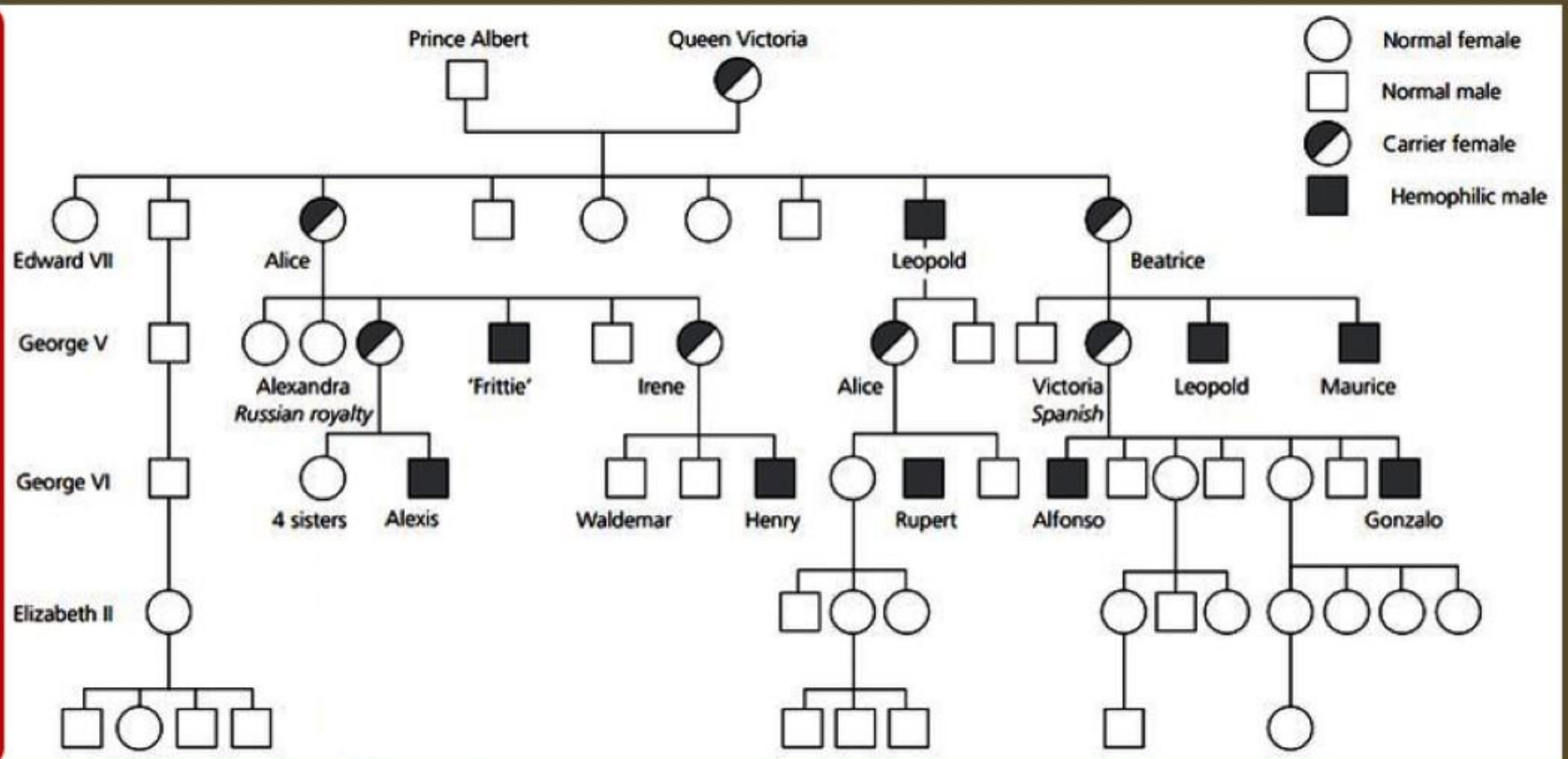
GENETIC DISORDERS

Mendelian Disorders

Haemophilia (Royal Disease)

In **females, haemophilia is very rare** because it happens only when **mother** is at least **carrier** and **father haemophilic** (unviable in the later stage of life).

Queen Victoria was a carrier of hemophilia. So her family pedigree shows many haemophilic descendants.

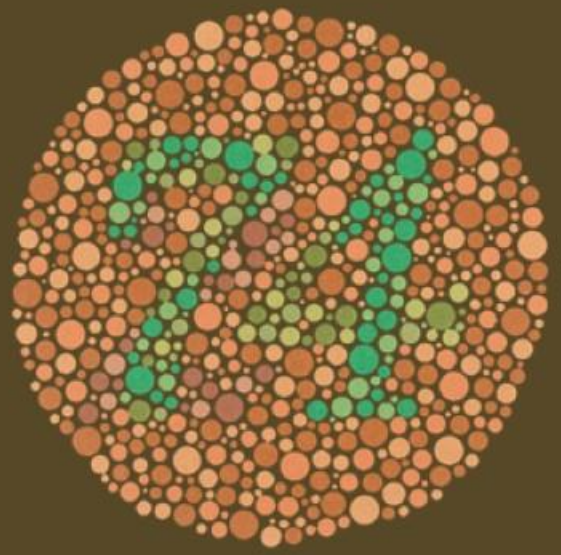


GENETIC DISORDERS

Mendelian Disorders

Colour blindness

- It is a **sex-linked (X-linked) recessive** disorder due to defect in either **red or green cone** of eye. It results in failure to discriminate between red and green colour.
- It is due to mutation in some genes in X chromosome.
- It occurs in **8% of males** and only **0.4% of females.** This is due to the genes are X-linked.

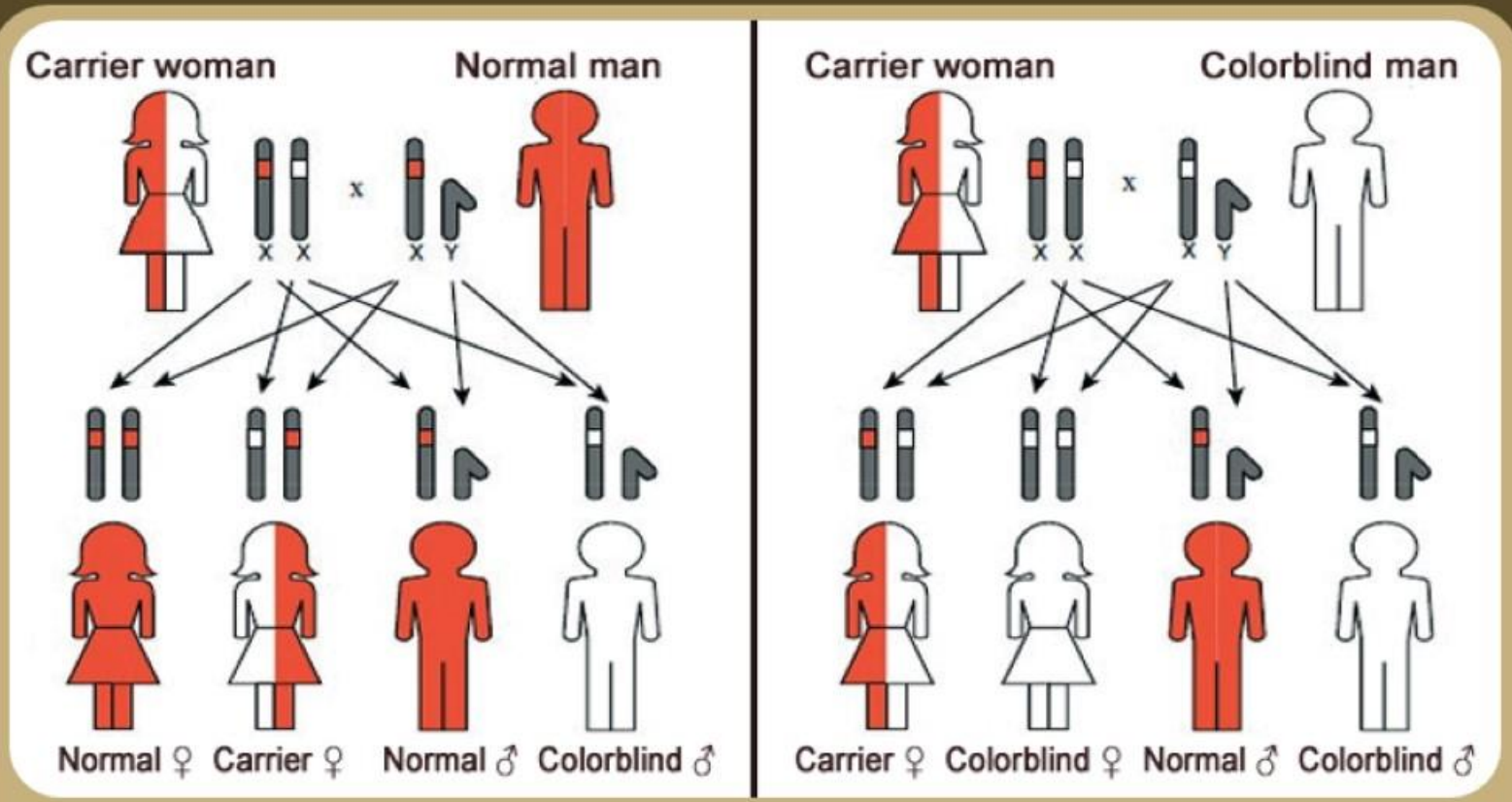


Can you read the number in this figure? If no, you may have colorblindness.

