Chapter III : Mutations

Mutations

- **I. Gene mutations (Nucleotides variations or microlesions)**

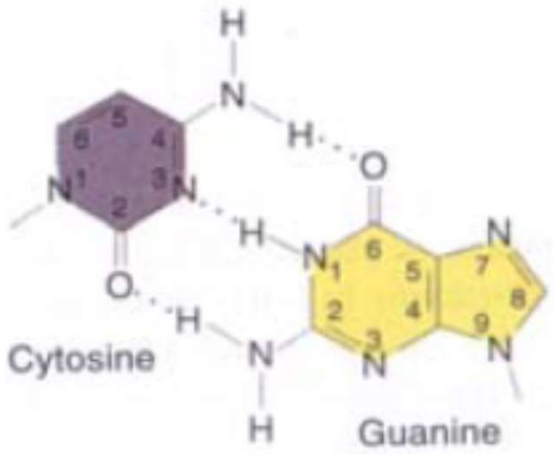
- **II. Chromosome aberrations (macrolesions)**

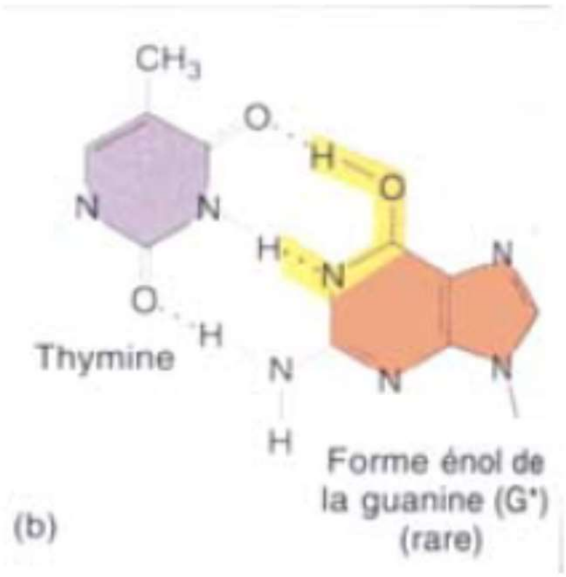
Mutations

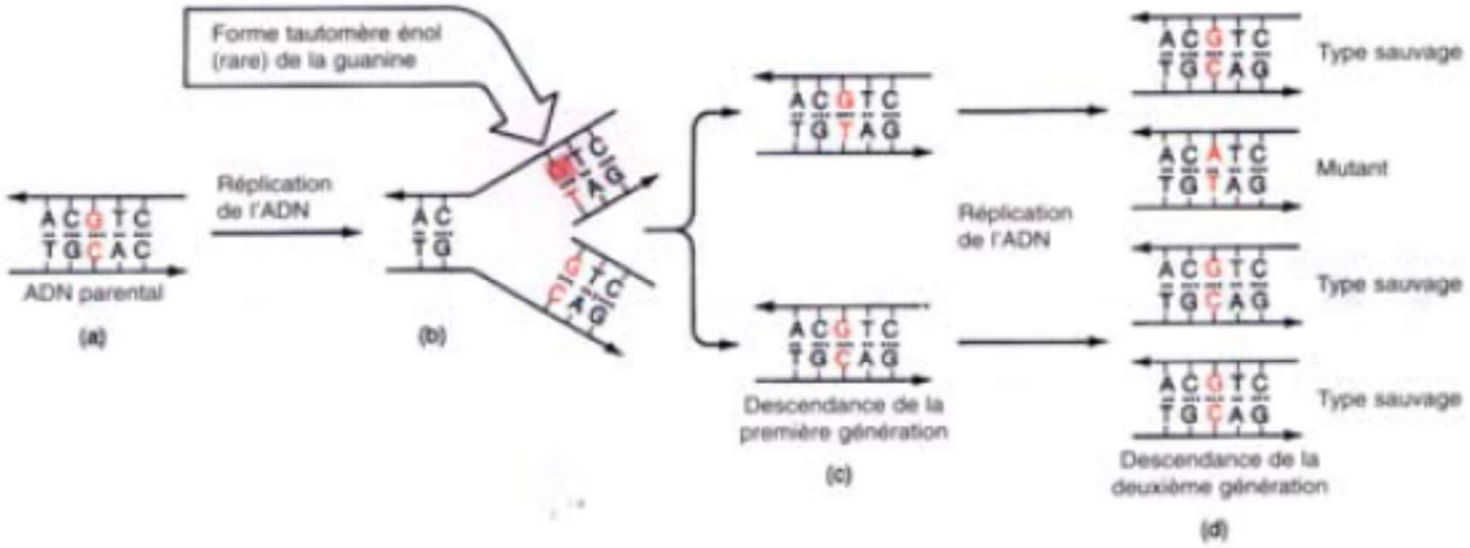
- **I. Gene mutations (Nucleotides variations or microlesions) :**
  - **1- Definition**

  – Base copying accidents most commonly occurring during DNA replication ➔ The newly synthesized DNA is then no longer an exact replica of the parental DNA.

  – Exposure to mutagenic agents







Apparition d'une paire de bases illégitime pendant la réplication

I. Gene mutations

- **The mutation may be:**
  - A) A mutation by substitution:
    - **A transition**: [a purine (A, G) > purine] or [pyrimidine (C, T, U) > pyrimidine]
    - **A Transversion:** [a purine > pyrimidine], or [pyrimidine > purine]
  - B) A forgotten base, it is then a mutation by **deletion**.
  - C) A base added, this is then a mutation by

I. Gene mutations

- Gene mutations – a mutation that affects a single gene
  - Substitution– an event in which a nucleotide is replaced by a different nucleotide
  - Insertion – an event in which one or more nucleotides are added into a DNA sequence coding for a gene
  - Deletion – an event in which one or more nucleotides are deleted from a DNA sequence of a gene

Type	Definition	Example
Insertion	one nucleotides is added	…TAGCCAGATA… …TAGC**G**CAGATA…
Deletion	one nucleotides is deleted	…TAGC**C**AGATA… …TAGCAGATA…
Substitution (mutation point)	a nucleotide is replaced by a different nucleotide	…TAGCCAGATA… …TAGCCAG**T**TA…

I. Gene mutations

- **Is a DNA mutation hereditary?**
  - In prokaryotes mutations are automatically transmitted to descendants.
  - In eukaryotes, a mutation is only transmitted to descendants if this mutation affects the sex (germ) cells.

