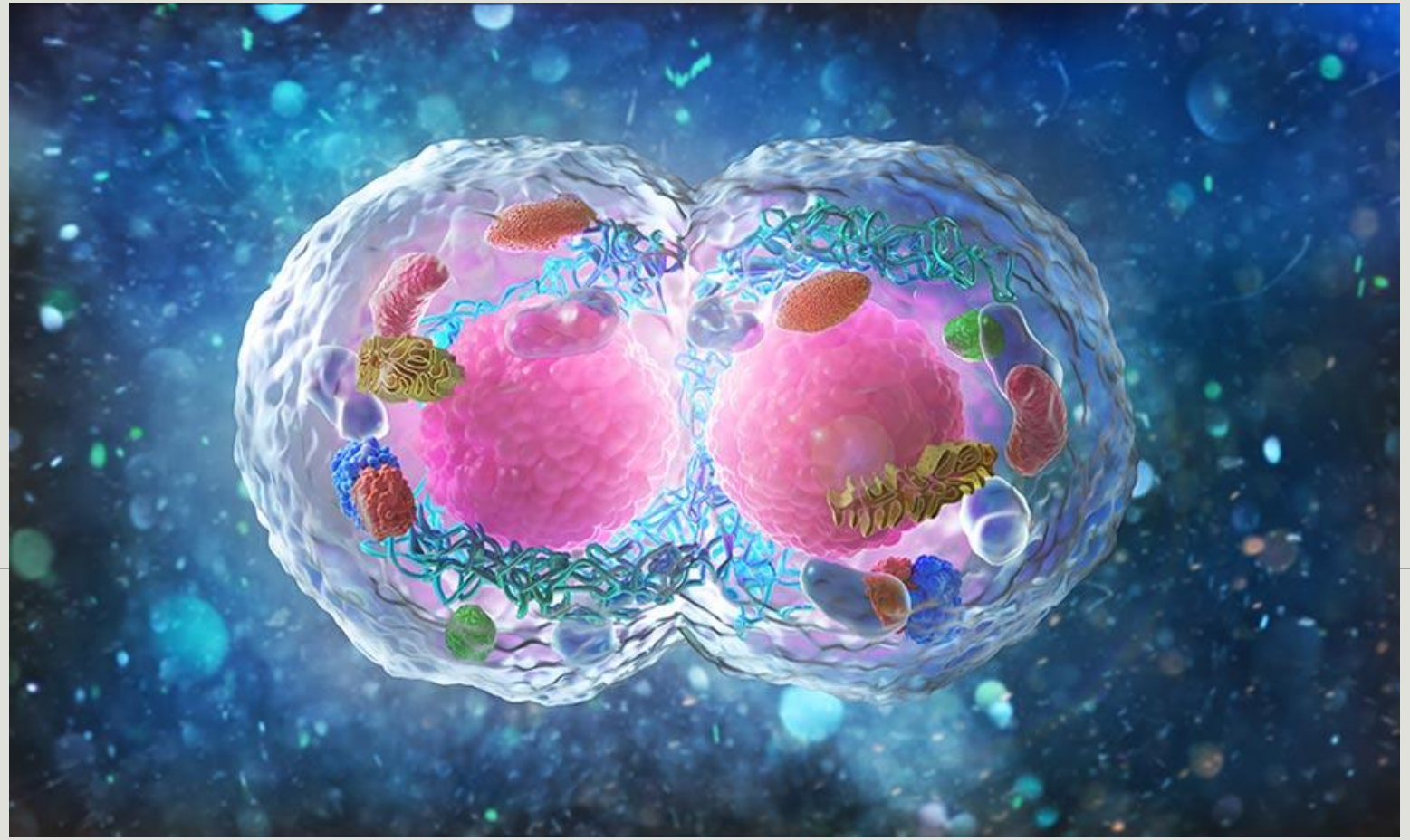
Genetic disorders



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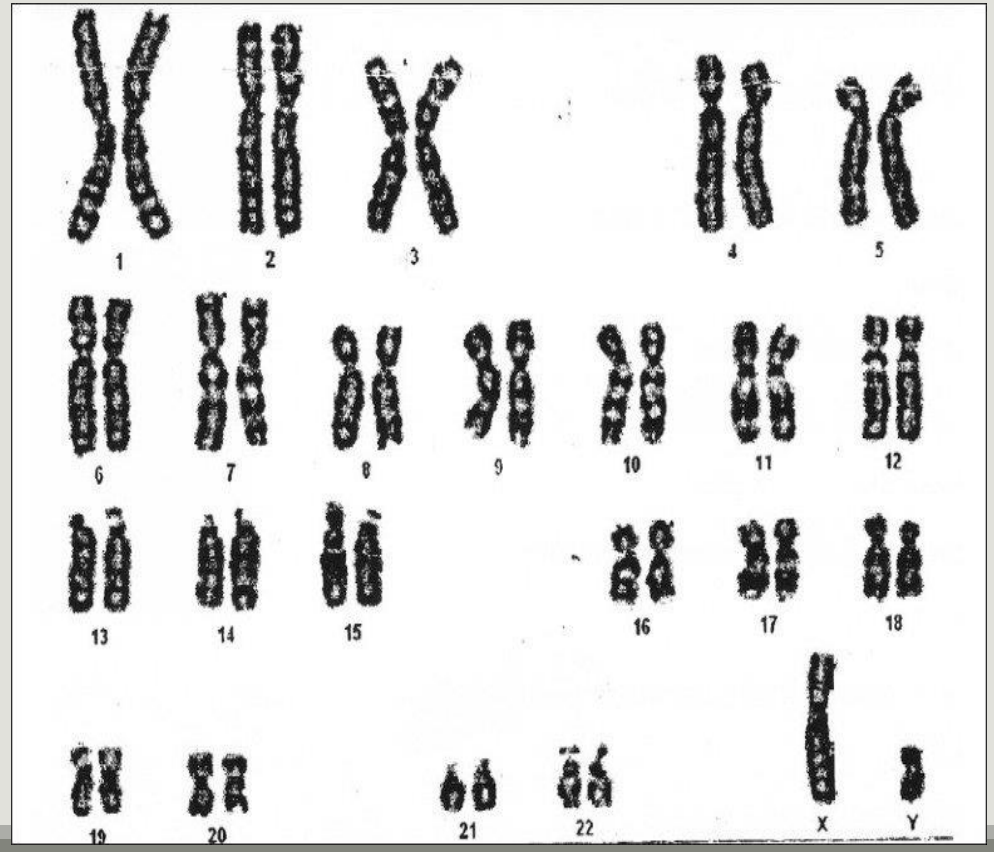
12/11/2025

Terminology

- Genetics: Study of heredity and its variation.
- Gene: part of chromosome and they code for a trait or character.
- Chromosome: long continuous strand of DNA that carries genetic information.
- Each somatic cell has 46 chromosomes (23 pairs).

22 pairs of autosomes + 23rd pair of sex chromosomes

- Sex chromosome pair is alike in female (two X chromosomes) whereas in male there is one X chromosome and one Y chromosome.

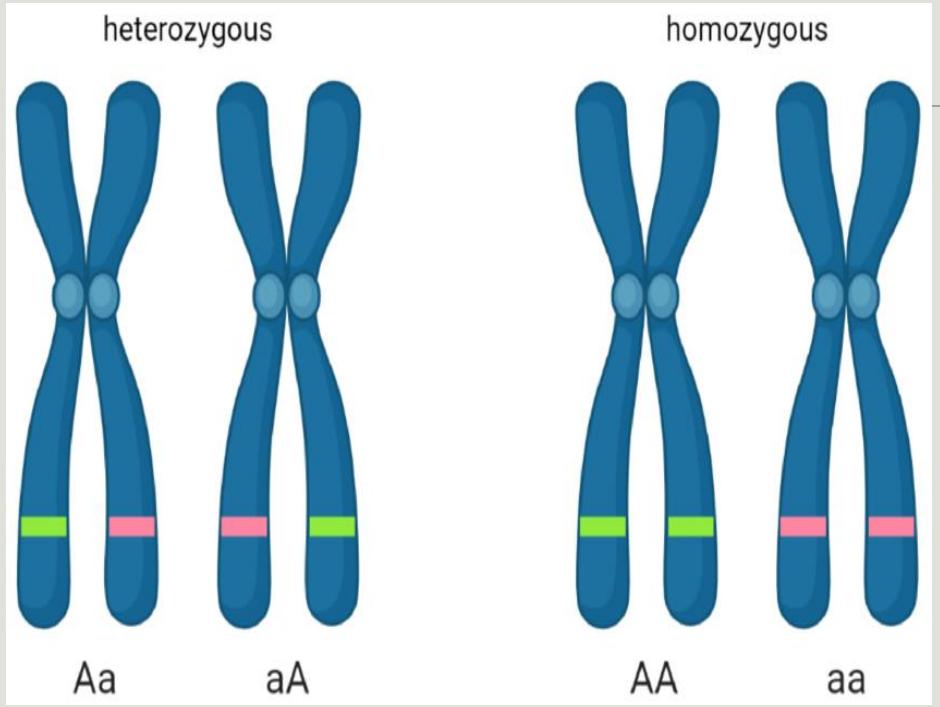


- An allele is a alternate form of a gene coding for different form of character. An individual inherits two alleles for each gene, one from each parent, which can be the same or different.

- Homozygous is a genetic term for having two identical alleles for a specific gene, one inherited from each parent
- Heterozygous: having two different alleles of a specific gene.
- Genome: all genetic information in the DNA.

- Genotype: specific genetic makeup of the individual.
- Phenotype: visible traits of a person.