GENETIC DISORDERS

Mendelian Disorders

Colour blindness



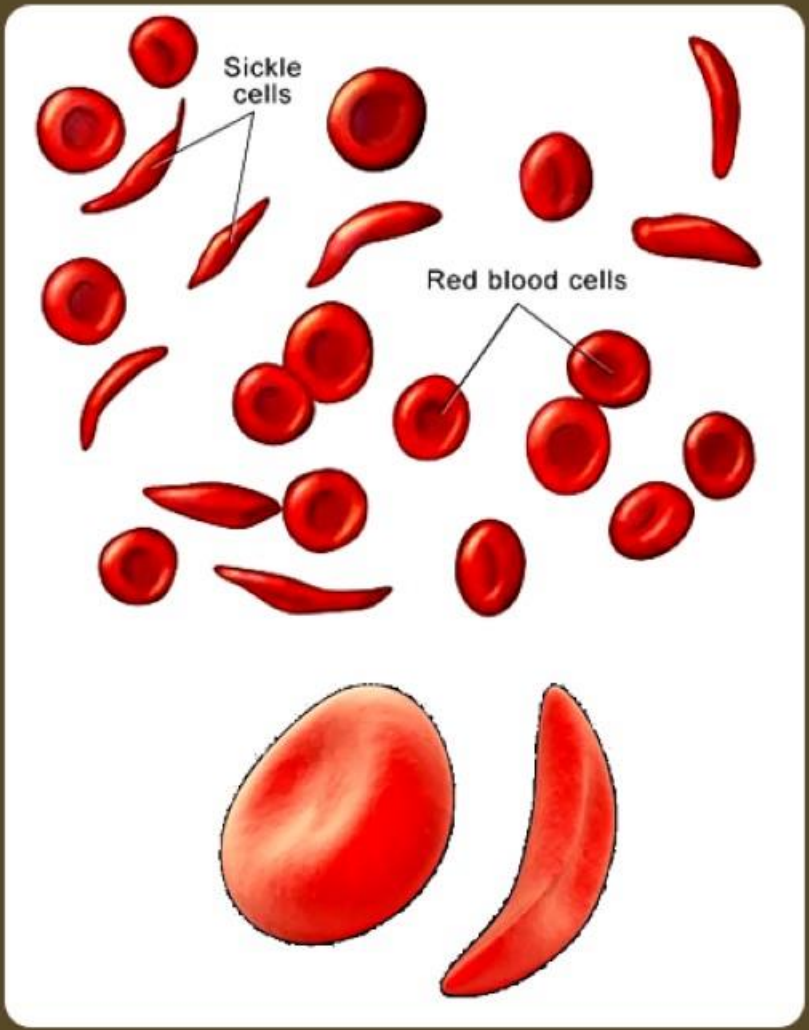
Inheritance of colorblindness

- Normal allele is dominant (C). Recessive allele (c) causes colour blindness.
- The son of a heterozygous woman (carrier, X^CX^c) has a 50% chance of being colour blind.
- A daughter will be colour blind only when her mother is at least a carrier and her father is colour blind (X^cY).

GENETIC DISORDERS

Mendelian Disorders

Sickle cell anaemia



- This is an **autosome linked recessive trait.**
- It can be transmitted from parents to the offspring when both the partners are carrier (heterozygous) for the gene .
- The disease is controlled by a pair of allele, **Hb^A & Hb^S.**

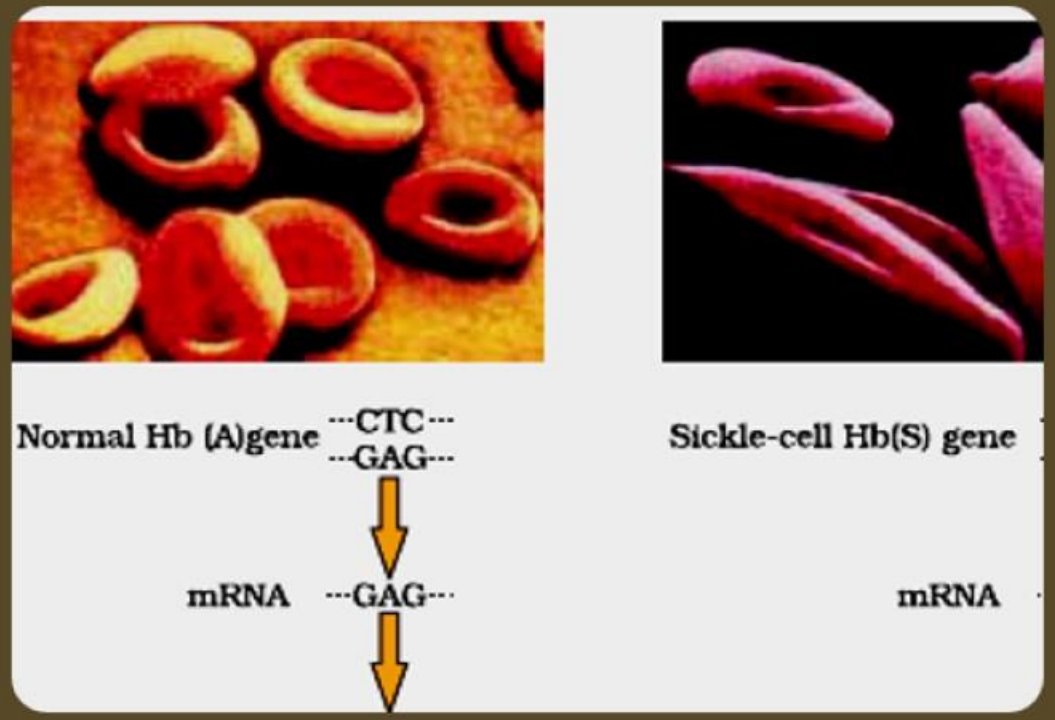
- ***Homozygous dominant (Hb^AHb^A): Normal***
- ***Heterozygous (Hb^AHb^S): Carrier; sickle cell trait***
- ***Homozygous recessive (Hb^SHb^S): Affected.***

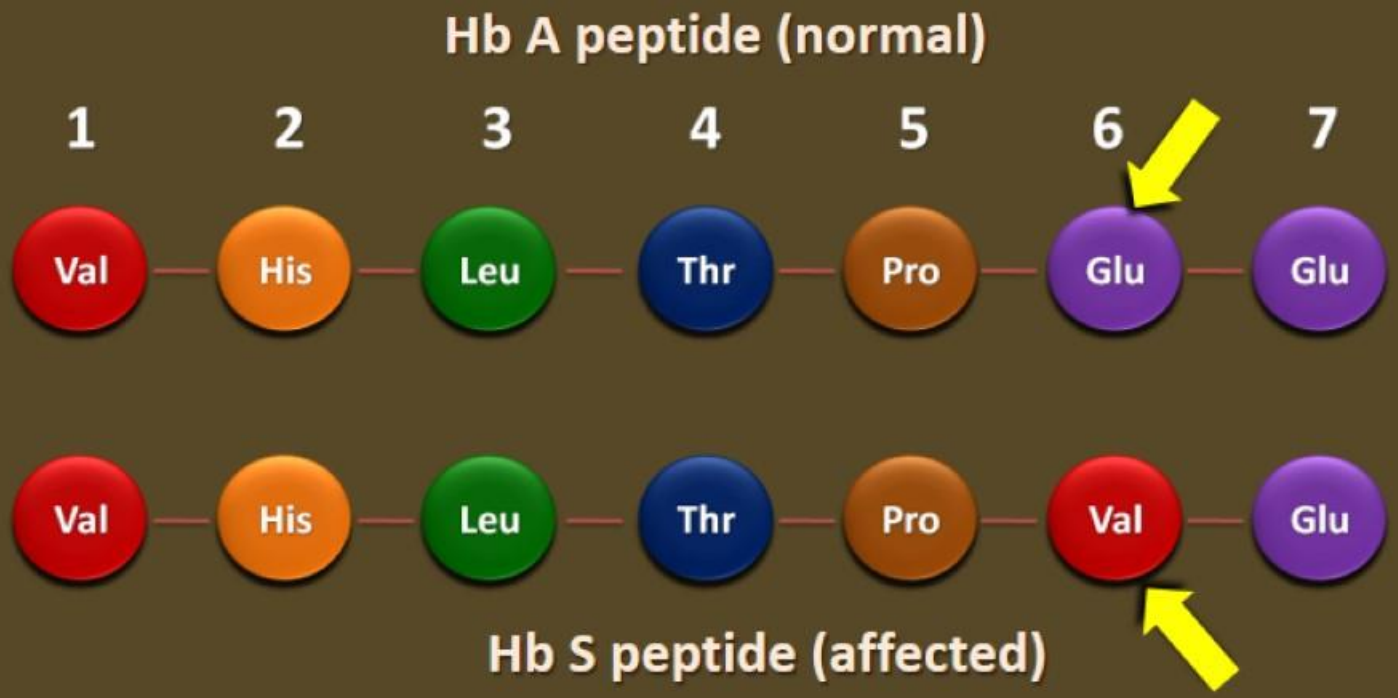
GENETIC DISORDERS

Mendelian Disorders

Sickle cell anaemia

- The defect is caused by the substitution of Glutamic acid (Glu) by Valine (Val) at the 6th position of the β-globin chain of haemoglobin.
- This is due to single base substitution at the 6th codon of β-globin gene from GAG to GUG.