I. Gene mutations

- **2) The different types of mutations :**
  - 2.1. Mutations without frameshifting:
    - A. Silent mutations
    - B. Missense mutations
    - C. Mutations involving the ‘stop’ codon (nonsense mutations)
  - 2.2. Frameshift mutations :
    - They are due to the insertion or deletion of one or more bases which causes a shift in the reading of the triplets.

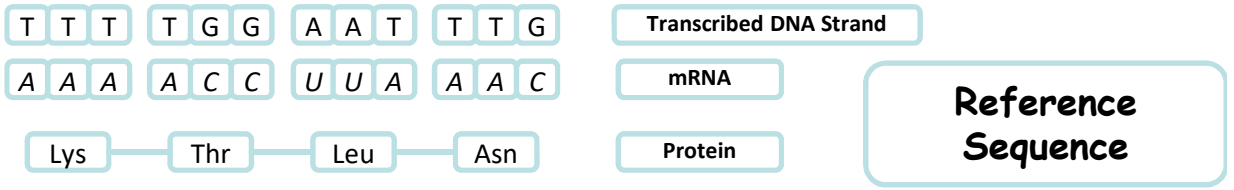
I. Gene mutations

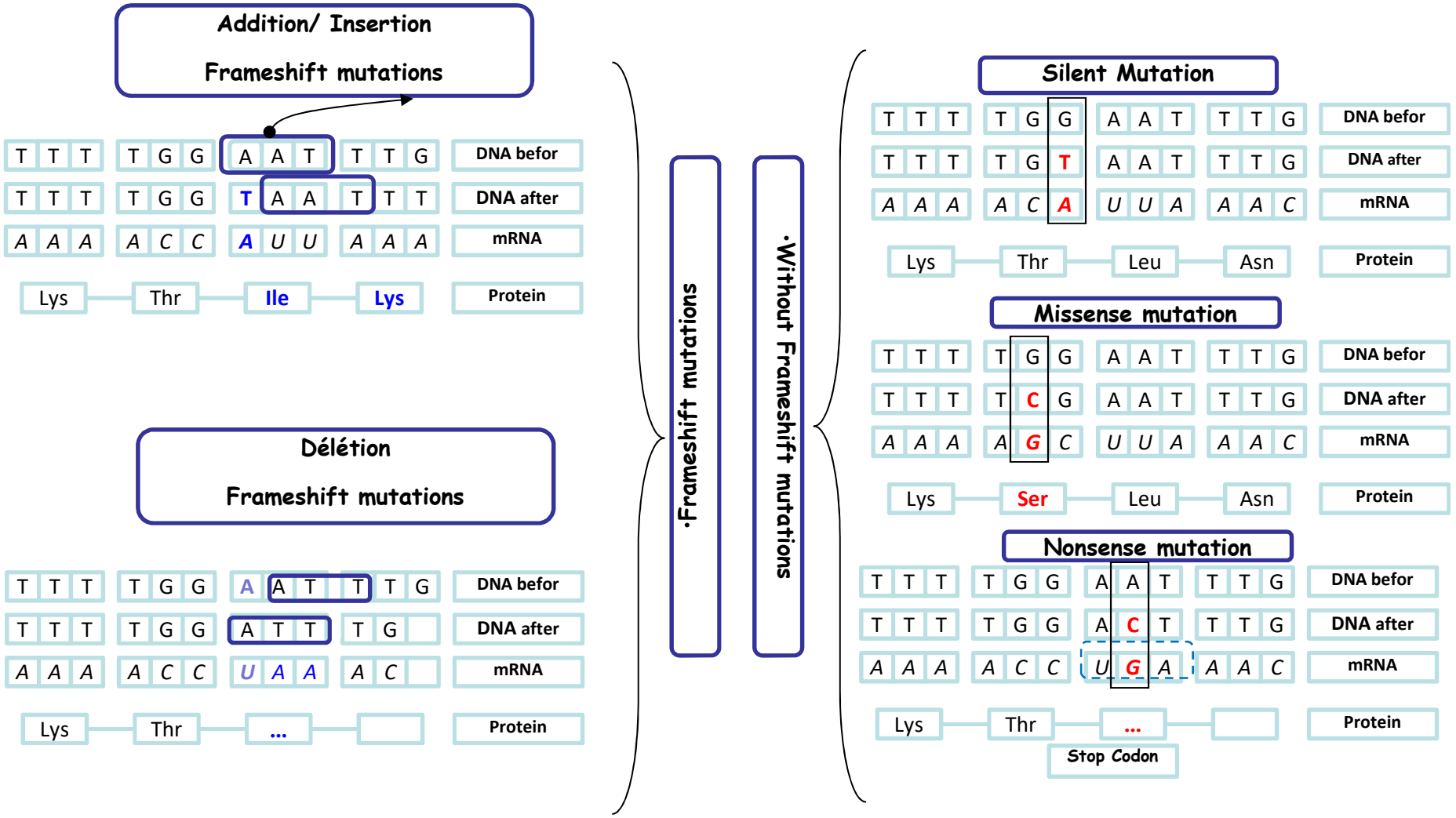
- 2.1. Mutations without frameshifting :
  - Silent mutations : a mutation in which there is no effect on the polypeptide chain created
    - No externally visible effect on the polypeptide
  - Missense mutations : a mutation that leads to the replacement of one amino acid by a different one
    - Different amino acids
    - Can change the created polypeptides
  - nonsense mutations : a mutation in which a stop codon is expressed early leading to the creation of a shorter polypeptide chain
    - Significantly affects the protein created

I. Gene mutations

- 2.2. Frameshift mutations :
  - Insertion and deletion mutations cause a frameshift
  - A mutation that causes reading frame shift
  - a mutation in which the reading frame of a codon is altered, which may change all subsequent codons
    - Codons are read in groups of three nucleotides
    - Adding or removing a nucleotide changes the reading frame
    - Different polypeptide is produced