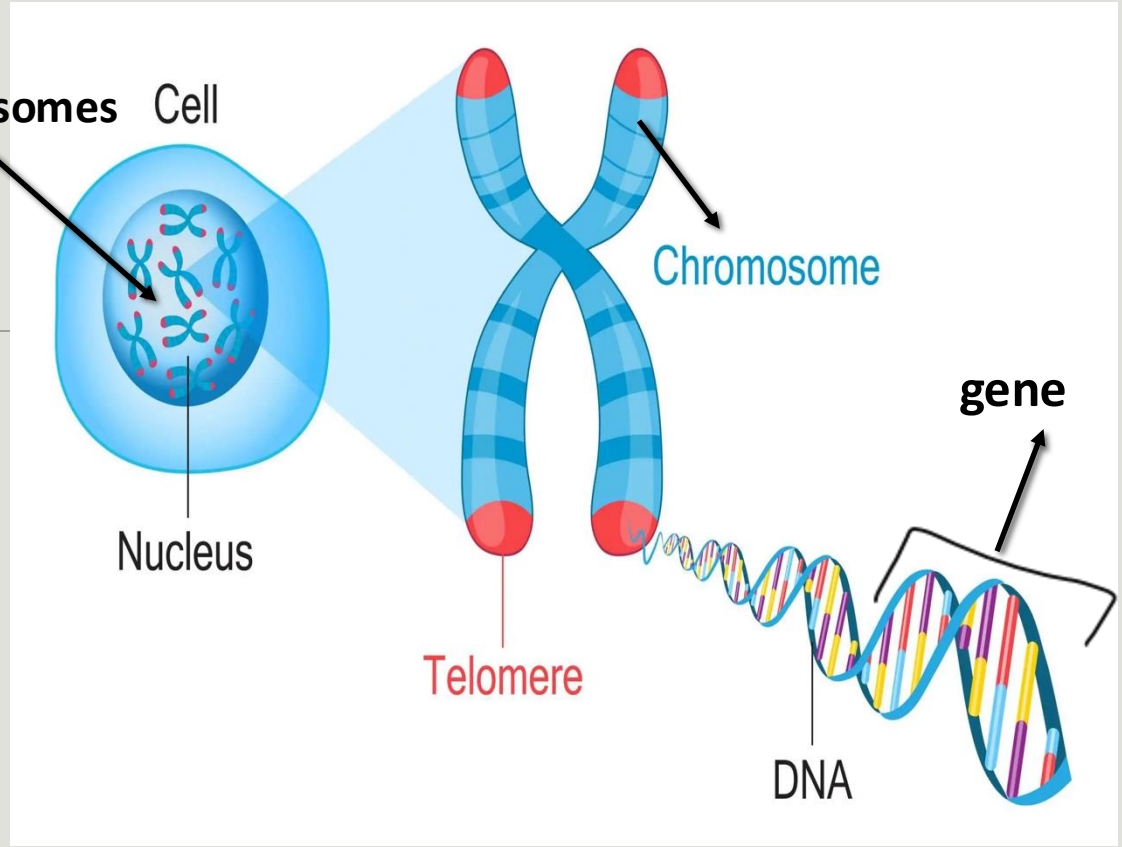
A: dominant allele
A: recessive allele

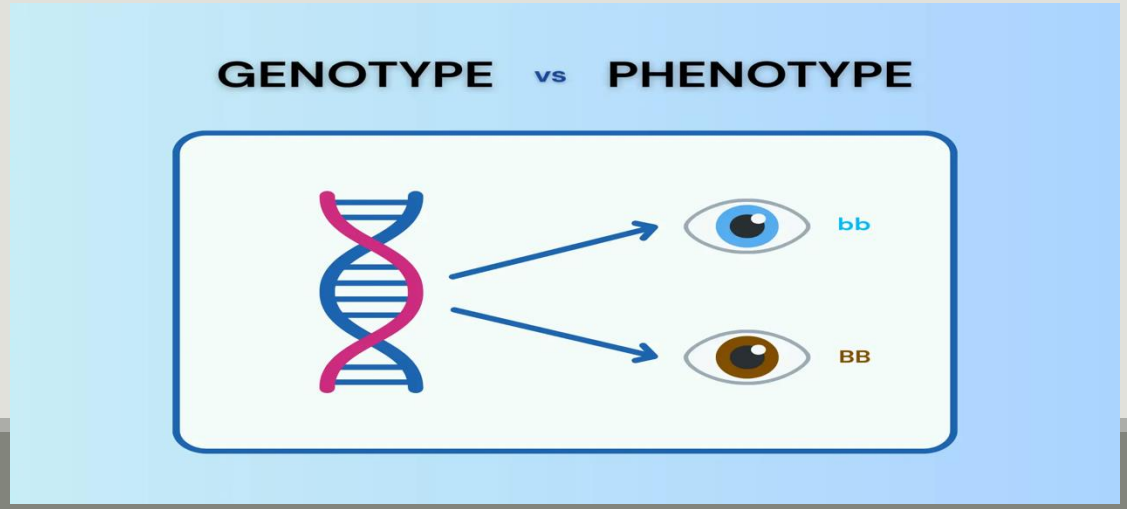


Net expression: A A A a

Each gene has two alleles, identical or different

46 chromosomes
23 pairs





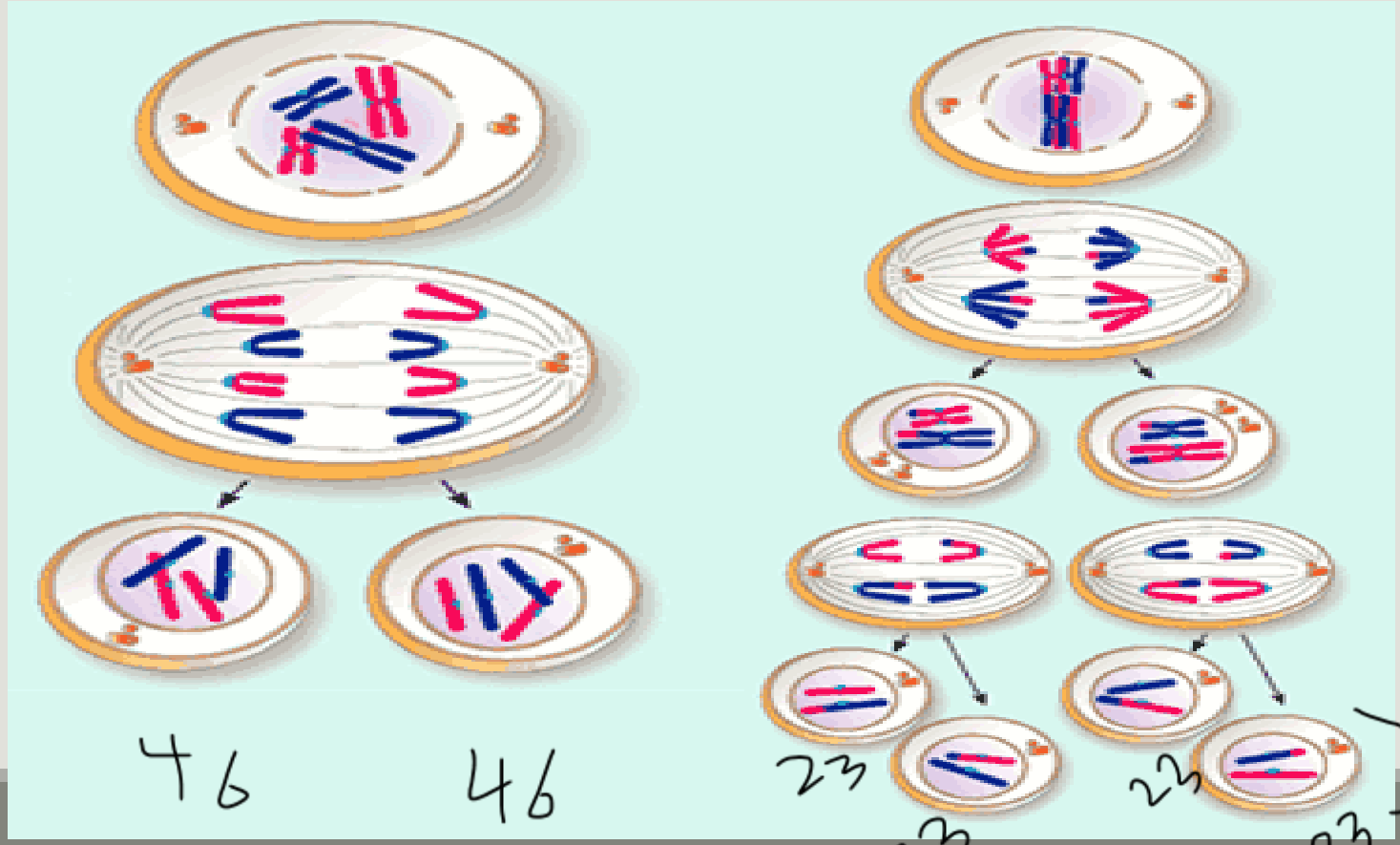
Mitosis vs. Meiosis

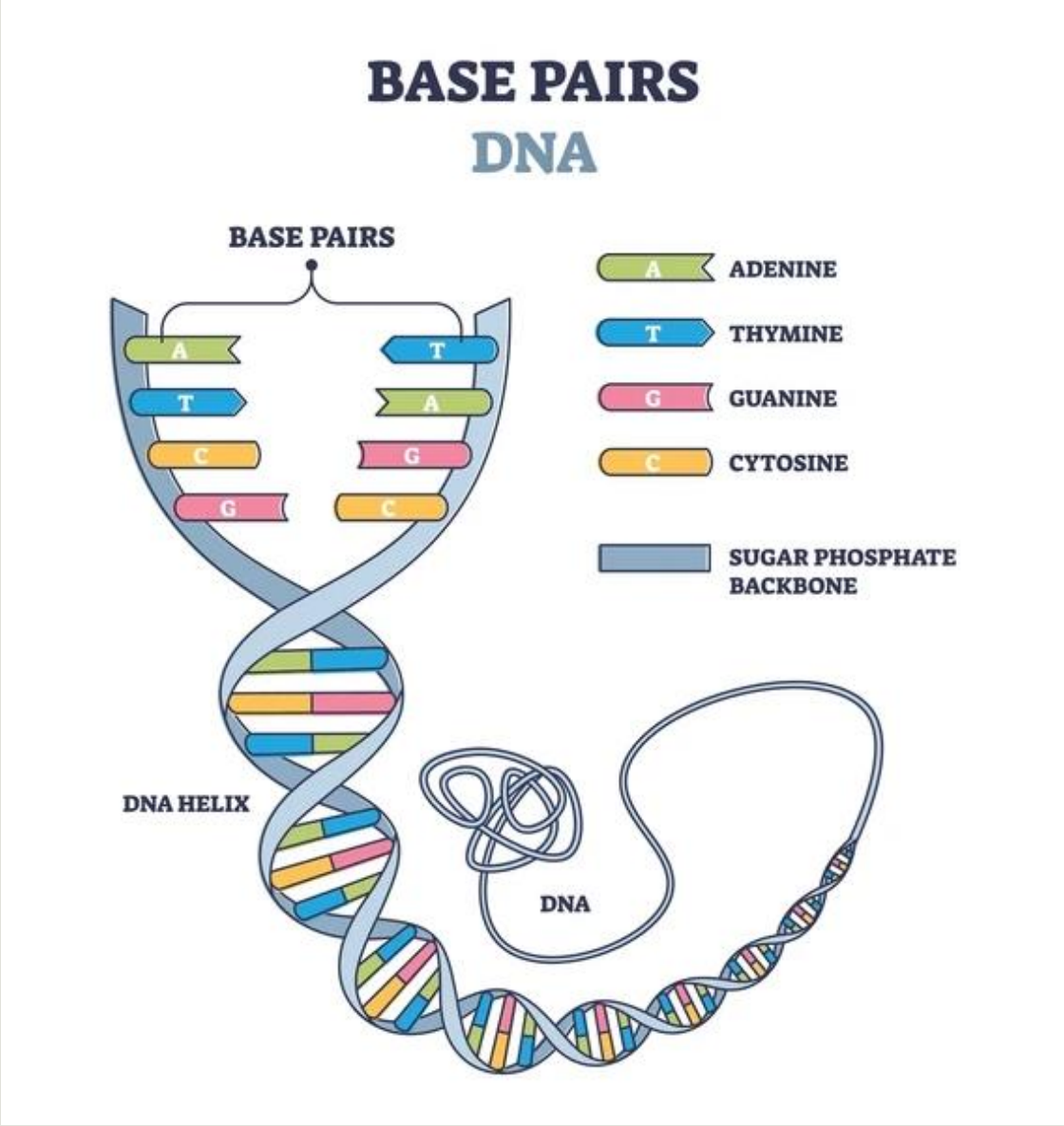
Mitosis

Mitosis is the type of cell division that results in the formation of two daughter cells each with the same number and kind of chromosomes as the parent cell.

Meiosis

Meiosis is a type of cell division that results in the formation of four daughter cells each with half the number of chromosomes as the parent cell. And genetically different from parent.

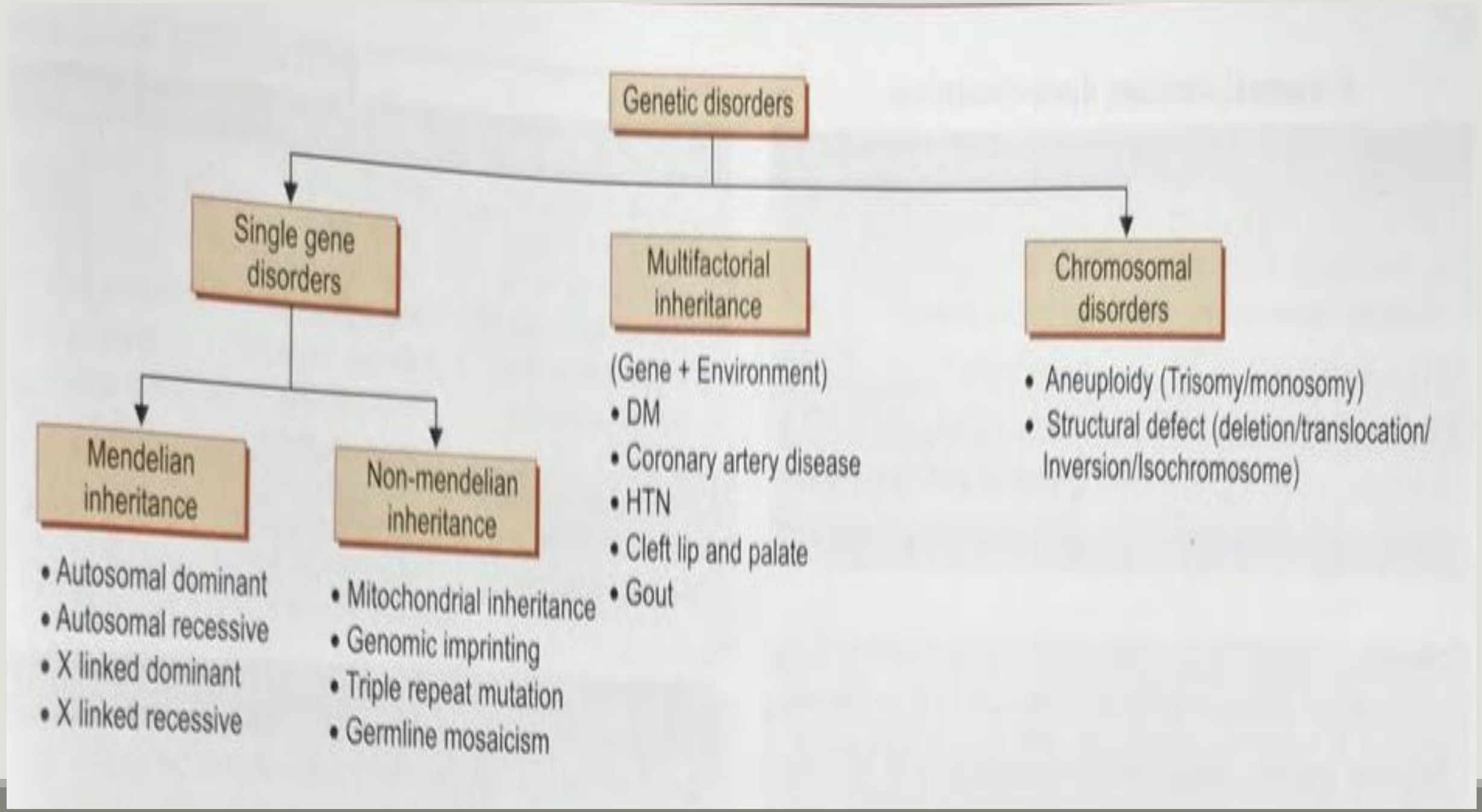




- DNA is the molecular basis for inheritance.
- Each strand of DNA composed of a chain of nucleotides matching each other in the center forming a twisted ladder.

Introduction

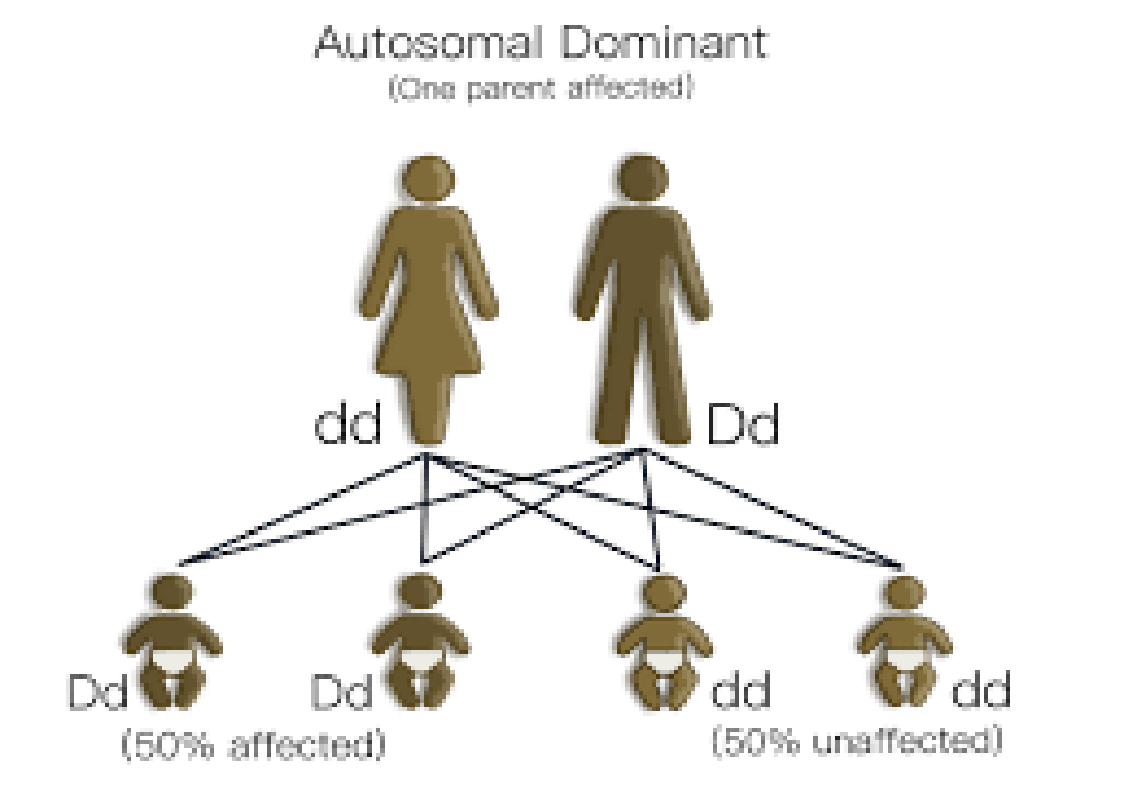
- Genetic disorder: disease caused by abnormalities in an individual's DNA.
- Abnormalities include small gene mutations or whole chromosome changes.
- Mutation: permanent change of DNA.


Genetic disorders
Single gene disorders
Multifactorial inheritance
Chromosomal disorders
Mendelian inheritance
Non-mendelian inheritance
• Autosomal dominant
• Autosomal recessive
• X linked dominant
• X linked recessive
• Mitochondrial inheritance
• Genomic imprinting
• Triple repeat mutation
• Germline mosaicism
(Gene + Environment)
• DM
• Coronary artery disease
• HTN
• Cleft lip and palate
• Gout
• Aneuploidy (Trisomy/monosomy)
• Structural defect (deletion/translocation/ Inversion/Isochromosome)

❖ Mendelian inheritance

1) Autosomal Dominant:

- Mutated genes can express themselves in heterozygous state.
- Homozygous of Dominant mutant genes will die prenatally.
- Usually cause defect in a structural protein.
- Individuals with Autosomal Dominant diseases have a 50 to 50 chance of passing the mutant gene and therefore the disorder onto each of their children.