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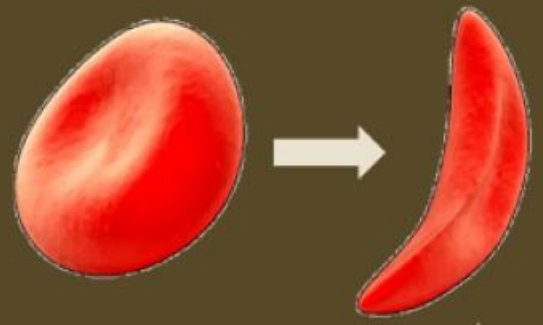
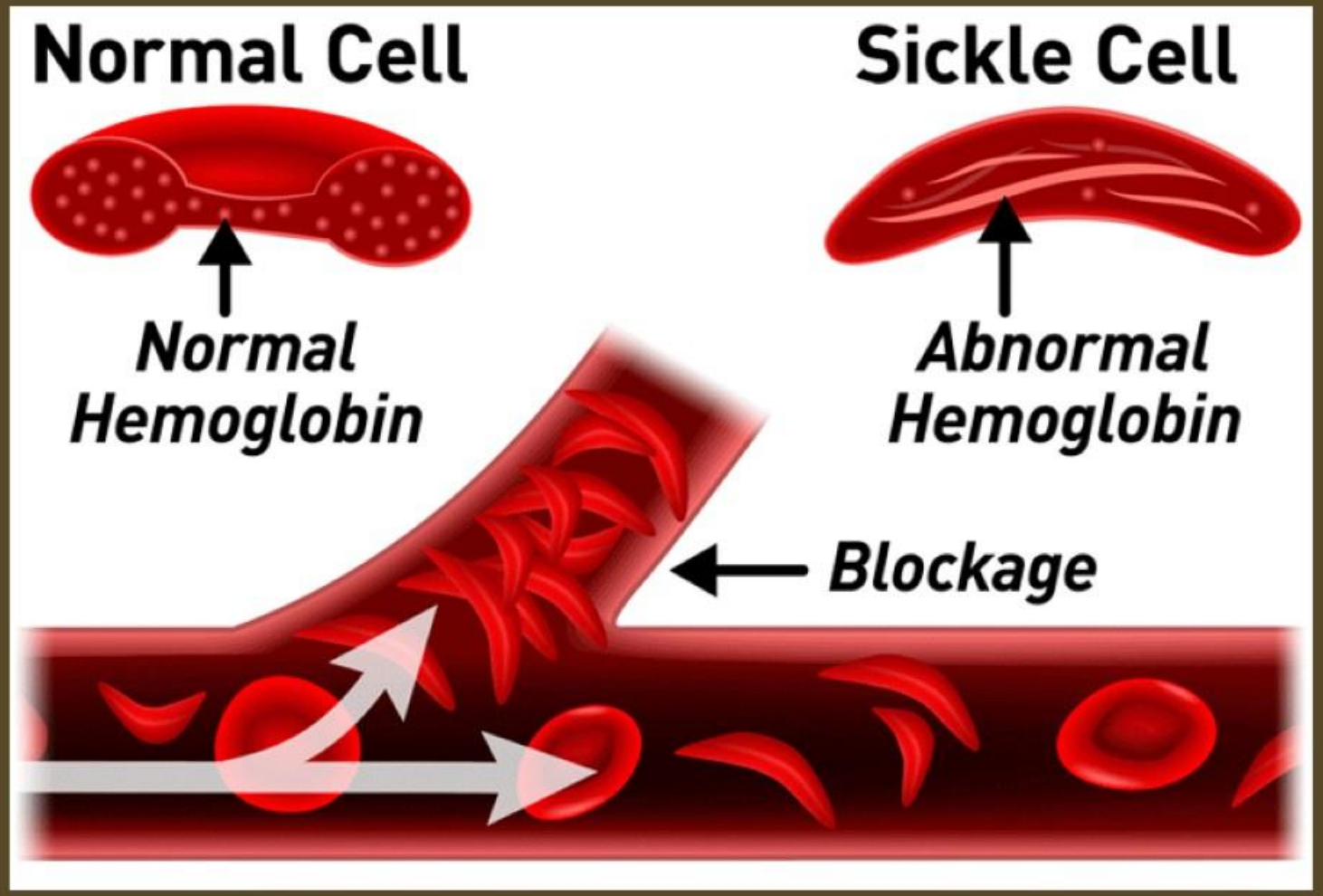
GENETIC DISORDERS

Mendelian Disorders

Sickle cell anaemia

The mutant haemoglobin molecule undergoes polymerization under low oxygen tension causing the change in shape of the RBC from biconcave disc to elongated sickle like structure.





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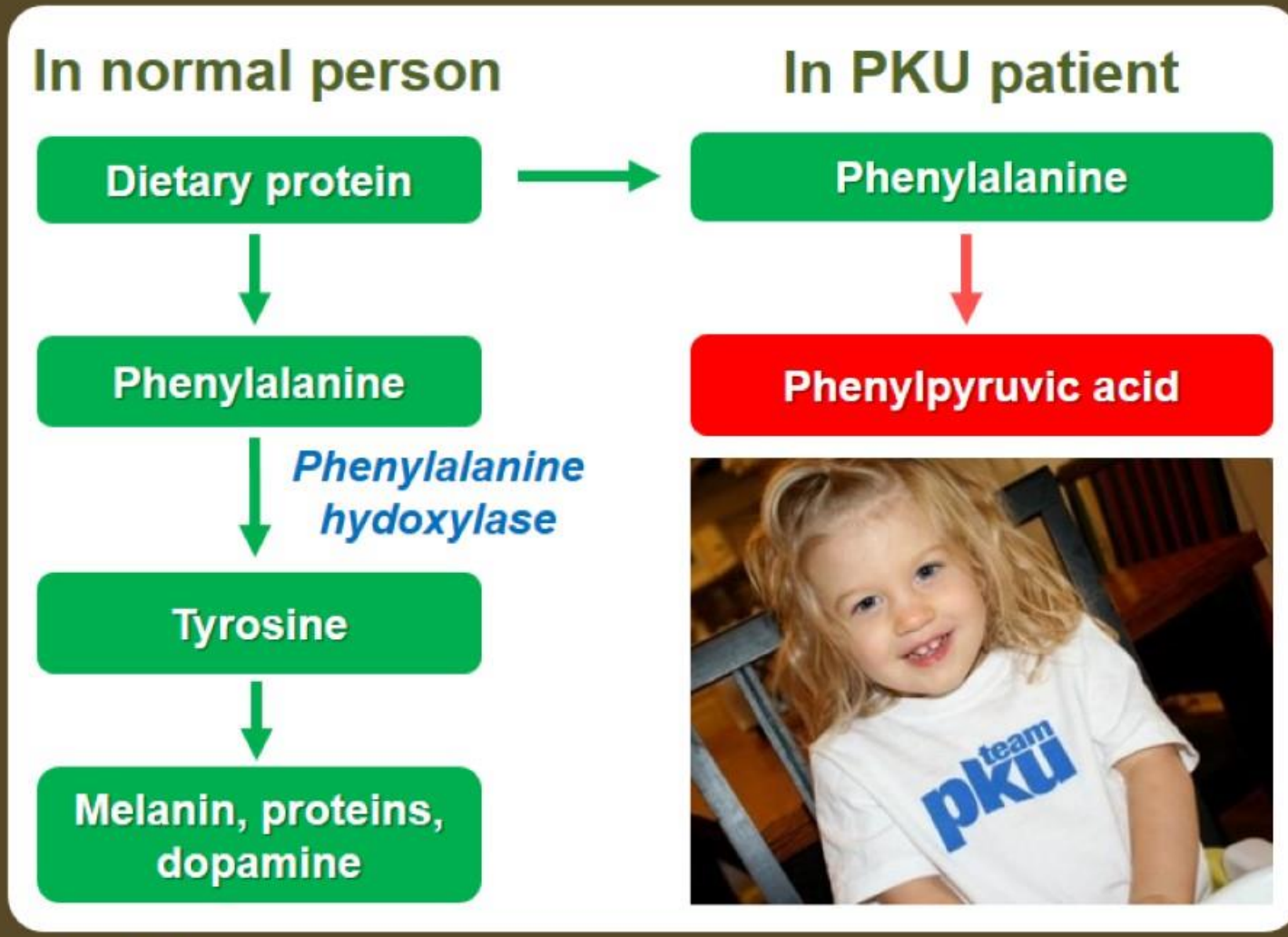
GENETIC DISORDERS

Mendelian Disorders

Phenylketonuria (PKU)

- An inborn error of metabolism.
- **Autosomal recessive trait.**
- It is due to mutation in the gene that codes for the enzyme ***phenyl alanine hydroxylase.*** This enzyme converts an amino acid **phenylalanine** into **tyrosine.**
- The affected individual lacks this enzyme. As a result, phenylalanine accumulates and converts into ***phenyl pyruvic acid*** and other derivatives.