Different Types of Gene Mutations & Consequences



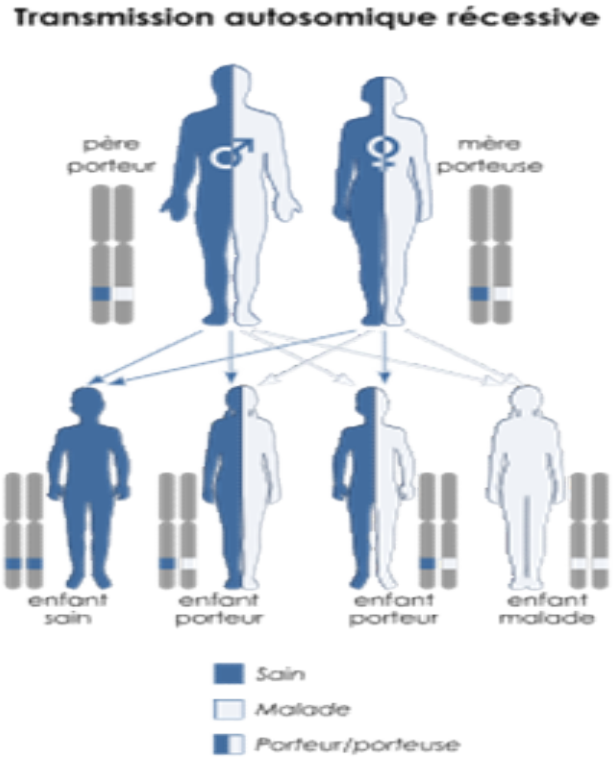


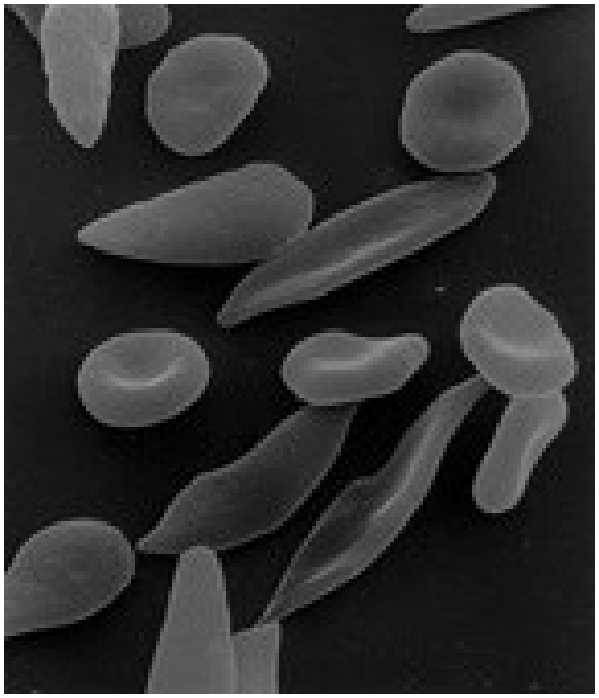
I. Gene mutations

- **4- Some consequences of mutations:**
  - 1- Diseases: A mutation of a single base on a structural gene can lead to serious pathological disorders, a classic example is **sickle cell disease** (*drepanocytosis*).

I. Gene mutations

- **4- Some consequences of mutations :**
  - 1- Diseases : exp. **sickle cell disease**.





I. Gene mutations

- **4- Some consequences of mutations :**

  - 2- Mutations and evolution (biodiversity):
    - Mutations that occur randomly can present an advantage.
    - Mutated individuals and their descendants survive better than non-mutated individuals because the best adapted who survive

I. Gene mutations

- **5. Mutagenic agents:**
  - **a. Chemical agents:**
    - Chemical substances that transform bases: exp, replacement of the NH2 of Cytosine by an OH which gives uracil,
    - Chemicals that disrupt replication by intercalating into DNA, exp BET (Ethidium bromide)
    - Chemical substances that behave as base analogues: For example 5-bromouracil which resembles thymine,

- **5. Mutagenic agents :**
  - **a. Chemical agents :**
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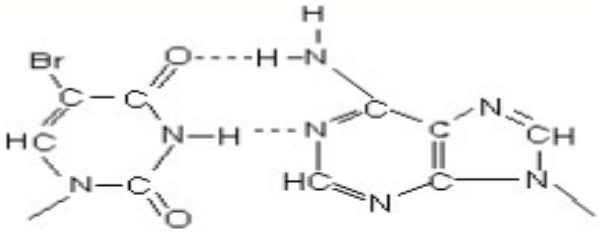
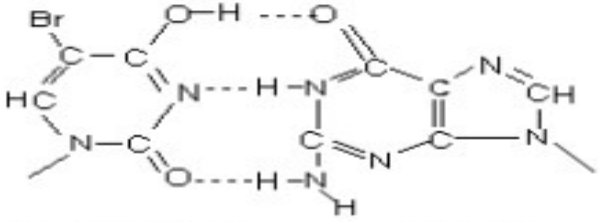


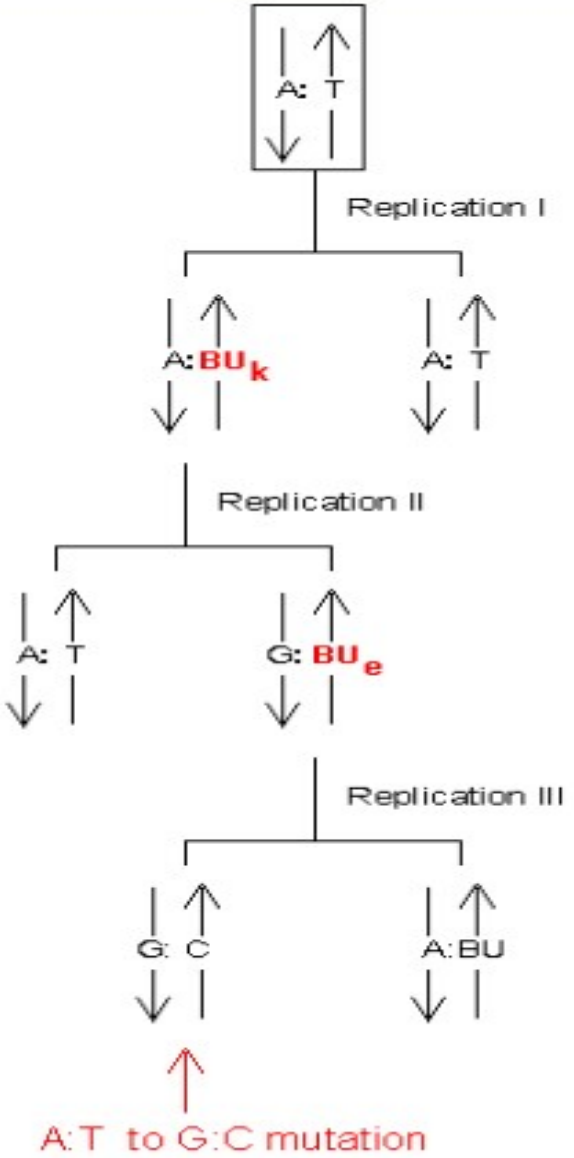
5-Bromouracil — Adenine

keto form (BU_k)