Examples:

Adult polycystic kidney

Marfan syndrome

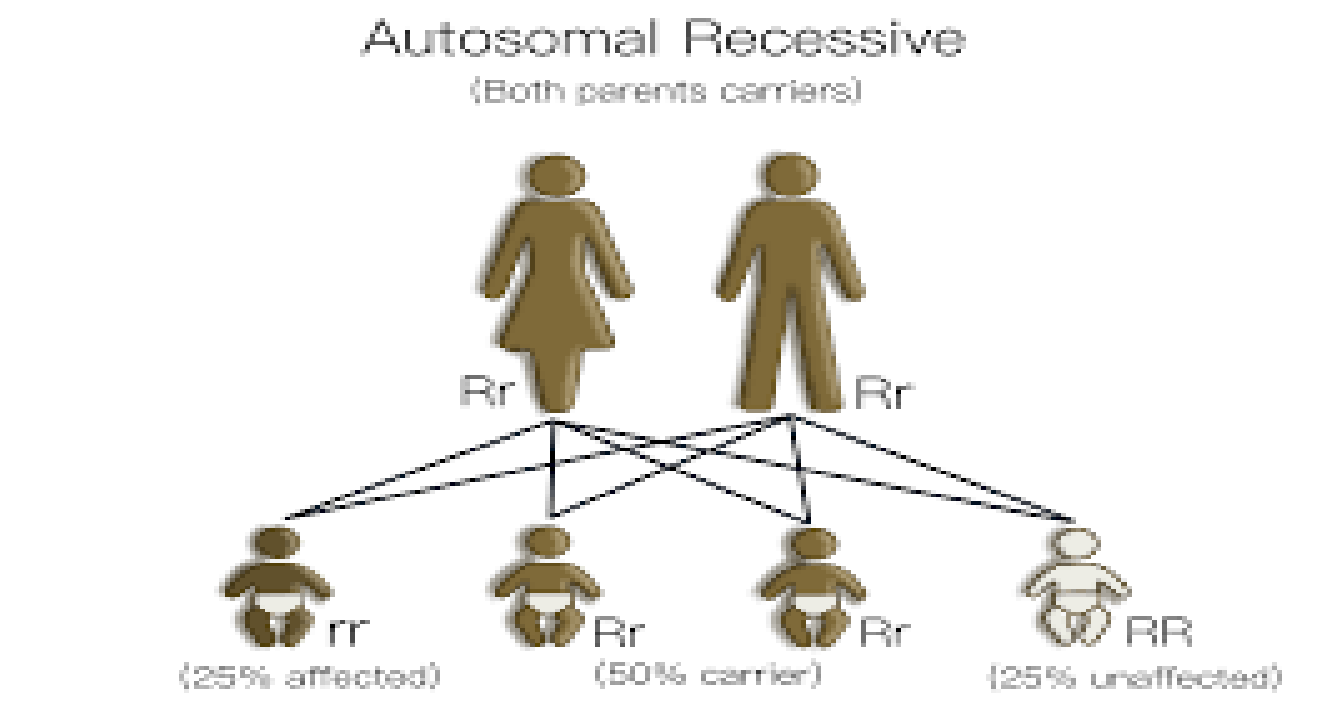
2) Autosomal Recessive:

- Mutant genes express themselves only in homozygous state.
- Usually cause defect in a enzyme protein.
- An affected person usually has an unaffected parents who each carry a single copy of the mutant gene and are refer to as carriers.
- _two unaffected carrier parents have a 25% chance with each pregnancy of having a male or female child affected by the disorder. And the risk of having a carrier child is 50%.

- Examples:

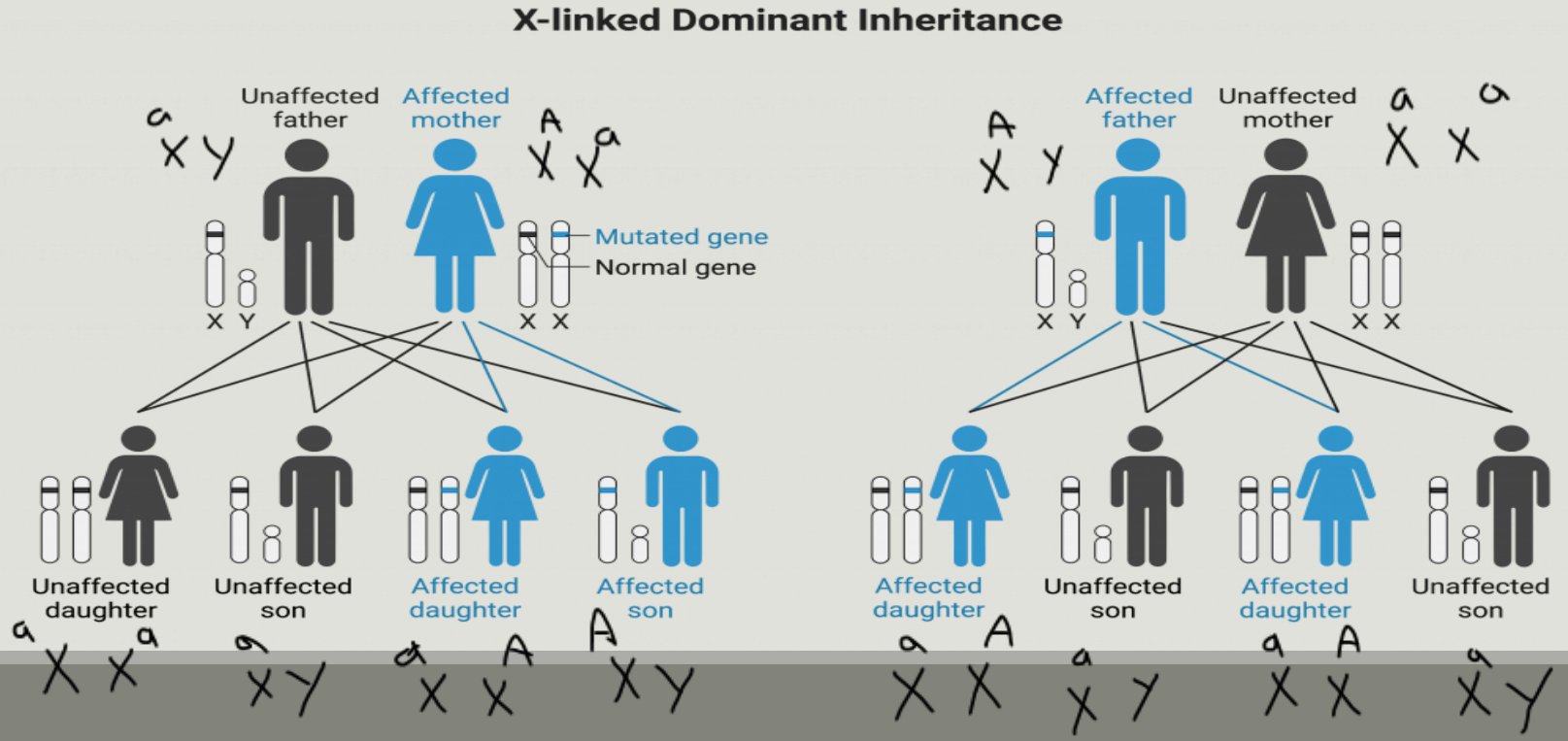
Sickle cell anemia

Inborn error of metabolism



3) X Linked Dominant:

- Caused by mutations of genes on the X chromosome. in heterozygous state.
- Homozygous state in female is extremely rare.
- A woman with an X-linked dominant disorder has a 50% chance of passing it to each child, regardless of sex
- Sons of an affected man will not inherit the disorder.
- All daughters of an affected man will inherit the disorder.

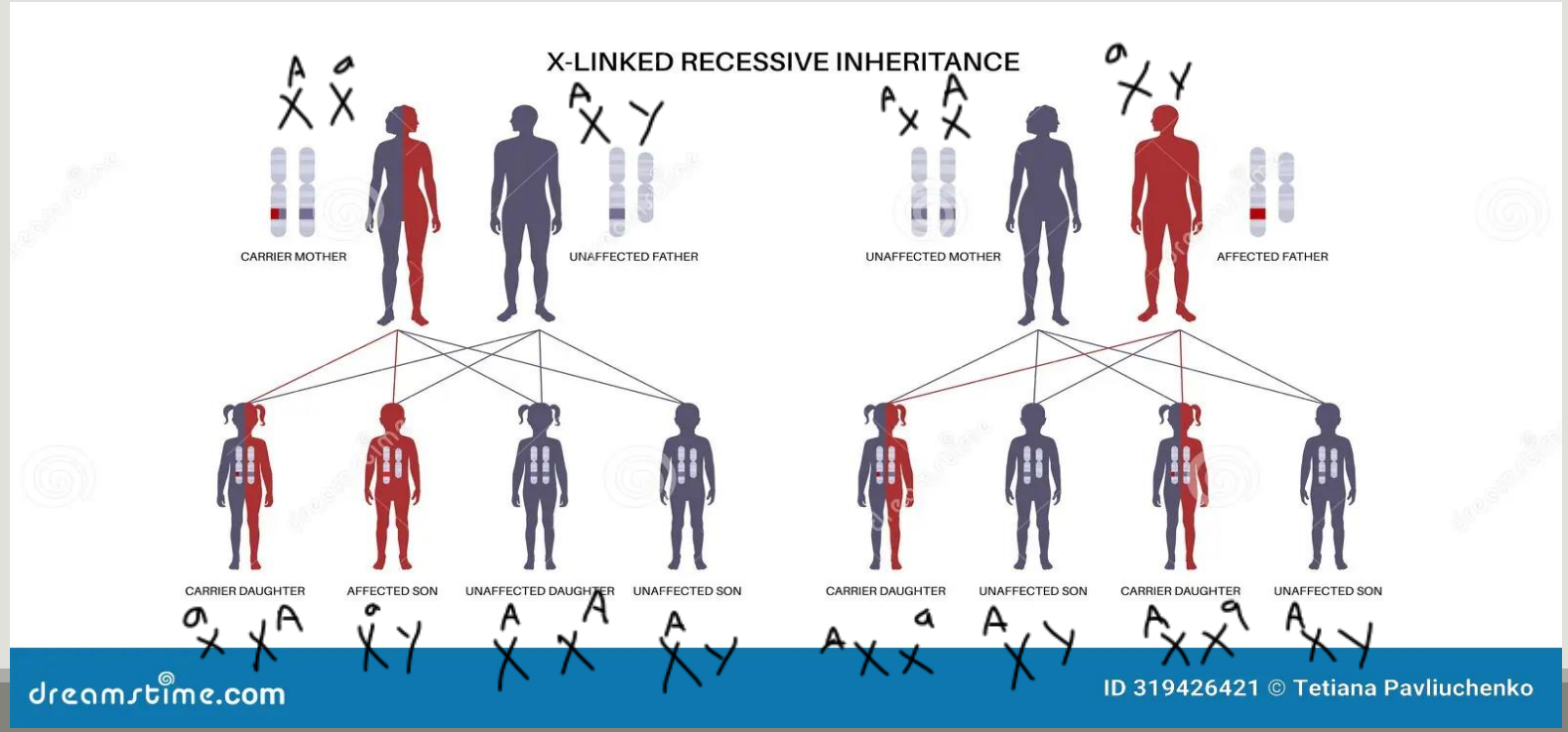


4) X liked Recessive:

- Also caused by mutant allele on the X chromosome.
- There is no corresponding allele on the Y chromosome for the Mutant allele on the X chromosome.