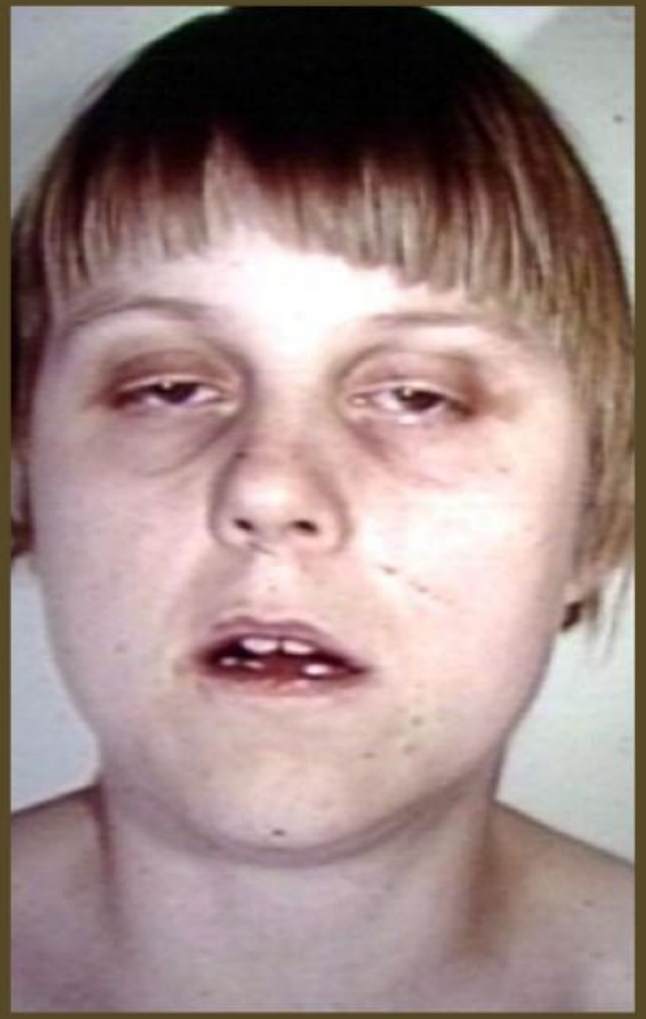


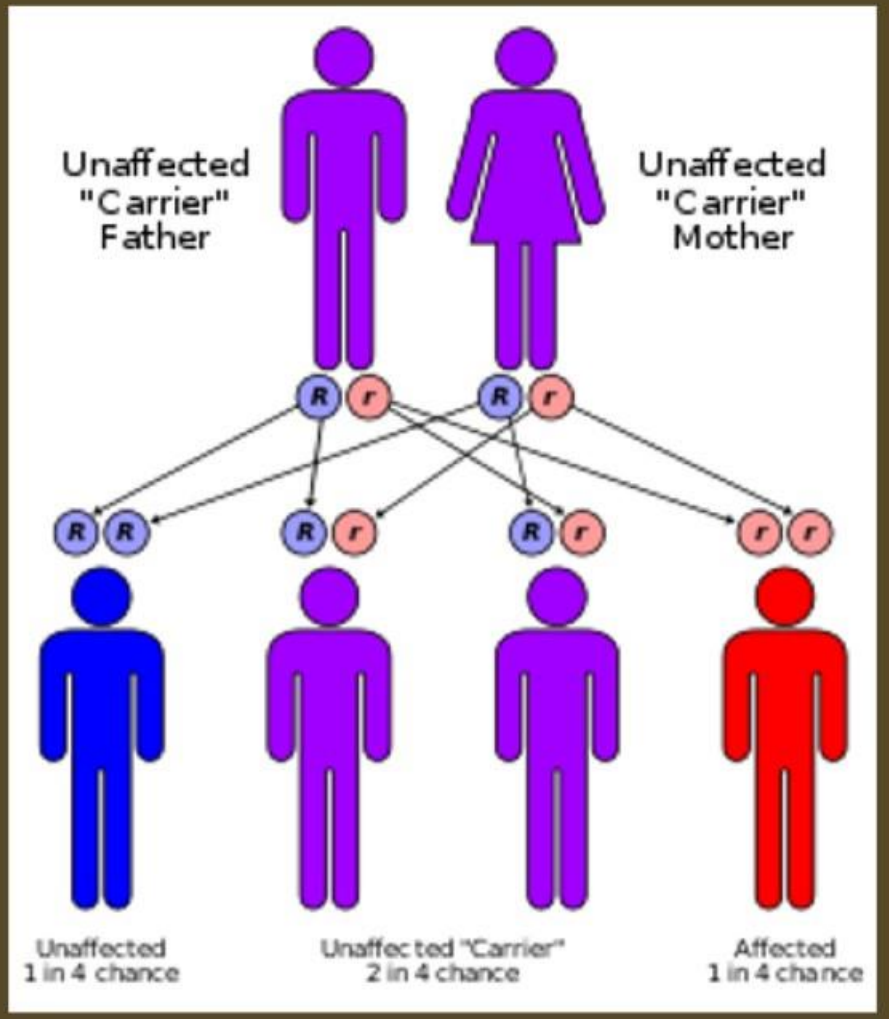
GENETIC DISORDERS

Mendelian Disorders

Phenylketonuria (PKU)

Phenyl pyruvic acid and other derivatives accumulate in brain resulting in mental retardation. These are also excreted through urine because of poor absorption by kidney.





GENETIC DISORDERS

Mendelian Disorders

Thalassemia

- It is an **autosome-linked recessive** blood disease.
- It is transmitted from unaffected carrier (heterozygous) parents to the offspring.
- It is due to **mutation or deletion.**
- It results in reduced synthesis of one of the **α or β globin chains** of haemoglobin. It forms abnormal haemoglobin and causes anaemia.

Thalassemia is a **quantitative problem** (synthesis of few globin molecules).
Sickle cell anaemia is a **qualitative problem** (synthesis of an incorrectly functioning globin).

GENETIC DISORDERS

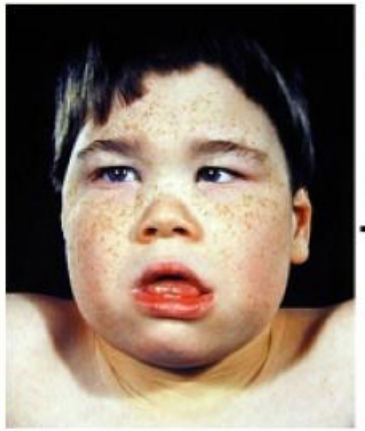
Mendelian Disorders

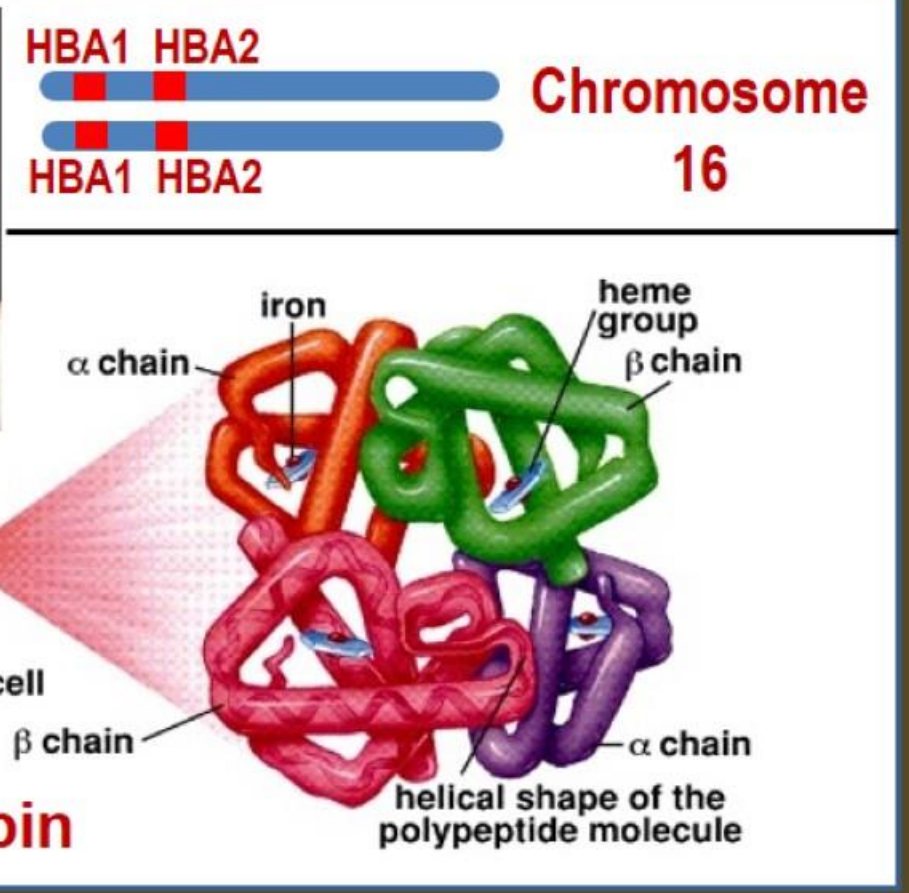
Thalassemia

Based on the chain affected, thalassemia is two types: α thalassemia and β thalassemia.

α Thalassemia

- Here, production of α globin chain is affected.
- It is controlled by two closely linked genes HBA1 & HBA2 on chromosome 16 of each parent.
- Mutation or deletion of one or more of the four genes causes the disease.
- The more genes affected, the less α globin molecules produced.





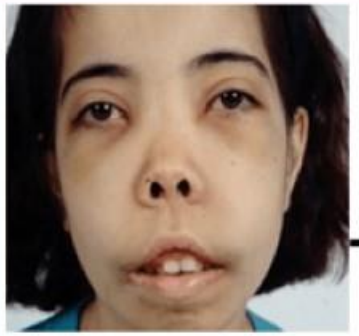
GENETIC DISORDERS

Mendelian Disorders

Thalassemia

β Thalassemia

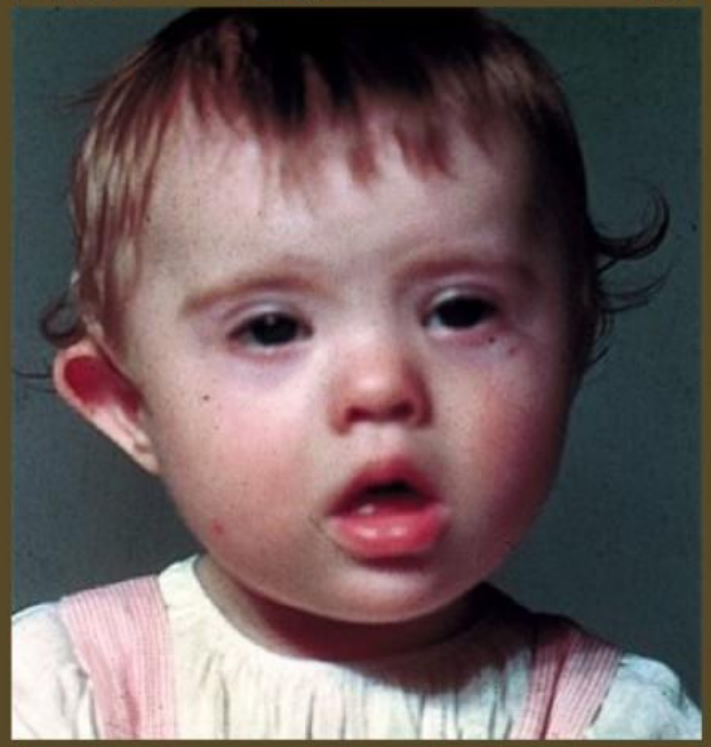
- Here, production of β globin chain is affected.
- It is controlled by a single gene HBB on chromosome 11 of each parent.
- Mutation of one or both the genes causes the disease.




