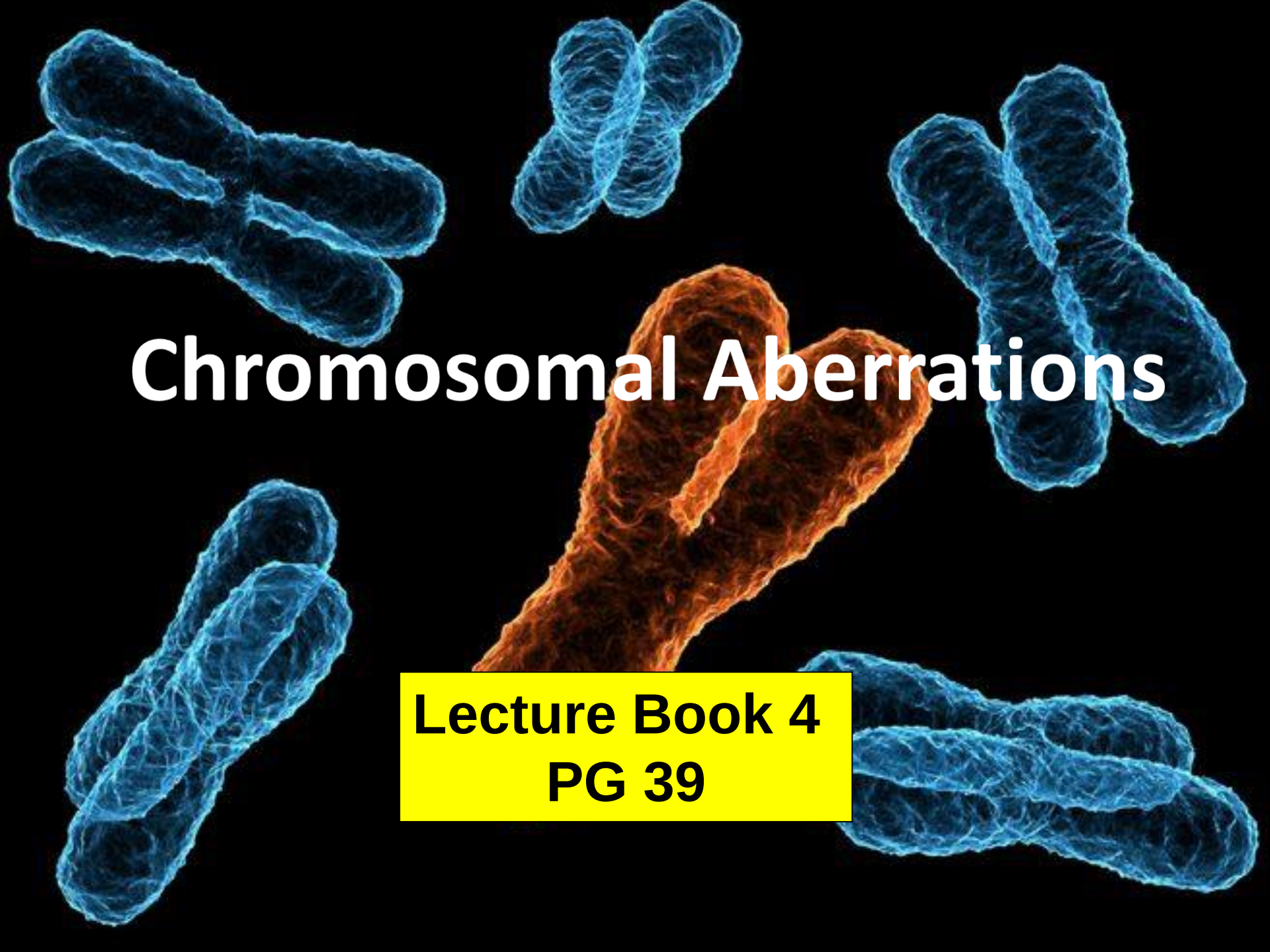


Chromosomal Aberrations

Lecture Book 4
PG 39

What you have learnt …

- 15(h)
  Describe mutation as a change in the structure of a gene such as in sickle cell anaemia, or in the chromosome number, such as the 47 chromosomes in the condition known as Down syndrome

BIOLOGY

GCE Ordinary Level (2016)

(Syllabus 5158)

Learning Objectives

- 2(d)
  Explain what is meant by the terms gene mutation and **chromosomal aberration**.