- In males: The mutant recessive gene on the X chromosome express itself because it is not suppressed by normal allele.
- In females: The presence of normal allele on the other X chromosome prevent the expression of the disease. So females only can act as carriers.

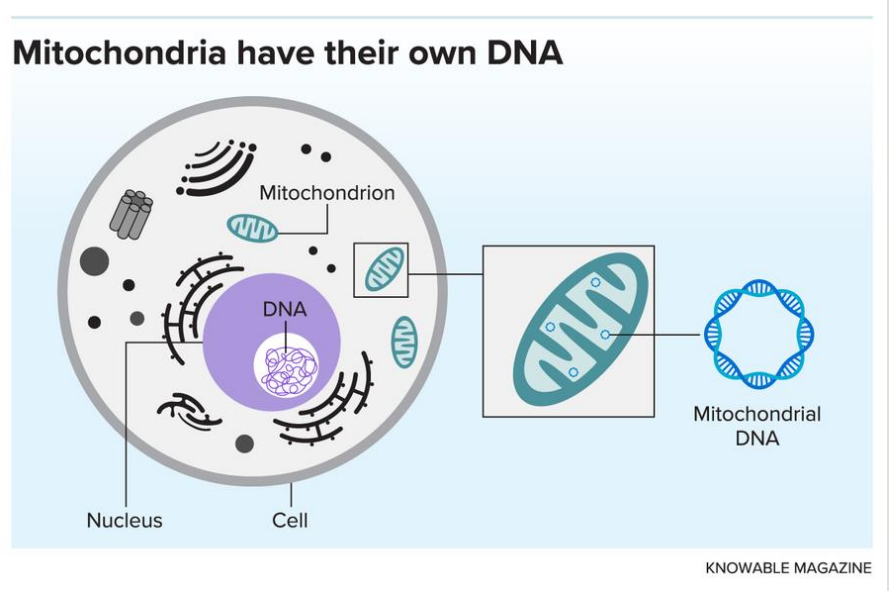
- Examples:
- Hemophilia type A, and B.

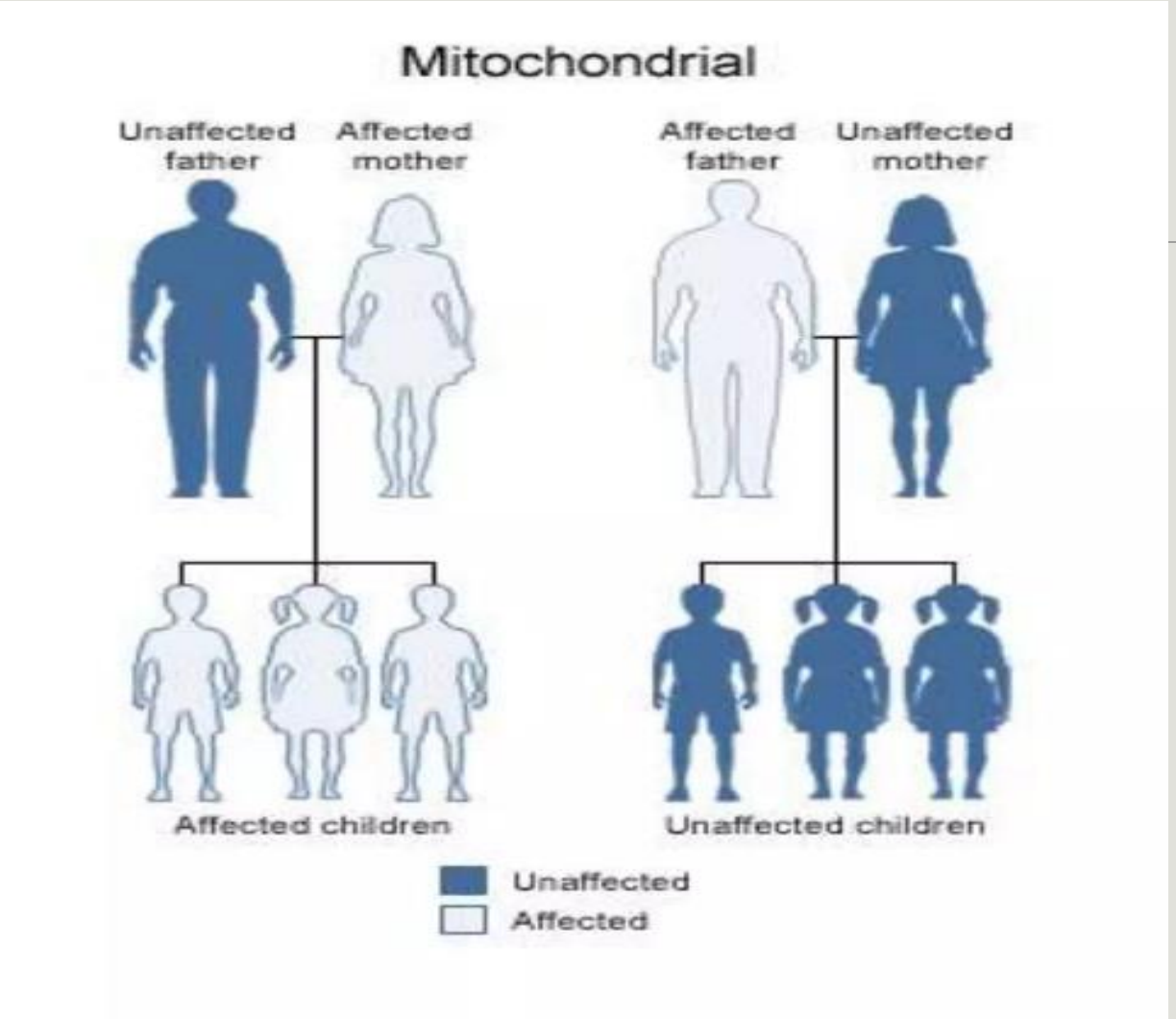


❖ Non-Mendelian inheritance

1) Mitochondrial inheritance:

- Mitochondria are inherited exclusively from the mother's egg.
  - ❖ Fertilized ovum will degrade the mtDNA in the sperm so only mother mtDNA will survive.
- Mothers transmit their mtDNA to both sons and daughters. Only the daughters will be able to transmit mtDNA to future generations.
- So Mitochondrial inheritance has a characteristic Maternal inheritance
- Diseases from mitochondrial inheritance often affect high-energy organs: heart, skeletal muscle, liver, kidneys.



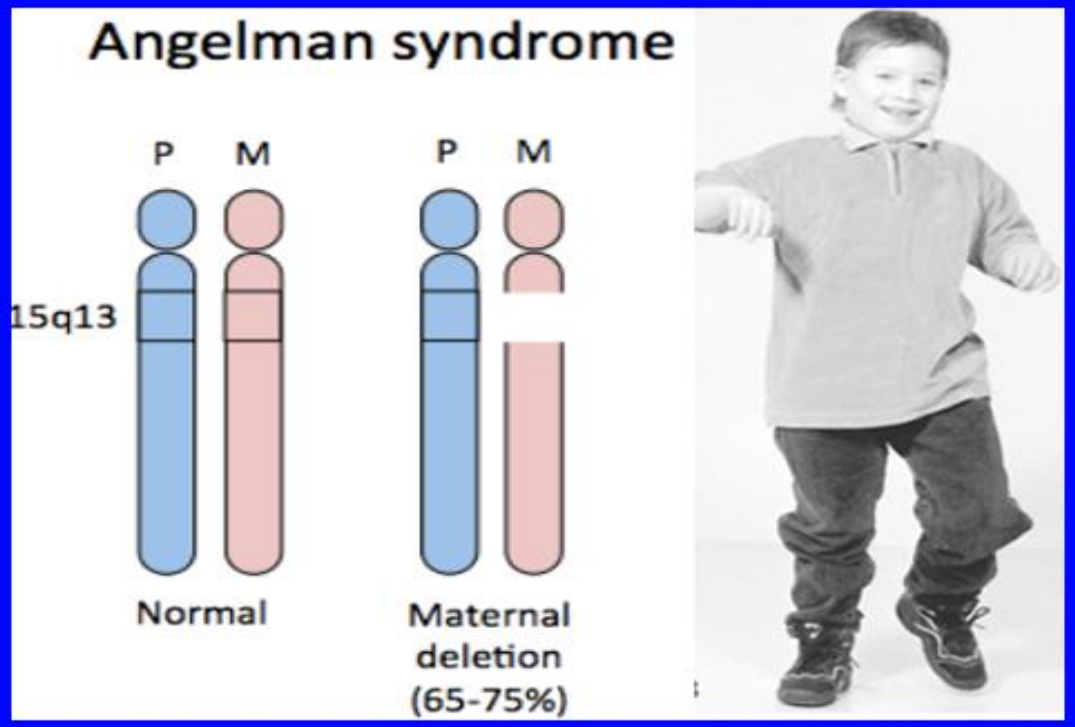

Mitochondrial
Unaffected father
Affected mother
Affected father
Unaffected mother
Affected children
Unaffected children
Unaffected
Affected