5-Bromouracil — Guanine

enol form (BU_e)



I. Gene mutations

- **5. Mutagenic agents :**
  - **a. Chemical agents:**
    - Chemical substances that transform bases: exp, replacement of the NH2 of Cytosine by an OH which gives uracil,
    - Chemicals that disrupt replication by intercalating into DNA, exp BET (Ethidium bromide)
    - Chemical substances that behave as base analogues: For example 5-bromouracil which resembles thymine,
  - **b. Physical agents:**
    - X Radiations
    - UV

II. Chromosome aberrations

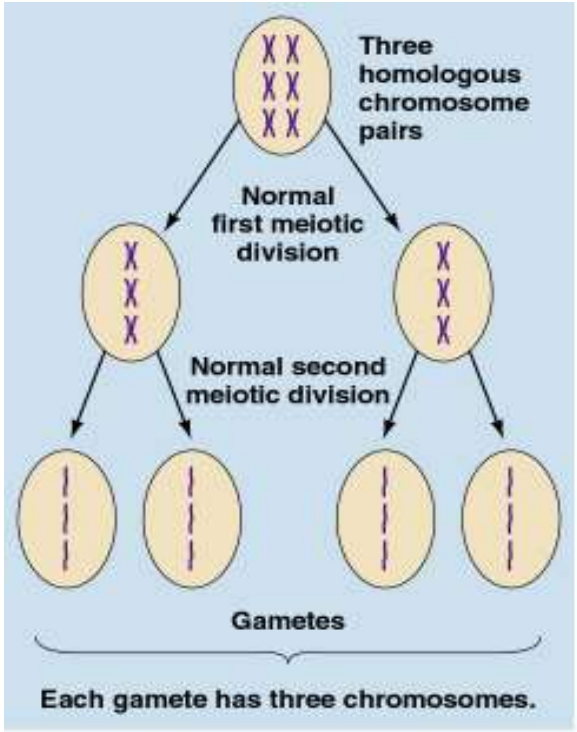
- a- Change in the number of chromosomes
- b- Change in chromosome structure

II. Chromosome aberrations

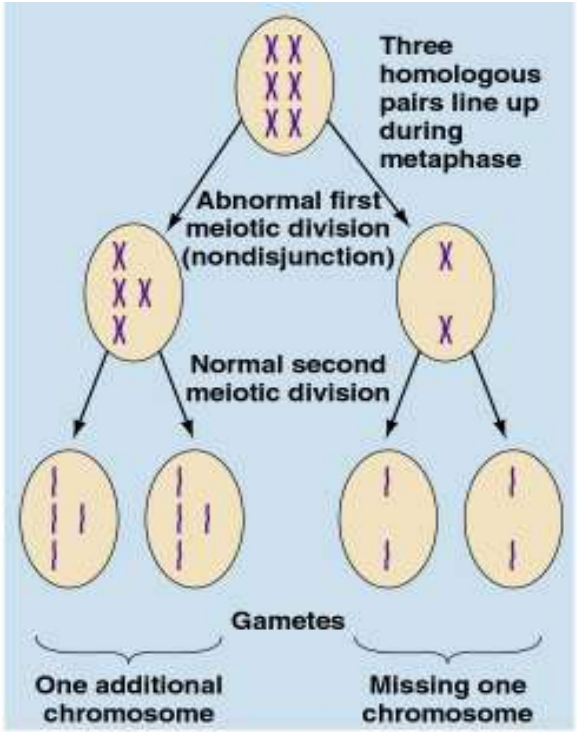
- **a- Change in the number of chromosomes**
  - Occurs by nondisjunction of homologous chromosomes during meiosis
    - **Non-disjonction** - an event in which homologous chromosomes do not separate and both go into the same daughter cell
  - Aneuploidy
  - Polyploidy

II. Chromosome aberrations

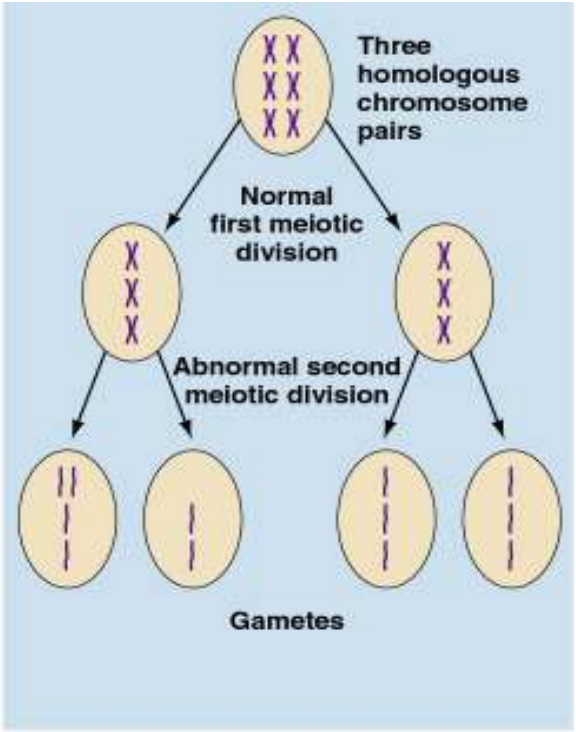
- **a- Change in the number of chromosomes**
  - Aneuploidy: monosomy and trisomy