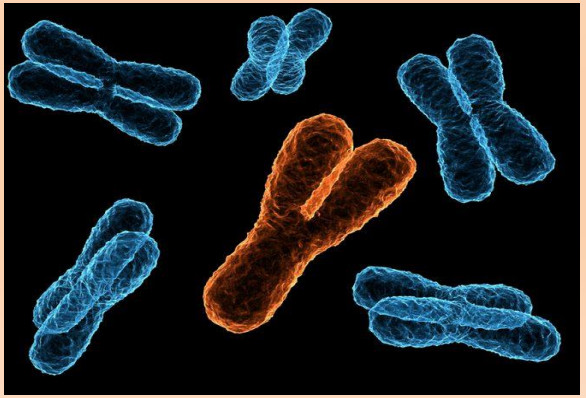
  For chromosomal aberration, knowledge of ***numerical aberration*** *(including aneuploidy, as in the case of trisomy 21, i.e. Down syndrome) and* ***structural aberration*** *(including translocation, duplication, inversion and deletion) is required.*

(iii) Nature of mutations?

Mutations

Gene mutation
(new alleles of a gene formed)

Chromosomal Aberration
(Change in number of copies of existing alleles OR reshuffling of existing alleles)



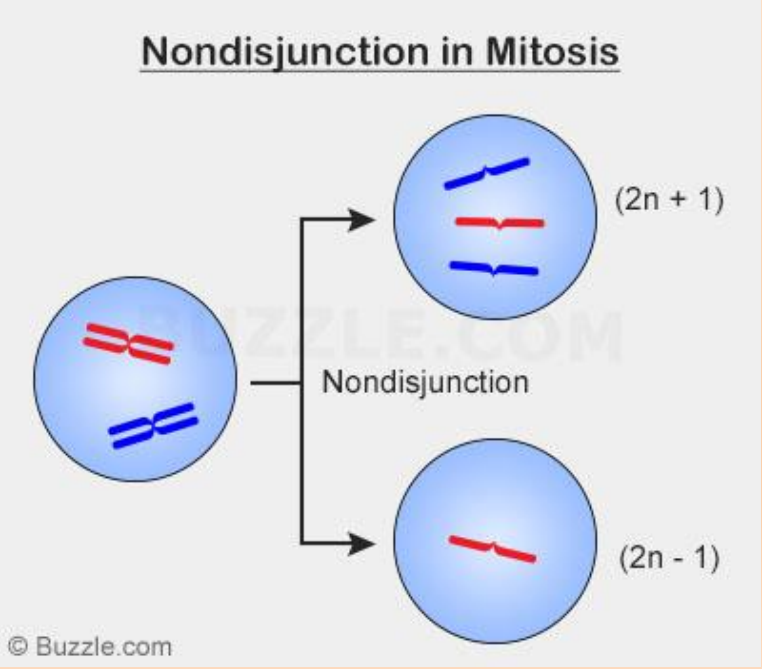
Chromosomal aberration

- A change in the **number or structure** of chromosomes
- Several gene loci are involved

Causes of chromosomal aberration

- **Errors in nuclear division** in **mitosis** and **meiosis**:
  1. **Non-disjunction** in mitosis or meiosis leads to a **change in the number of chromosomes (Numerical aberration)**

Failure of one of more pairs of homologous chromosomes or sister chromatids to separate normally during nuclear division, => **Abnormal distribution of chromosomes** in daughter nuclei