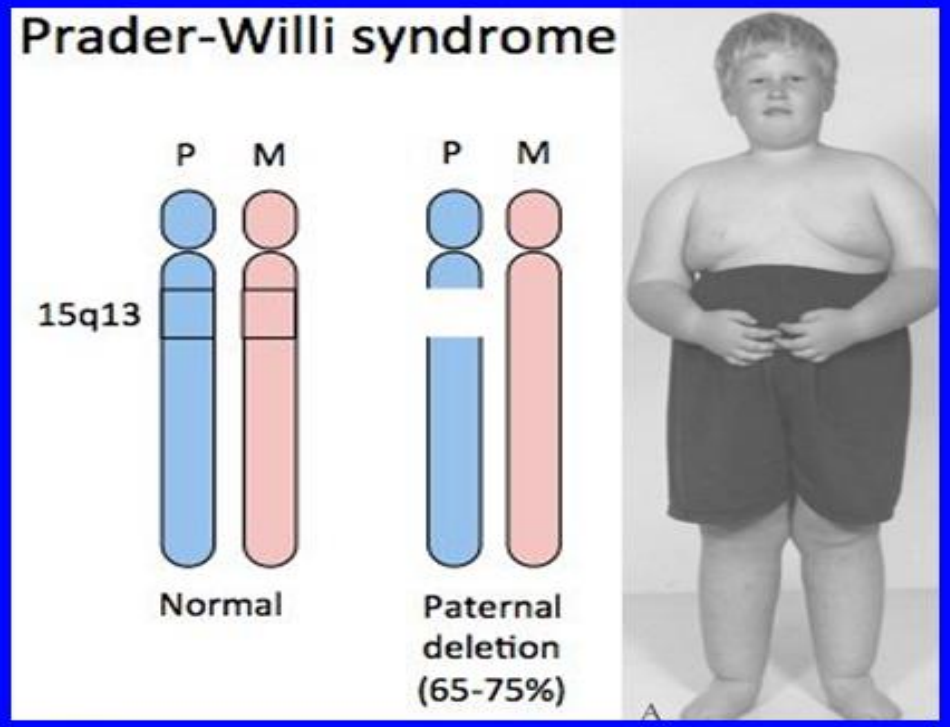
2) Genomic imprinting:

- Only one copy of a gene (either from the mother or the father) is expressed, while the other is silenced.

- If the chromosome containing the gene which is expressed undergo deletion there will be disease, whereas if the corresponding chromosome undergo deletion nothing will happen.

- Example:
- Microdeletion of chromosome 15q11-13
- If microdeletion occurs on maternal chromosome, Angelman syndrome result.
- If the microdeletion occurs on paternal chromosome, Pradder-willi syndrome result





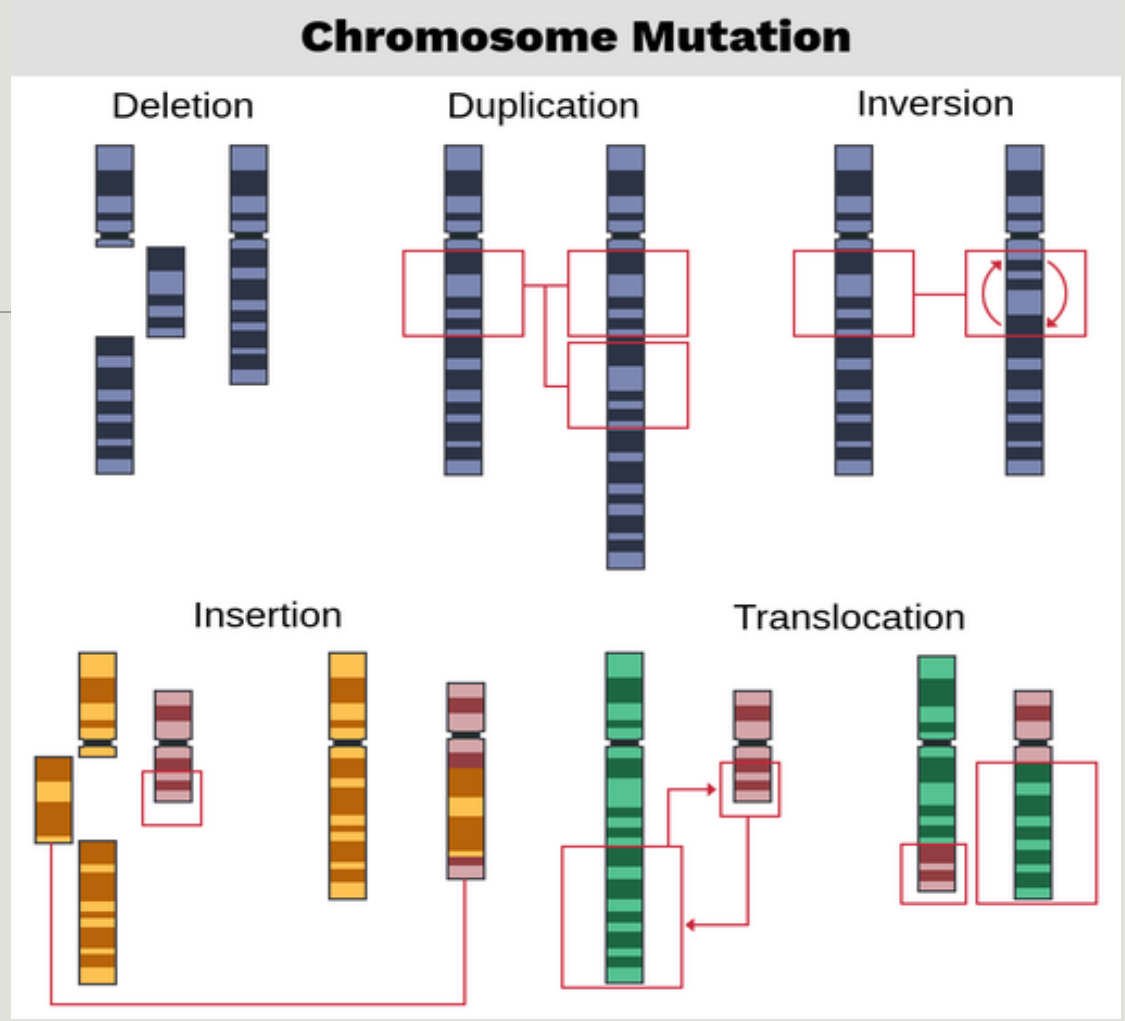
severe intellectual disability, a happy demeanor, seizures, and movement issues

hypotonia, poor feeding in infancy, followed by **hyperphagia** (insatiable hunger) and obesity

❖ Chromosomal disorders

- **1) structural defects:**
- **Inversion:** Chromosome segment rotates 180 degrees.
- **Translocation:** Chromosomal segment moves to a non-homologous chromosome.
- **Deletion:** Part of the chromosome breaks off.
- **Duplication:** A chromosome segment repeats itself.

2) Aneuploidy (Trisomy/Monosomy)

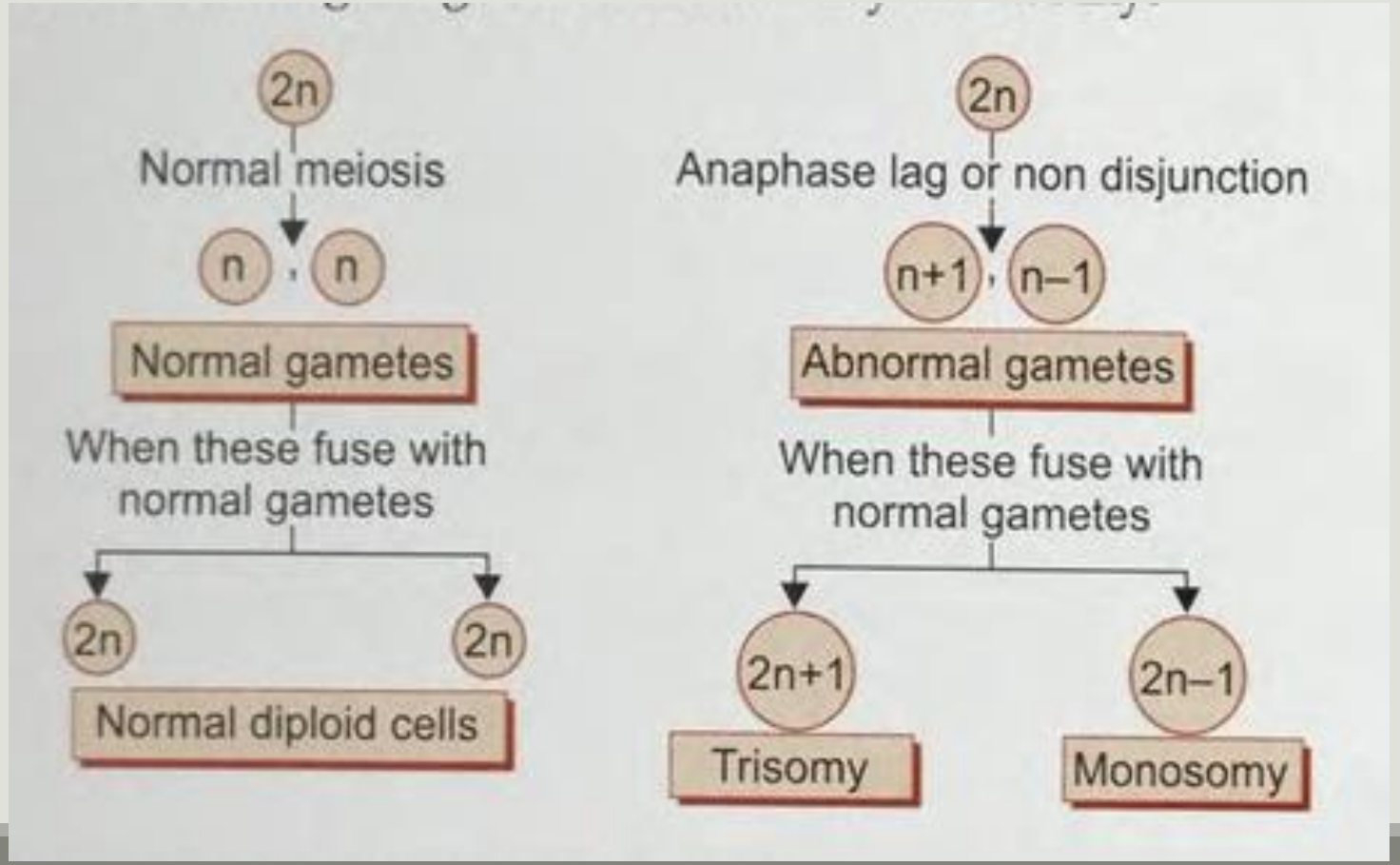


Aneuploidy (Trisomy/Monosomy)