Meiosis Normale



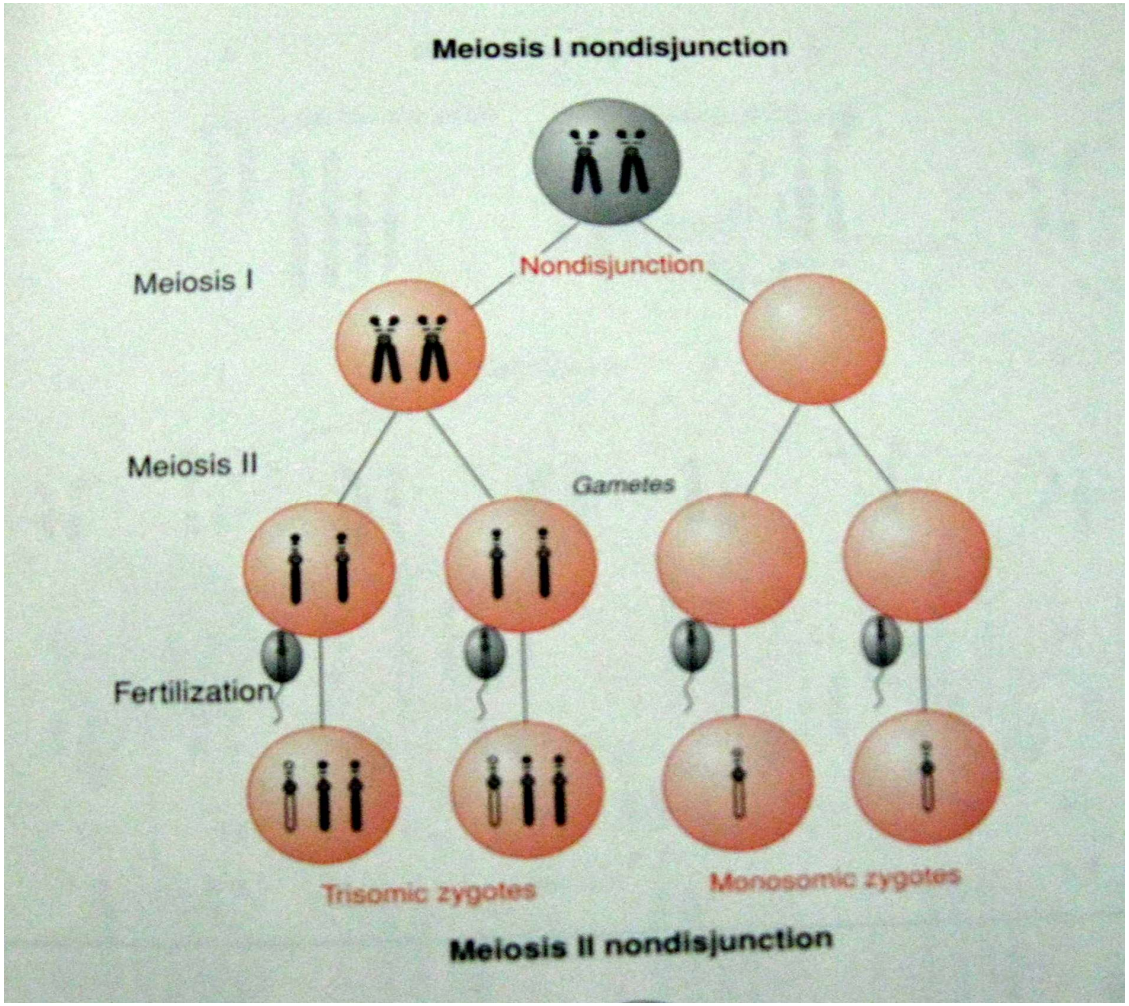
Non-disjonction in Meiosis I



Non-disjonction in Meiosis II

II. Chromosome aberrations

- **a- Change in the number of chromosomes**
  - Aneuploidy: monosomy and trisomy



II. Chromosome aberrations

- **a- Change in the number of chromosomes**
  - Aneuploidy: monosomy and trisomy

    - Monosomy – one less chromosome

      (23 x 2) – 1 = 45

    - Trisomy – one more chromosome

      (23 x 2) + 1 = 47

II. Chromosome aberrations

Autosomal Aneuploidies

Down Syndrome	Trisomy 21
Edward Syndrome	Trisomy18
Patau Syndrome	Trisomy 13

Trisomy: 3 copies of a chromosome

II. Chromosome aberrations

- **a- Change in the number of chromosomes**
  - Aneuploidy: exp **Trisomy 21**

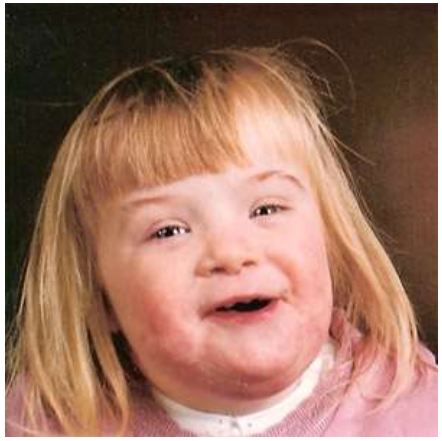
-Characteristic facial features

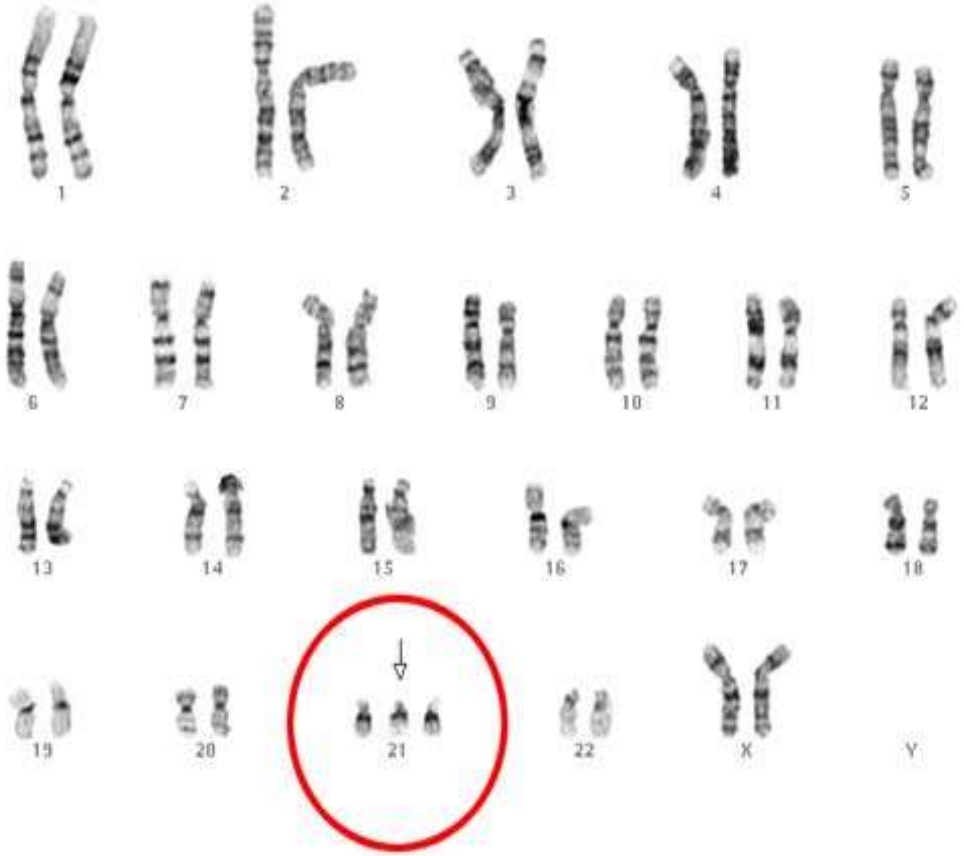
-Susceptibility to respiratory infections