Part 9
CHROMOSOMAL
DISORDERS

GENETIC DISORDERS

Chromosomal Disorders



The disorders caused due to absence or excess or abnormal arrangement of one or more chromosomes.

Chromosomal disorders

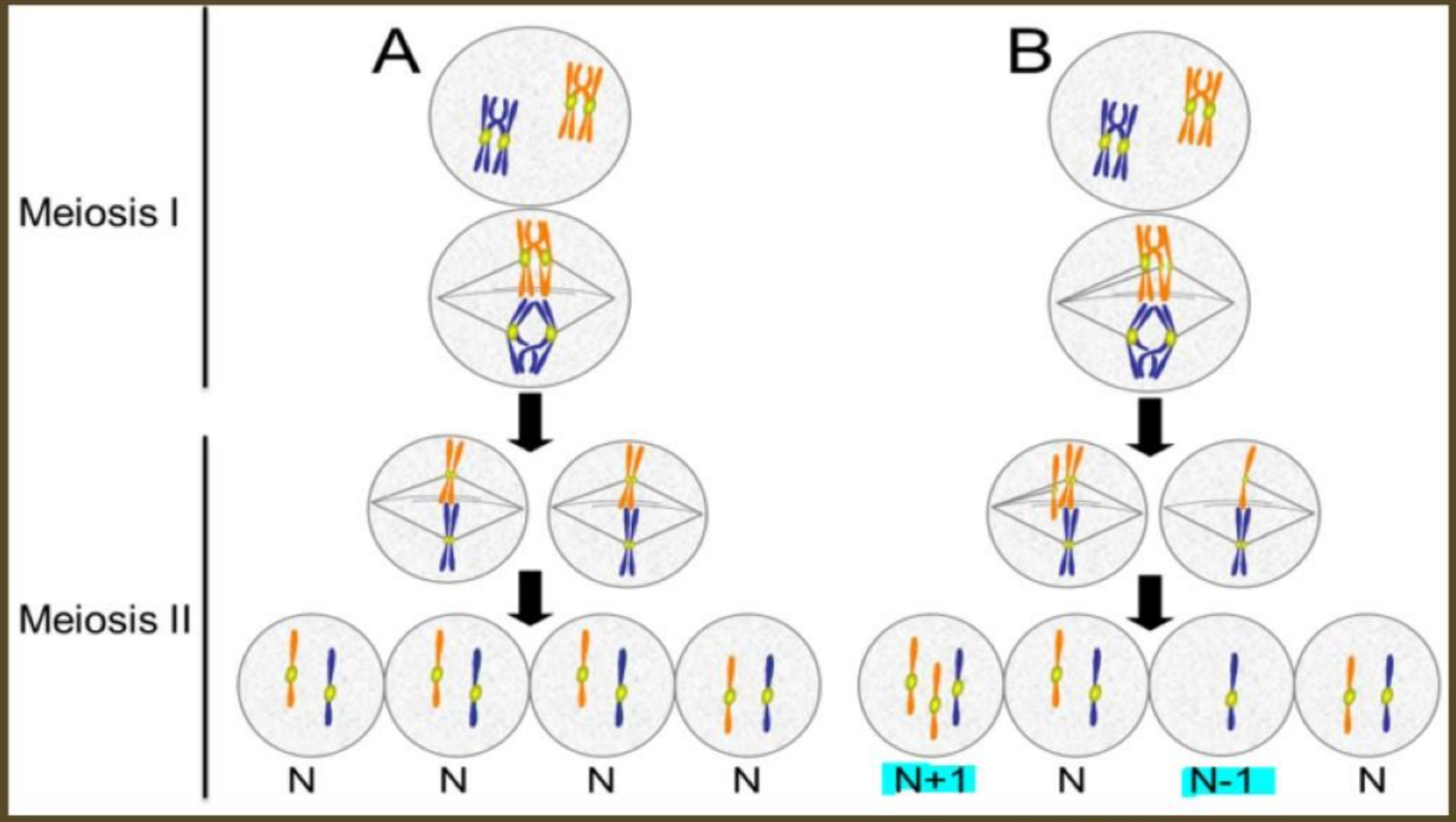
- Aneuploidy
- Polyploidy

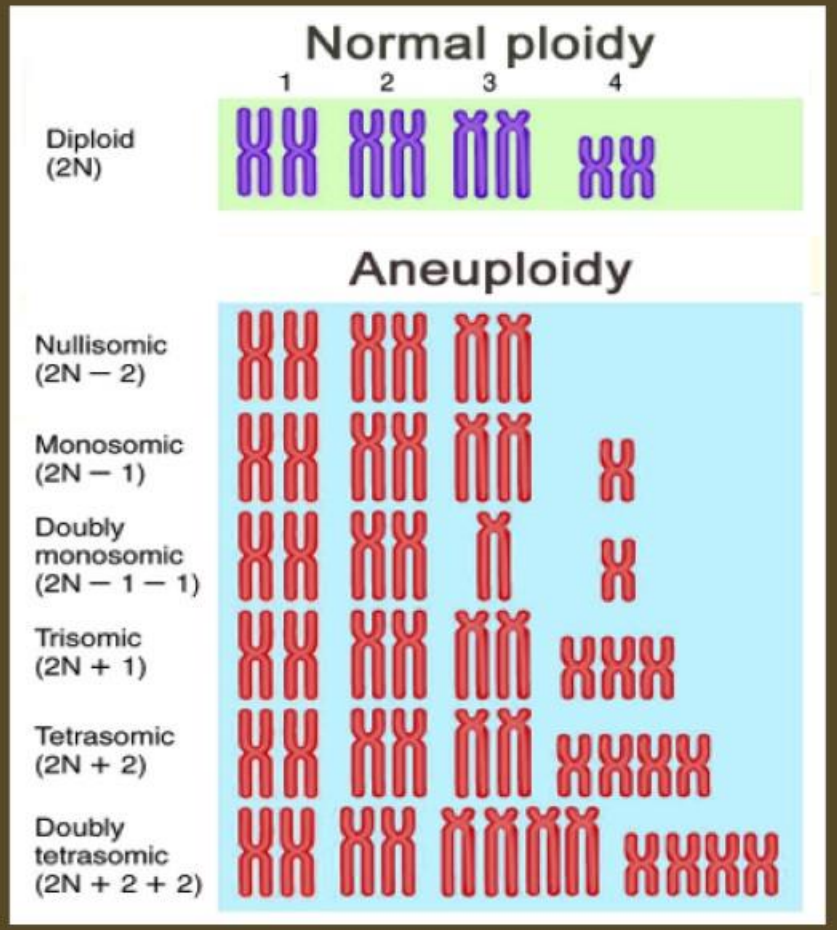
GENETIC DISORDERS

Chromosomal Disorders

Aneuploidy

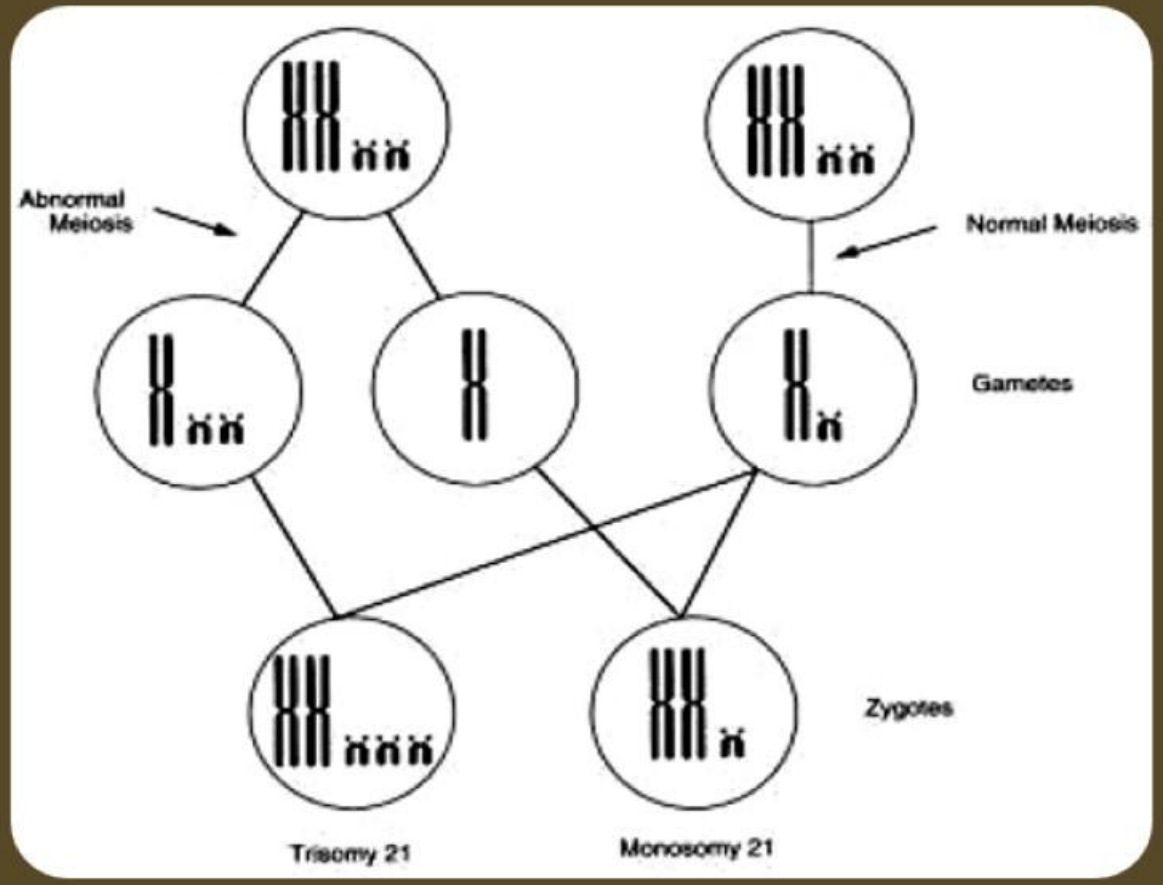
It is the gain or loss of chromosomes due to **failure of segregation of chromatids** during cell division.