- **C**aused by **Nondisjunction:** failure of chromosomes to separate during replication, causing abnormal autosomal chromosome numbers

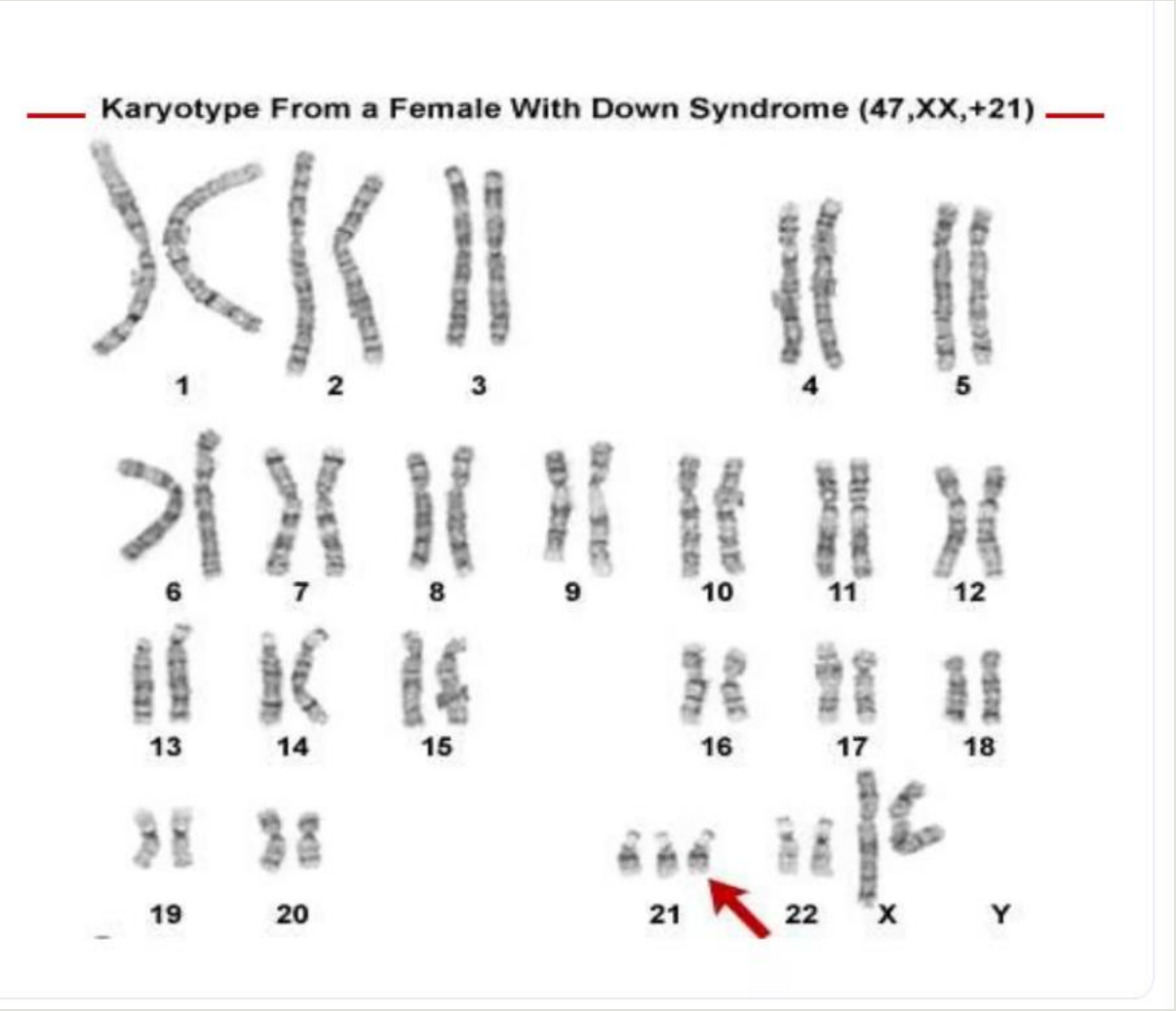
- **Monosomy:** 2n - 1 chromosomes
- **Trisomy:** 2n + 1 chromosomes,

  example: Down syndrome



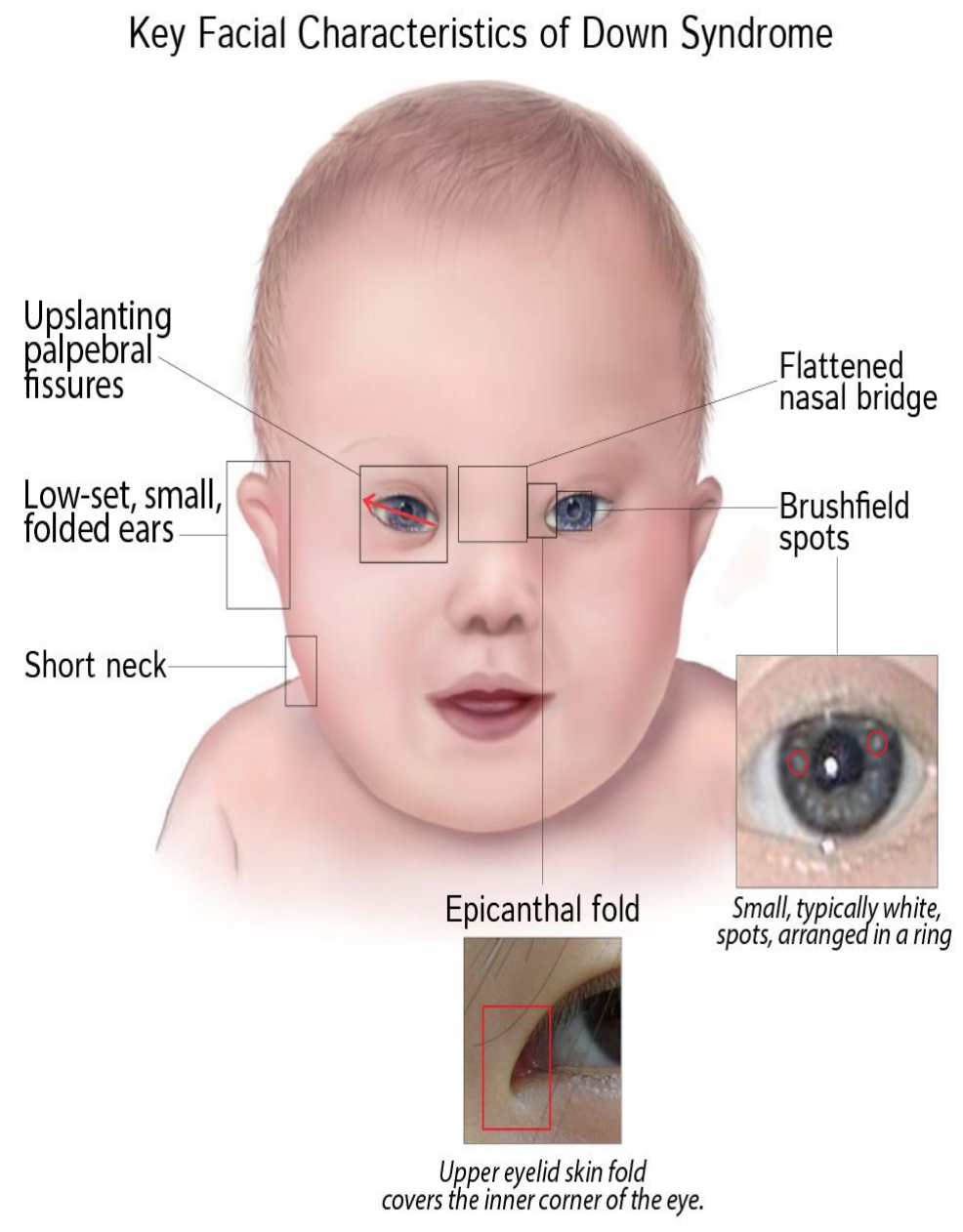
Down Syndrome (Trisomy 21)

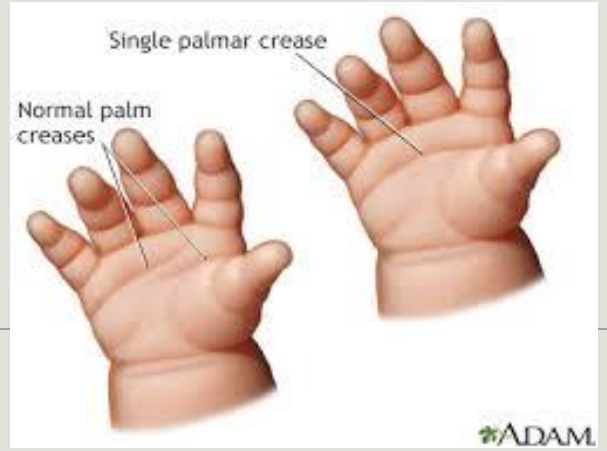
- Down syndrome usually results from an extra copy of chromosome 21
- This condition is known as Trisomy 21
- 47, XX or 47, XY
- The most common cause for mental retardation worldwide.
- Advance maternal age has a strong influence on the incidence of trisomy 21.