-Mental retardation

-Predisposition to Alzheimer's disease and leukemia

-Sterility

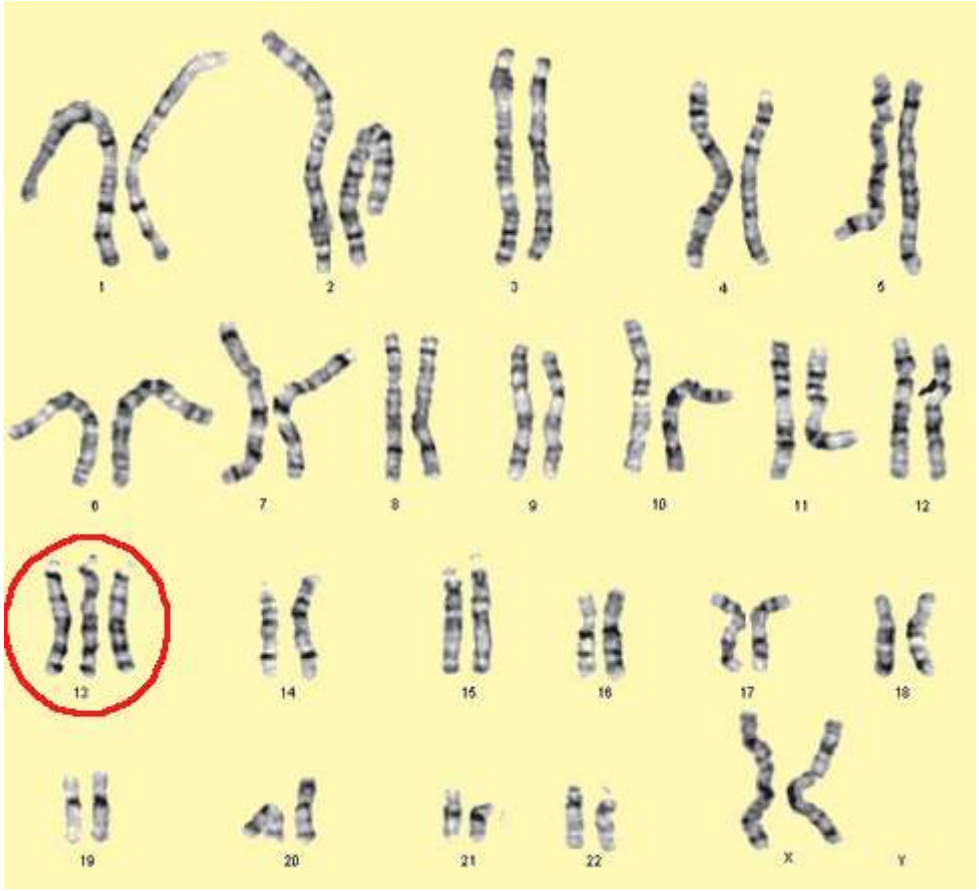




II. Chromosome aberrations

- **a- Change in the number of chromosomes**
  - Aneuploidy: exp **Patau Syndrome**

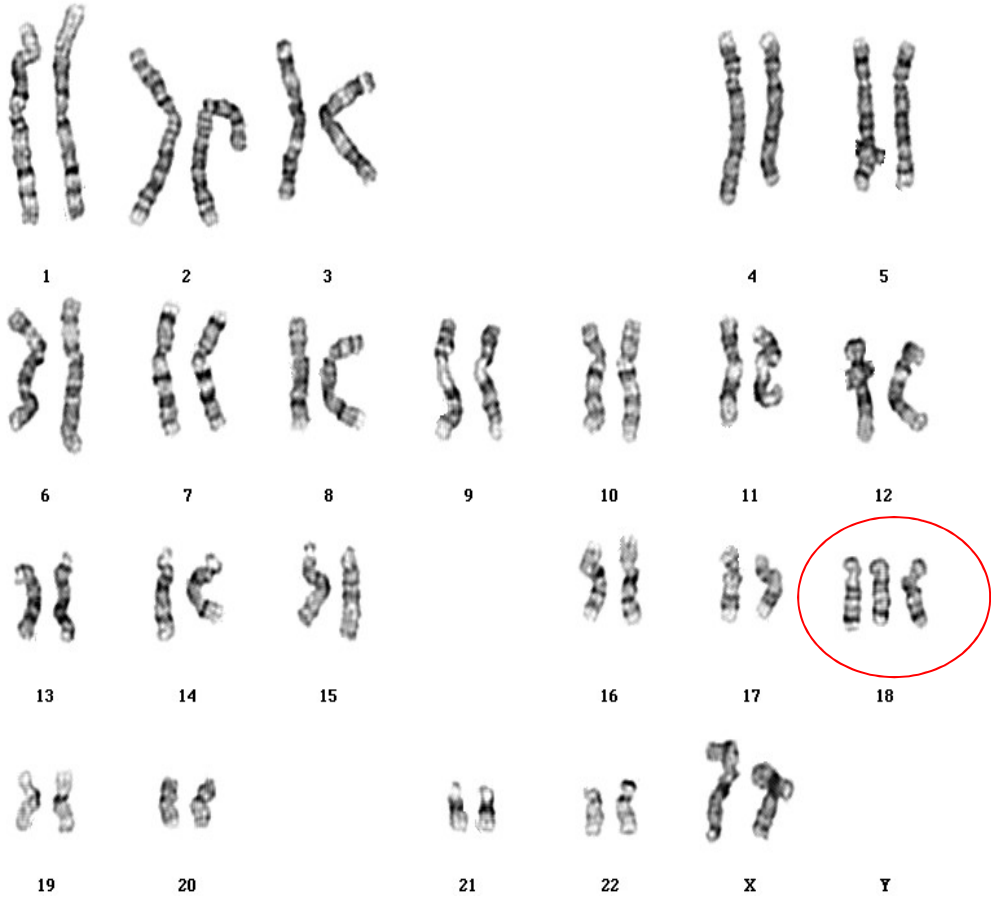
- Severe malformations of the eyes, brain and circulatory system
- Cleft lip