Aneuploidy

- **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.

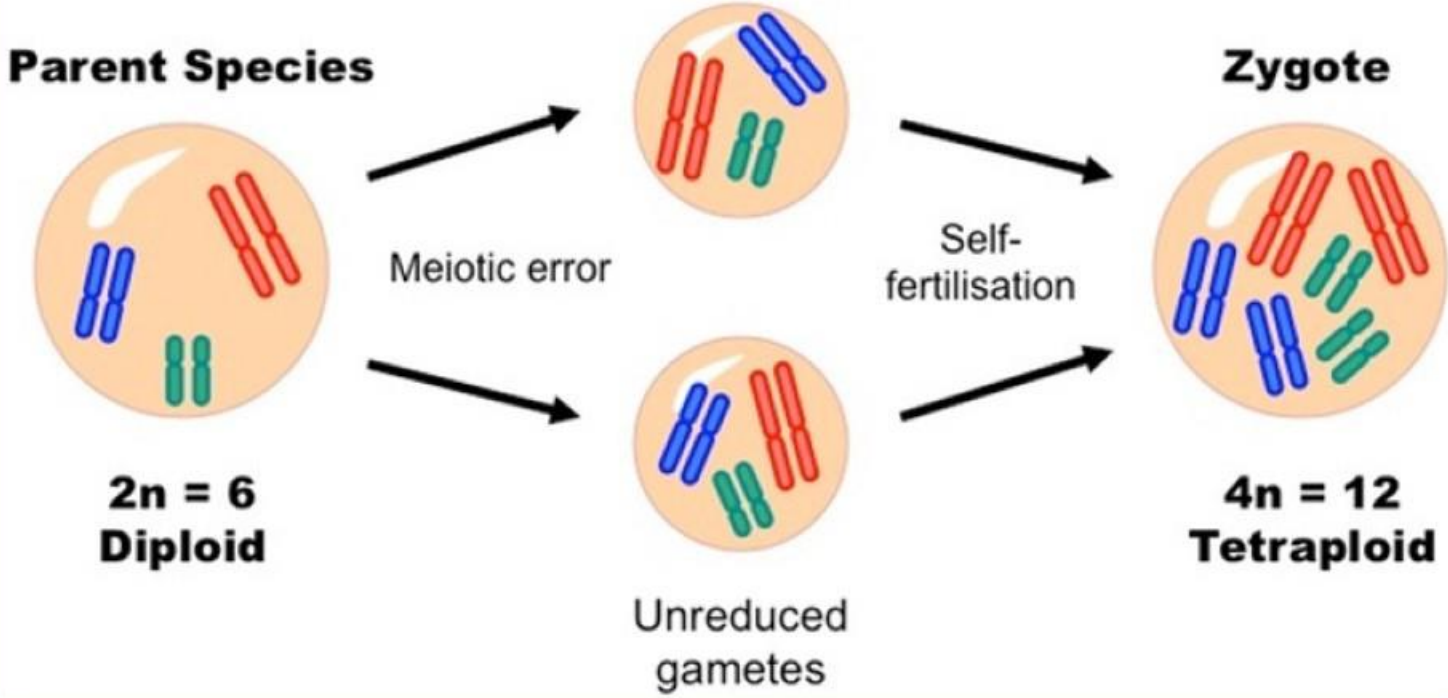


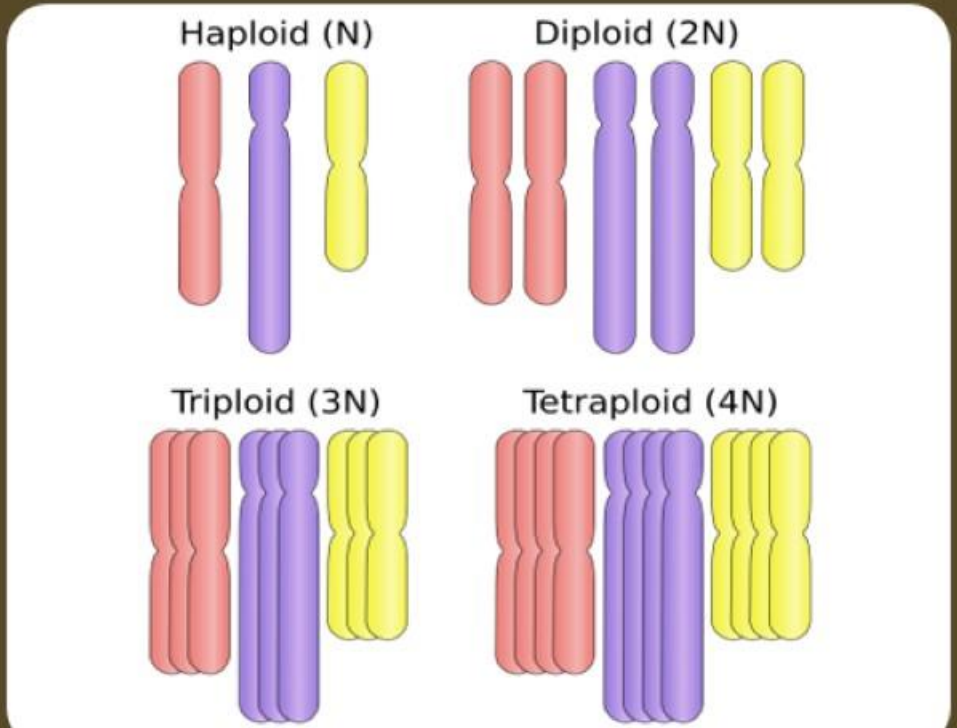
GENETIC DISORDERS

Chromosomal Disorders

Polyploidy (Euploidy)

- It is an increase in a ***whole set of chromosomes*** due to **failure of cytokinesis** after telophase stage of cell division.
- This is **very rare in human** but often seen in plants.



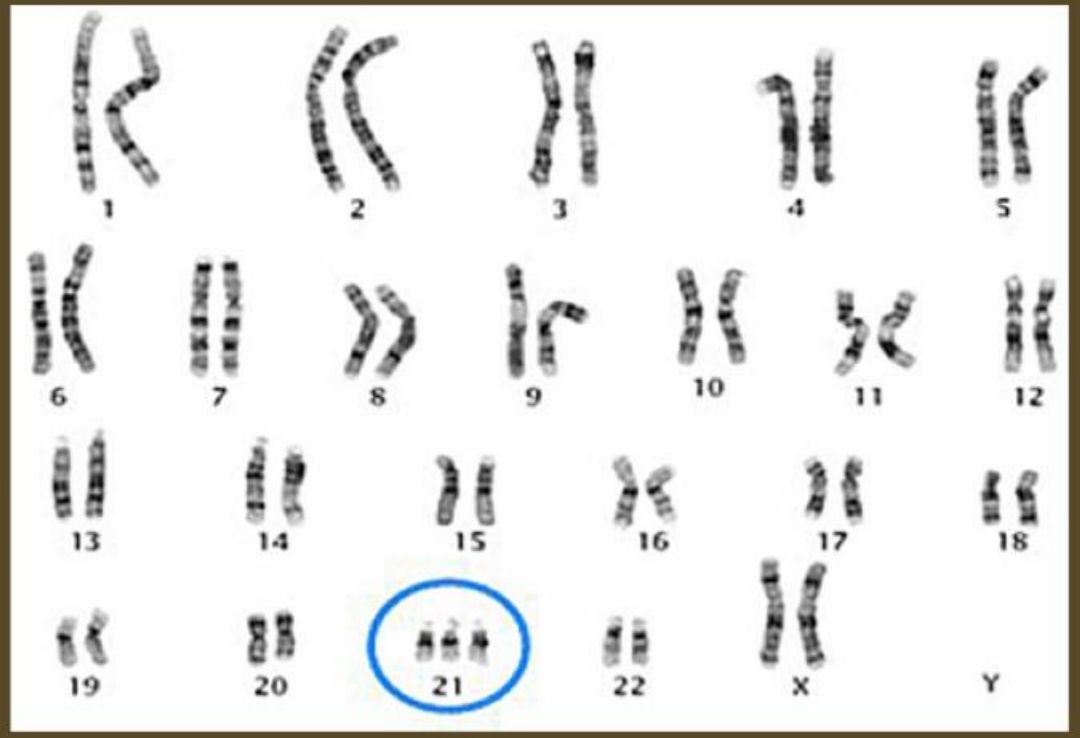


GENETIC DISORDERS

Chromosomal Disorders

Down's syndrome (Mongolism)

- It is the presence of an additional copy of chromosome number 21 (trisomy of 21).
- Genetic constitution: 45 A + XX or 45 A + XY (i.e. 47 chromosomes).