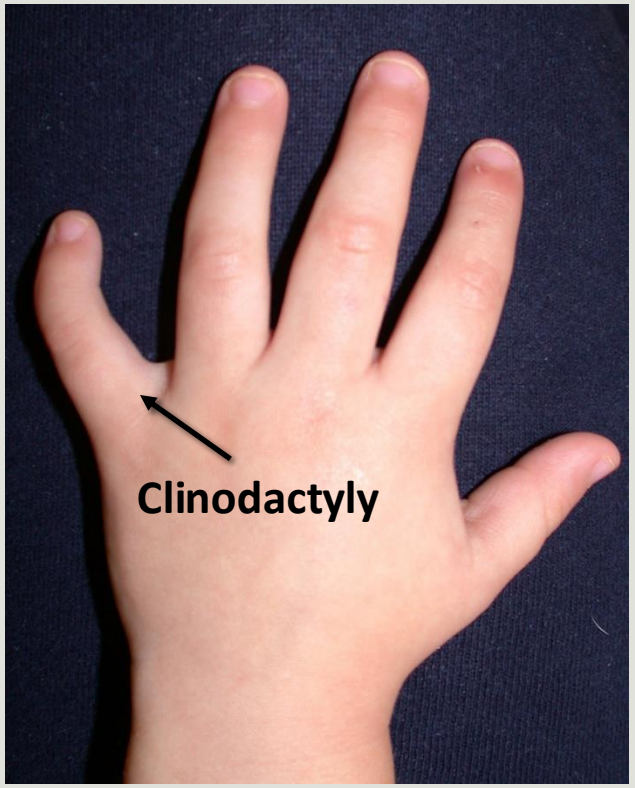


Characteristic physical features are commonly recognized

- Decreased or poor muscle tone.
- Short neck, with excess skin at the back of the neck.
- Flattened facial profile and nose.
- Small head, ears, and mouth.
- Upward slanting eyes, often with a skin fold that comes out from the upper eyelid and covers the inner corner of the eye.
- Clinodactyly: Small pinky finger that points inward towards the thumb.
- One crease in the palm of their hand (palmar crease).
- Shorter-than-average height.


Key Facial Characteristics of Down Syndrome
Upslanting palpebral fissures
Flattened nasal bridge
Low-set, small, folded ears
Brushfield spots
Short neck
Epicanthal fold
Small, typically white, spots, arranged in a ring
Upper eyelid skin fold covers the inner corner of the eye.


Single palmar crease
Normal palm creases
A.D.A.M.


Clinodactyly


DOWN SYNDROME

Complications:

- Congenital cardiac defect
- Increased risk for Leukemia
- Reduced fertility in females. (males are totally infertile)
- Alzaheimer’s disease
- Hirshbrung disease
- Duodenal atresia
- Respiratory tract infection

Screening for Down Syndrome

- Many standard prenatal screens can discover down syndrome.

First and second trimester Down syndrome screens

Screen	When performed (weeks gestation)	Detection rate	False positive rate	Description
Triple test	15-20	70%	5%	Maternal serum α-feto protein (Low) + Estriol (Low) + hCG (High)
Quad screen	15–20	81%	5%	Triple test + inhibin-Alpha (High)
First Trimester Combined Test	10–13	85%	5%	Ultrasound to measure: *Nuchal Translucency (Increased) *Ductus venosus flow (reversed) *Nasal bone (hypoplasia) + hCG + Pregnancy associated plasma protein A; PAPPA (Low)
Integrated Test	10-13 and 15–20	95%	5%	Measurements from both the 1st Trimester Combined test and the 2nd trimester Quad test to yield a more accurate screening result.

Diagnostic tests

1) chorionic villous sampling:

- taking tiny sample of the placenta.
- Through the cervix or needle inserted into the abdomen.
- During first trimester
- Risk of abortion

2) Amniocentesis:

- Taking small amount of amniotic fluid
- Through needle inserted into the abdomen
- Risk of abortion

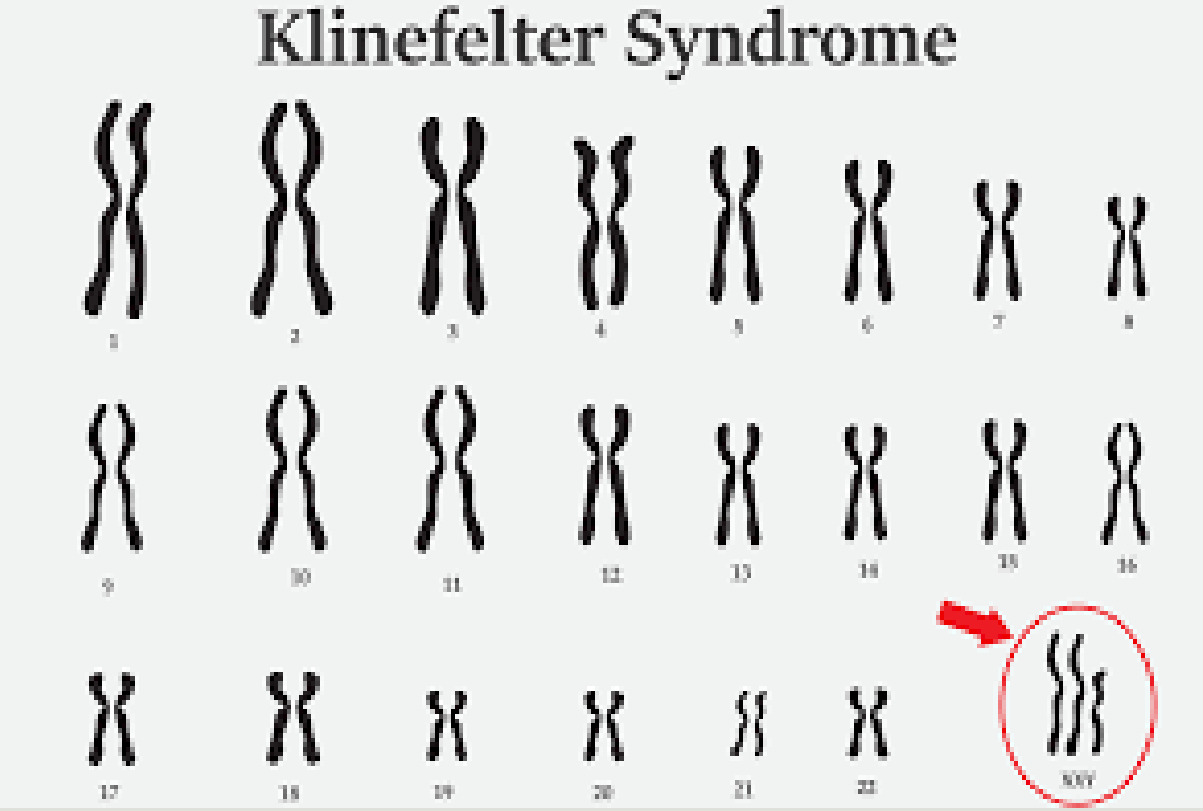
3) Percutaneous umbilical blood sampling:

- small sample of umbilical blood
- Also needle into the abdomen
- Risk of abortion

Karyotyping
خريطة جينية

Klinefelter syndrome

- The most common chromosomal disorder of males.
- Due to extra X chromosome, 47 XXY
- Extra X chromosome increase Female like features in males

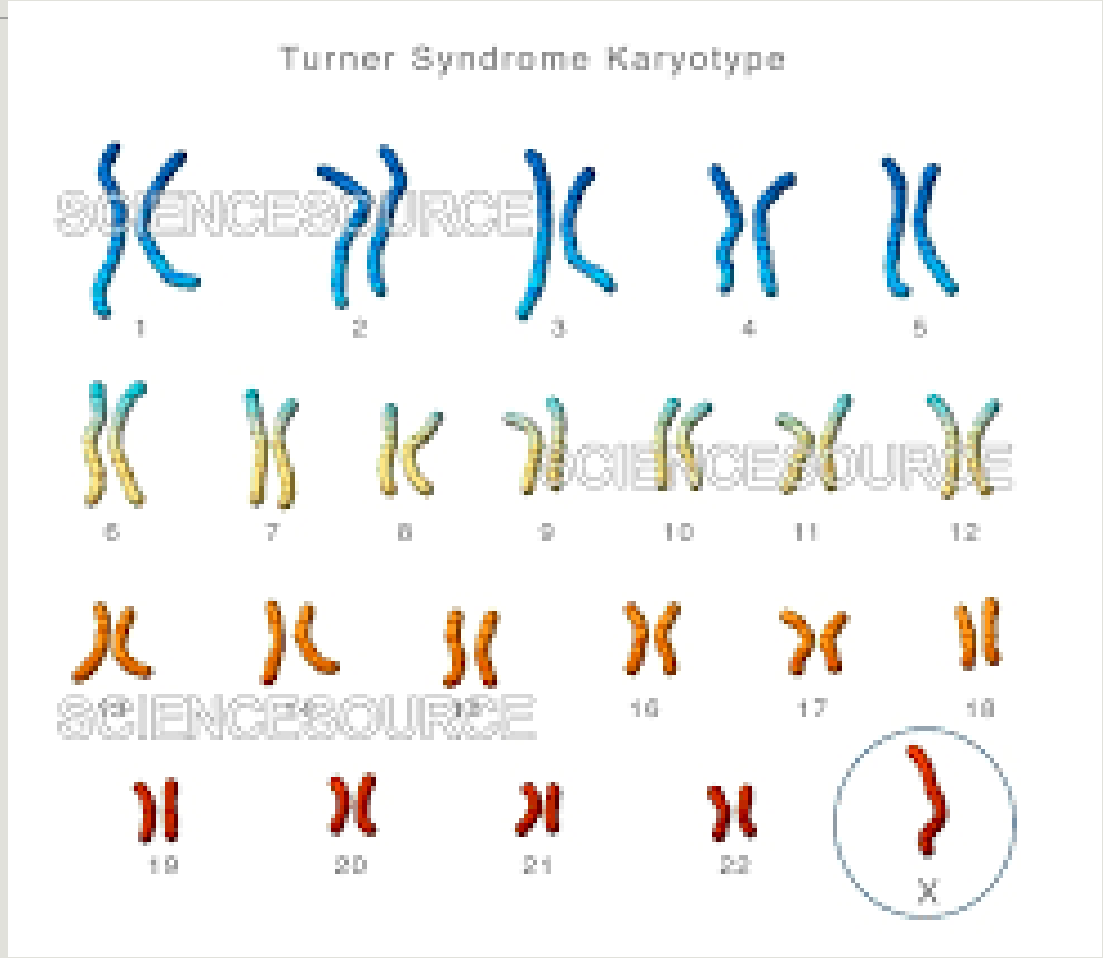


- **Symptoms:**
- Hypogonadism and infertility
- Subnormal IQ
- Gynecomastia
- Loss of secondary sexual characteristic
- Mitral valve prolapse

Turner Syndrome

- Most common cause of sex chromosomal abnormality in females
- Monosomy of X chromosome, 45, X

- **Symptoms:**
- Hypogonadism
- Primary amenorrhea




Thank You