II. Chromosome aberrations

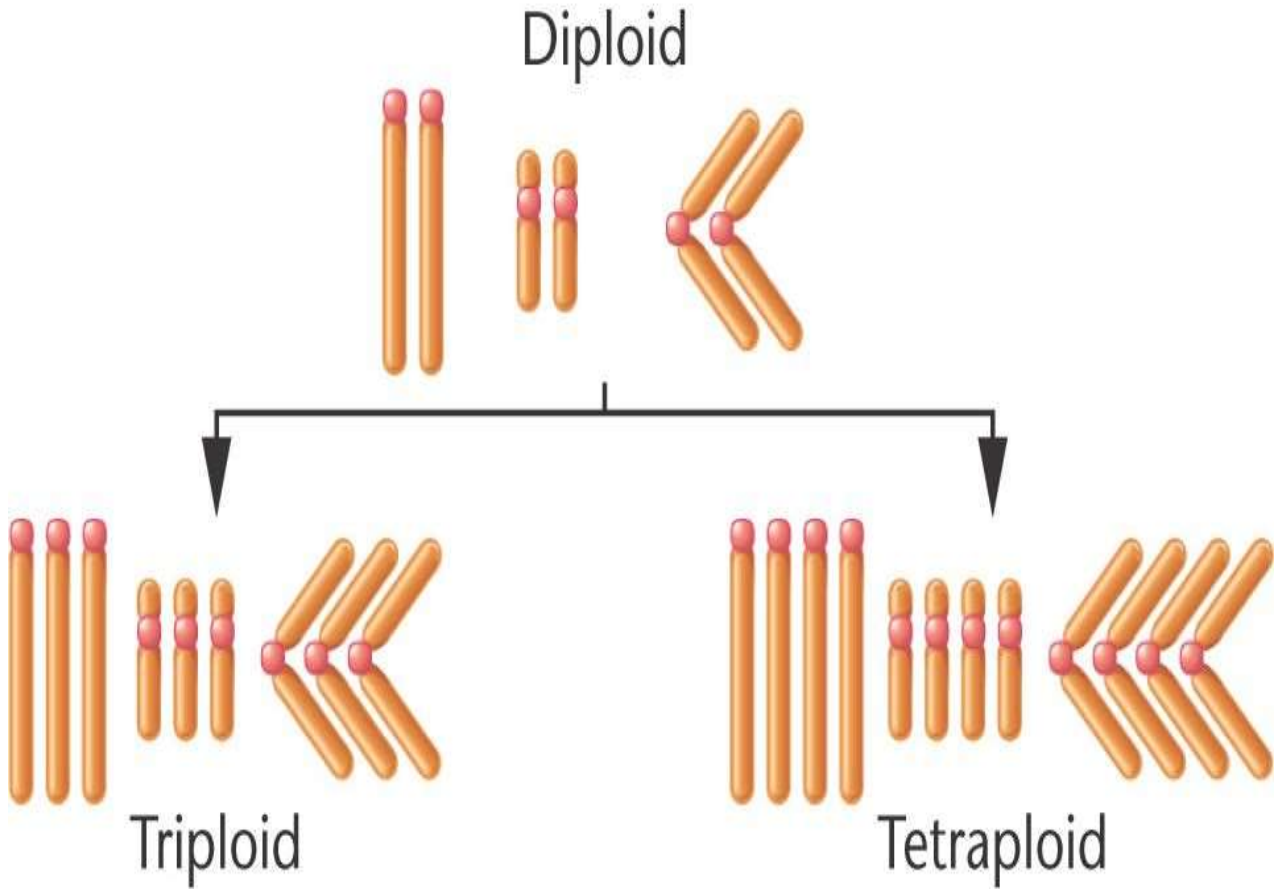
- **a- Change in the number of chromosomes**
  - Aneuploidy: exp **Trisomy 18 (Edward Syndrome)**