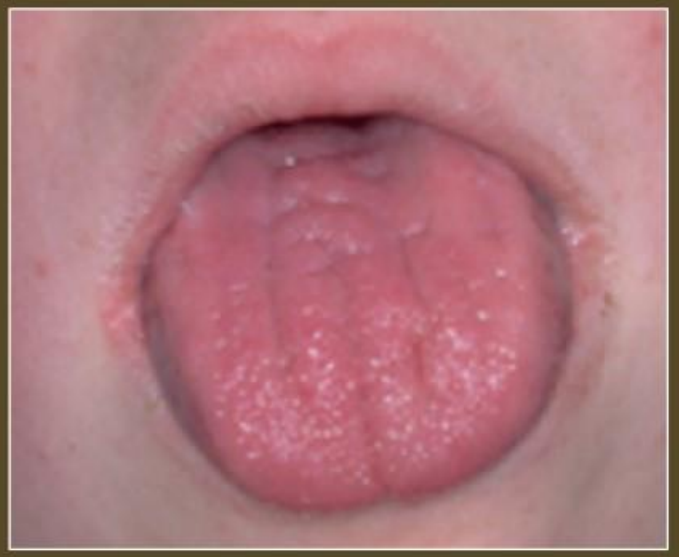
GENETIC DISORDERS

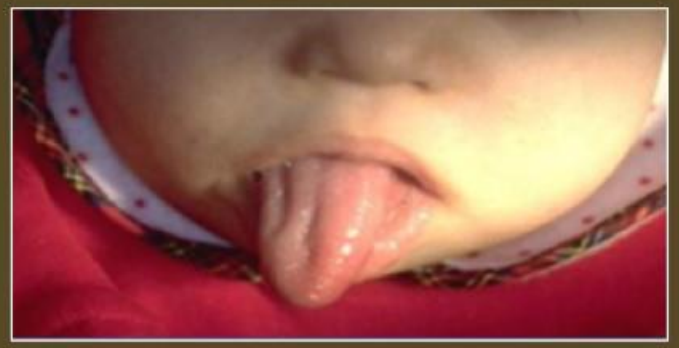
Chromosomal Disorders

Down's syndrome (Mongolism)

Features

- ✓ Short statured with small round head.
- ✓ Broad flat face.
- ✓ Furrowed big tongue & partially open mouth.





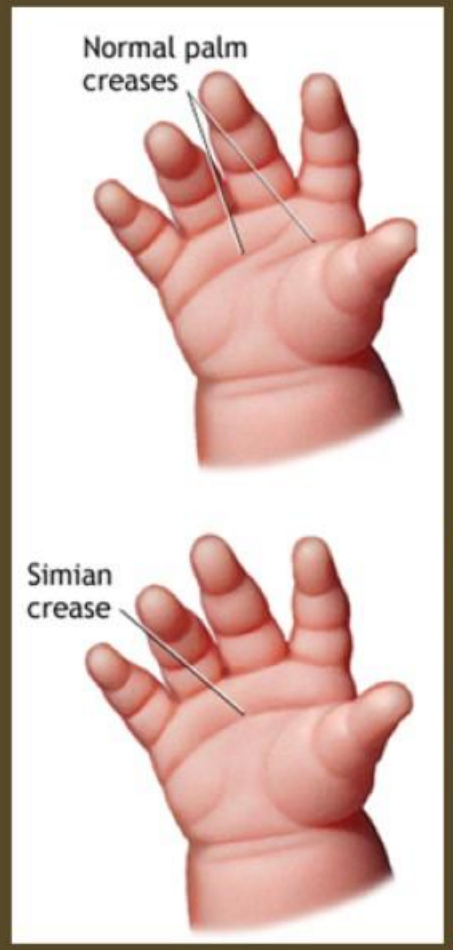
GENETIC DISORDERS

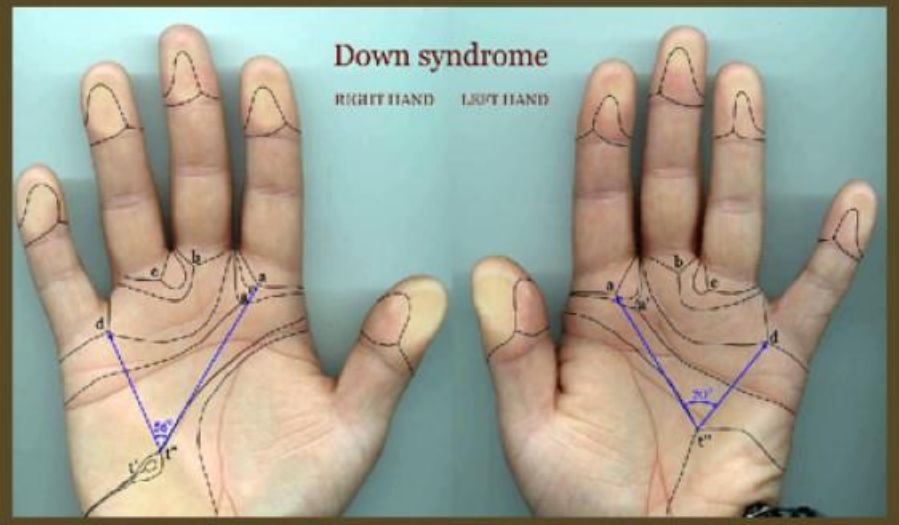
Chromosomal Disorders

Down's syndrome (Mongolism)

Features

- ✓ Short statured with small round head.
- ✓ Broad flat face.
- ✓ Furrowed big tongue & partially open mouth.
- ✓ Broad palm with characteristic palm simian crease.
- ✓ Many "loops" on finger tips.
- ✓ Retarded physical, psychomotor & mental development.
- ✓ Congenital heart disease.





GENETIC DISORDERS

Chromosomal Disorders

Down's syndrome (Mongolism)

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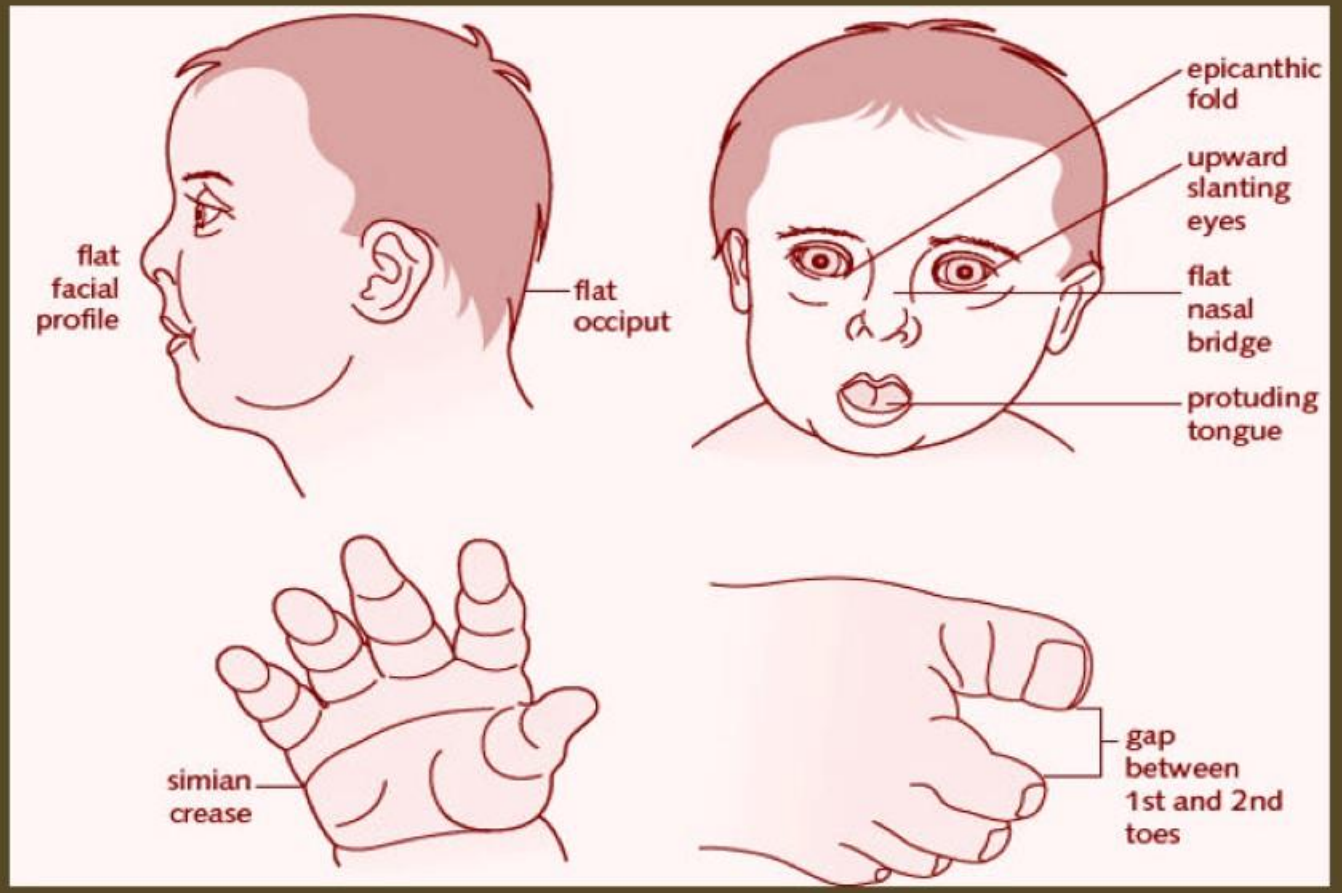
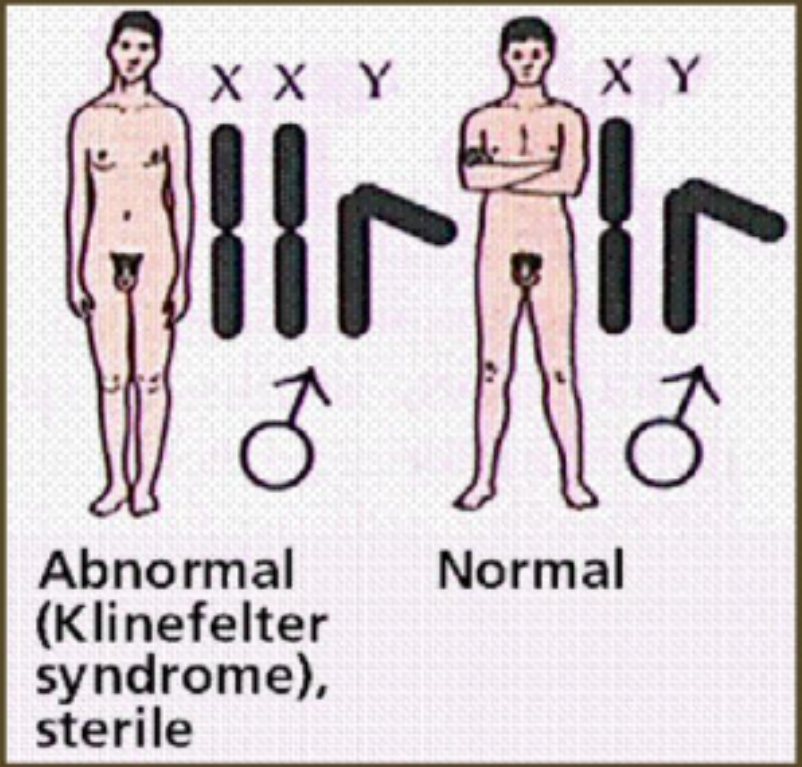