-Affects almost all body systems
-Affected children die before the age of one



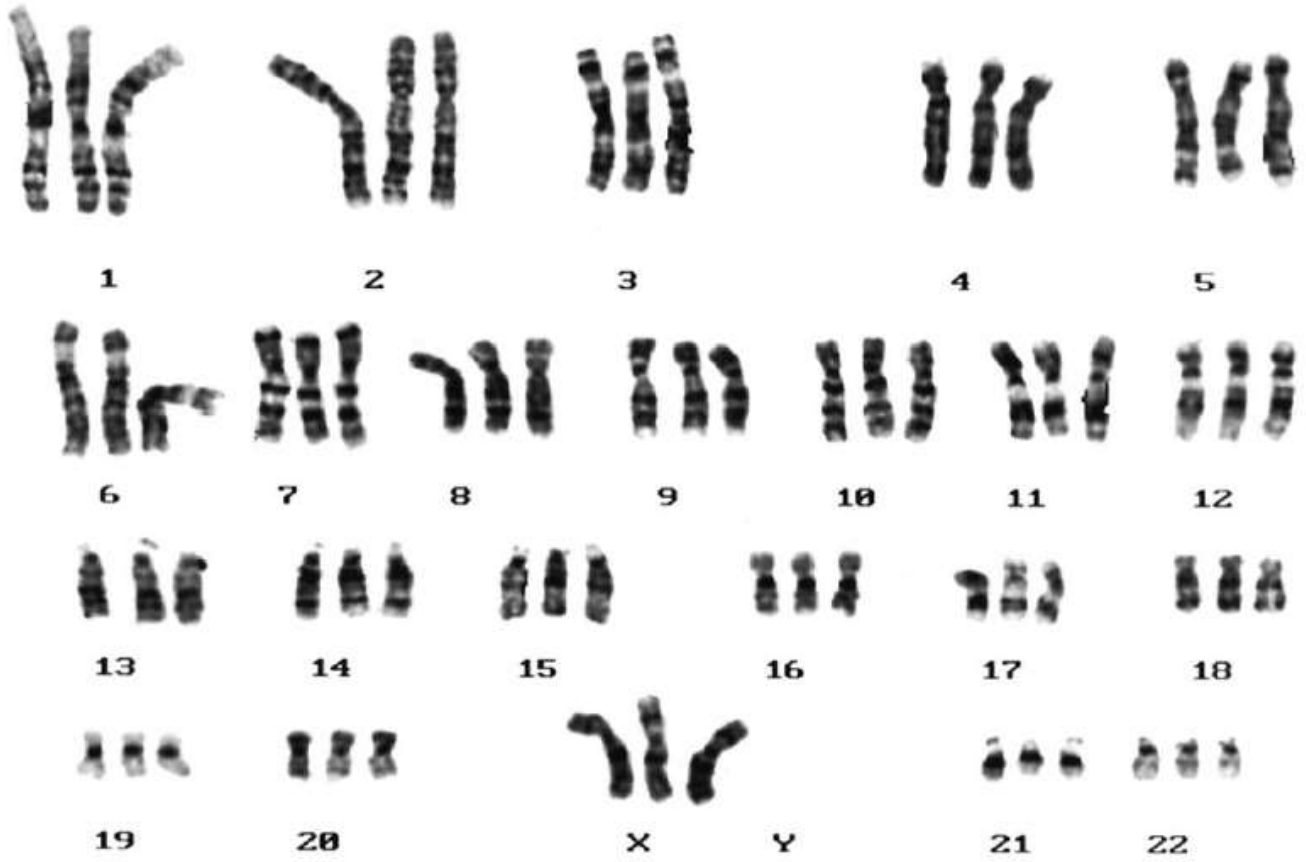
II. Chromosome aberrations

- **a- Change in the number of chromosomes**
  - Polyploidy:



II. Chromosome aberrations

- **a- Change in the number of chromosomes**
  - Polyploidy: **Triploidy**



II. Chromosome aberrations

- **a- Change in the number of chromosomes**
  - **Polyploidy:**
    - Triploidy – 3 quantity of chromosomes

      23 x 3 = 69
    - Tetraploidy – 4 quantity of chromosomes

      23 x 4 = 92

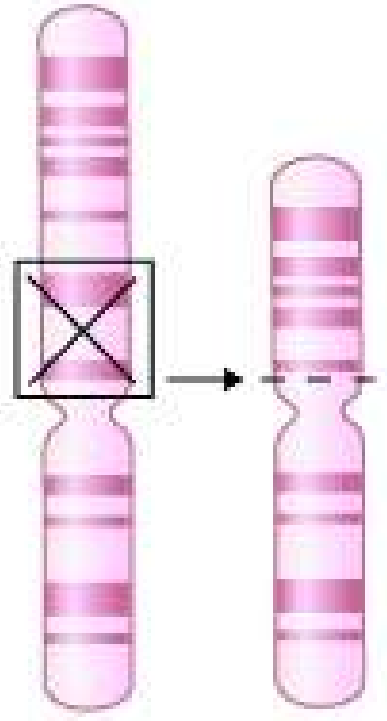
II. Chromosome aberrations

- a- Change in the number of chromosomes
- b- Change in chromosome structure

II. Chromosome aberrations

– **b- Change in chromosome structure**

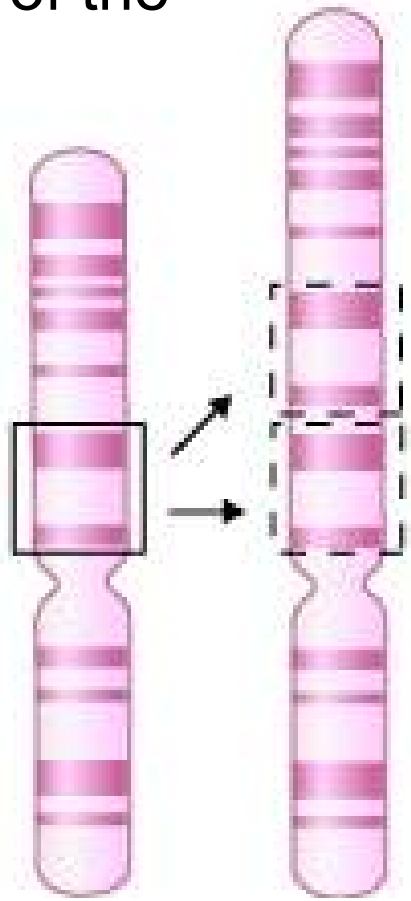
- **Chromosomal Mutation** – a mutation that affects multiple genes
  - Chromosomal deletion – an event in which part of a chromosome is deleted
    - Can remove one or more genes from the chromosome



II. Chromosome aberrations

– **b- Change in chromosome structure**

- **Chromosomal Mutation** – a mutation that affects multiple genes
  - – Duplication – an event in which a large part of the chromosome repeats itself
    - Causes the duplication into two or more copies of one or more genes



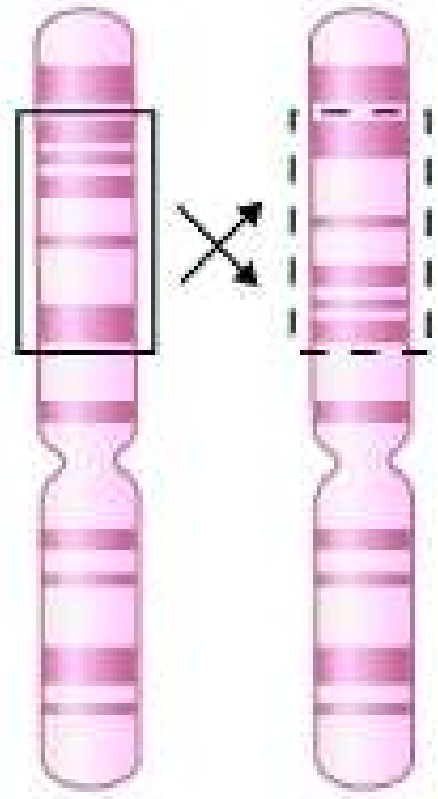
II. Chromosome aberrations

– b- Change in chromosome structure

- **Chromosomal Mutation** – a mutation that affects multiple genes

  Inversion – an event in which one or more fragments are removed and reversed before being inserted

  - inverse orientation

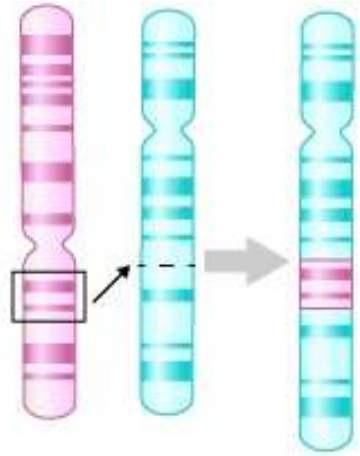


II. Chromosome aberrations

– **b- Change in chromosome structure**

- **Chromosomal Mutation** – a mutation that affects multiple genes
  - – Chromosomal Insertion – an event in which part of a chromosome is removed and inserted into another chromosome
  - – Translocation - an event in which two fragments of two different chromosomes are interchanged

Chromosomal Insertion



Translocation