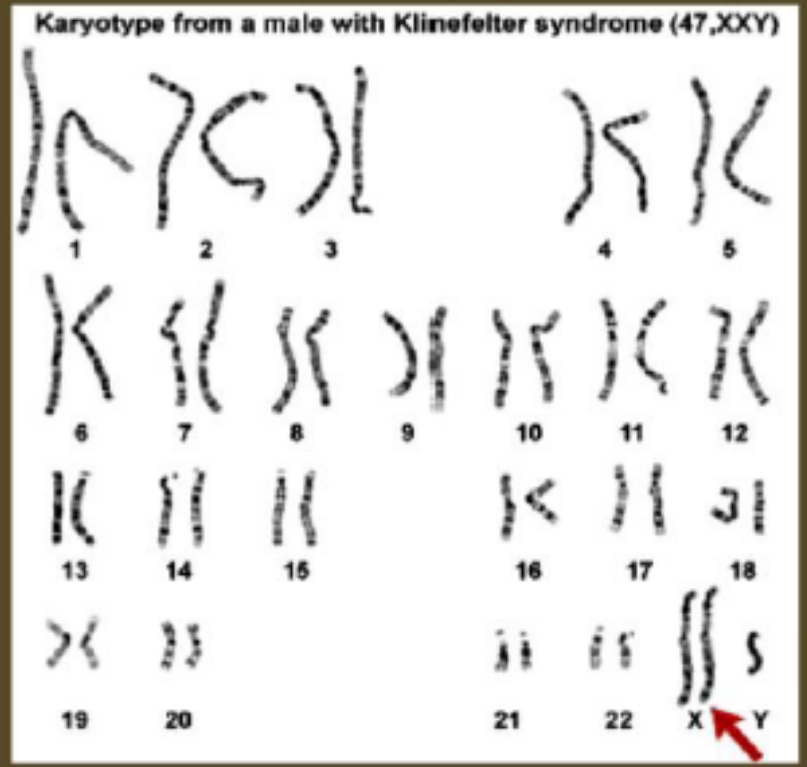
GENETIC DISORDERS

Chromosomal Disorders

Klinefelter's syndrome

- It is the presence of an additional copy of X-chromosome in male.
- Genetic constitution: 44 A + XXY (i.e. 47 chromosomes).





GENETIC DISORDERS

Chromosomal Disorders

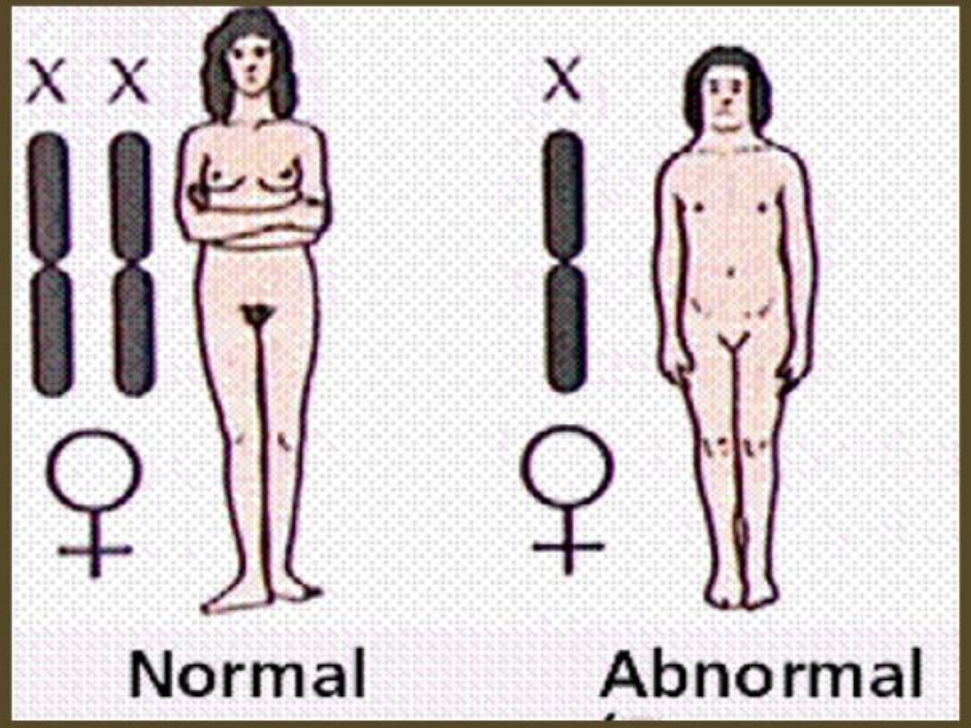
Klinefelter's syndrome

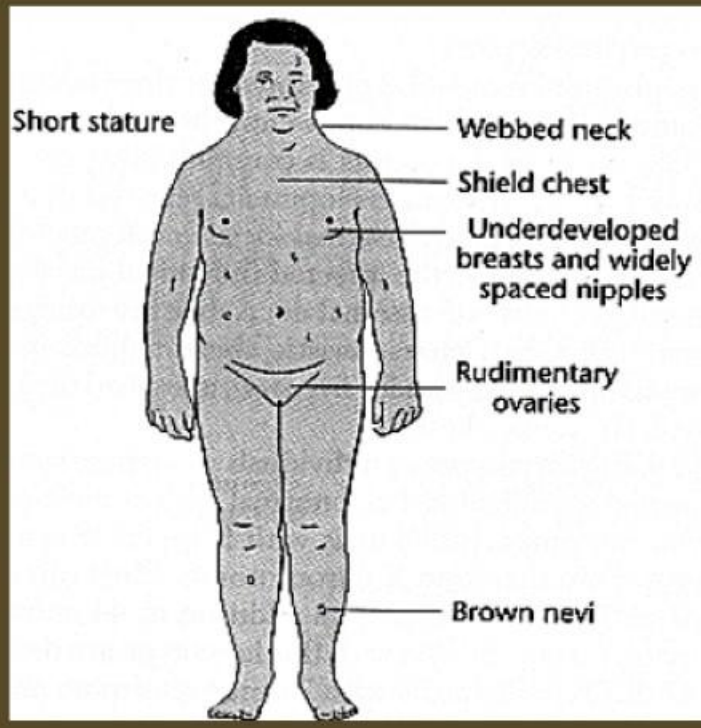
Features

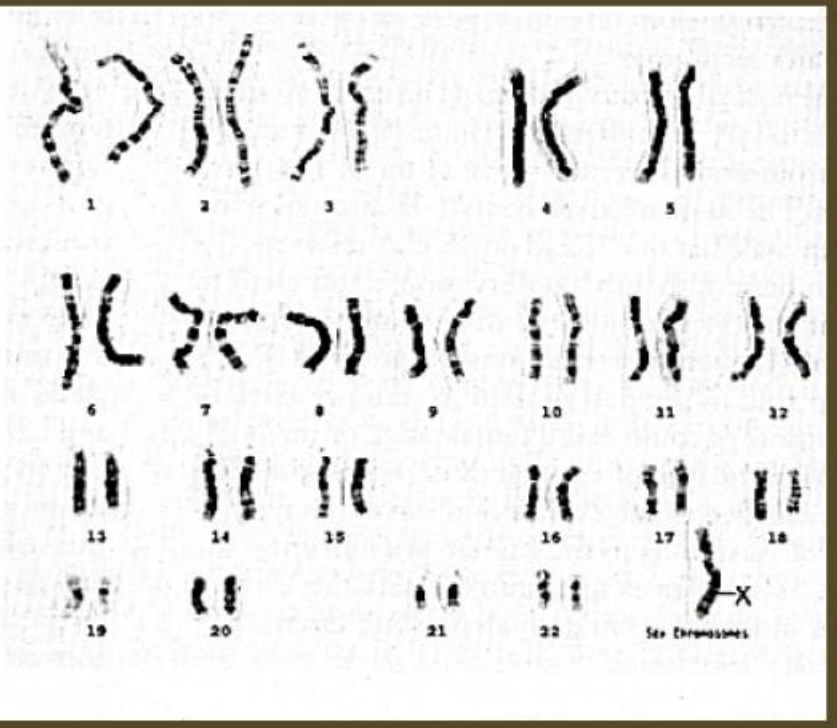
- ✓ Overall masculine development, however, feminine development (development of breast, i.e., Gynaecomastia) is also expressed.
- ✓ Sterile.
- ✓ Mentally retarded.

Turner's syndrome

- This is the absence of one of the X chromosomes in female.
- Genetic constitution: 44 A + X0 (i.e. 45 chromosomes).







GENETIC DISORDERS

Chromosomal Disorders

Turner's syndrome

Features

- ✓ Sterile, Ovaries are rudimentary.
- ✓ Lack of other secondary sexual characters.
- ✓ Dwarf.
- ✓ Mentally retarded.