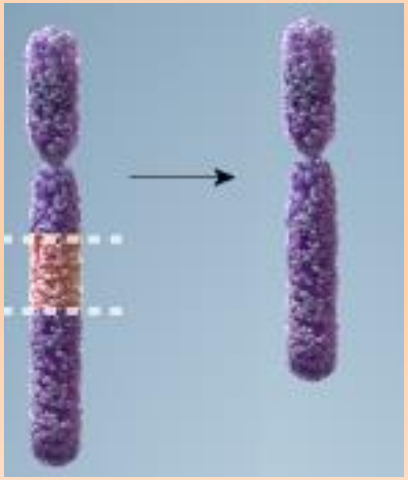
Causes of chromosomal aberration

- **Errors in nuclear division**, i.e. in mitosis and meiosis:

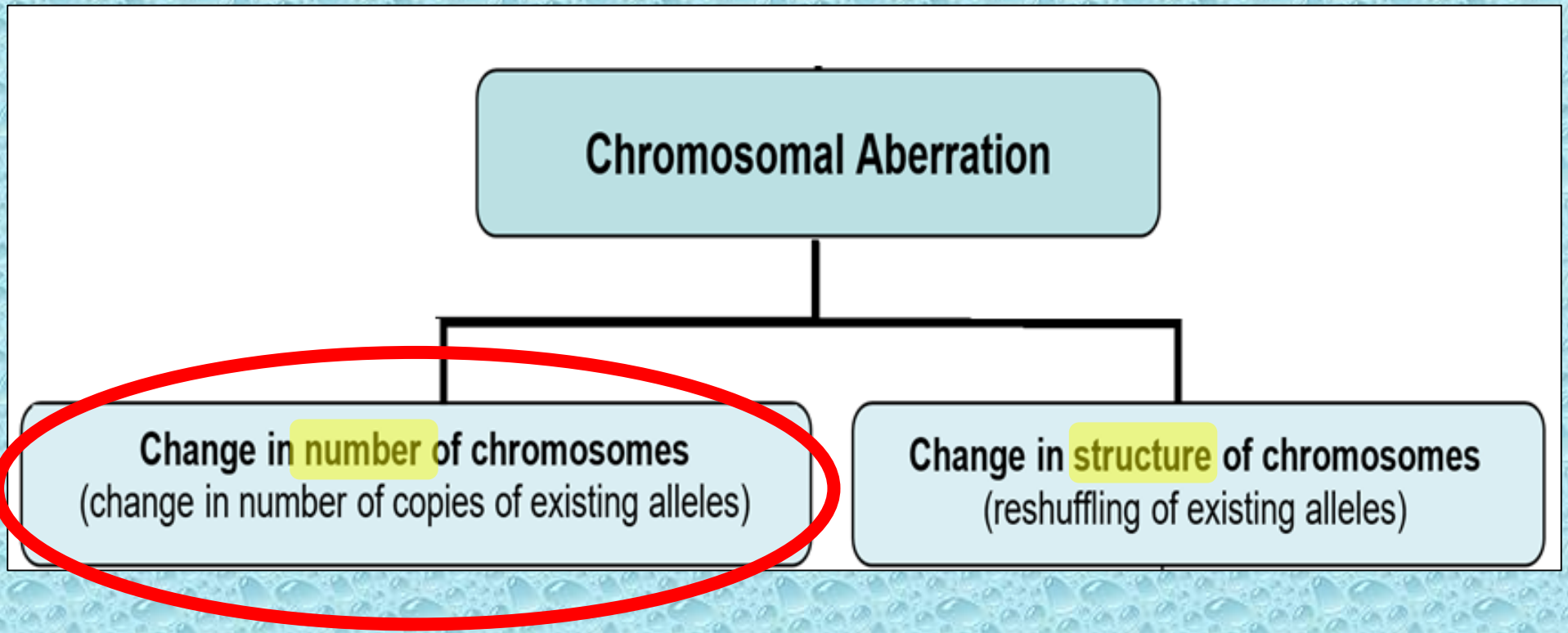
  2. **Chromosomal breaks** that occur during mitosis or meiosis resulting in

     deletion, duplication, inversion or **translocation** of chromosomal segments

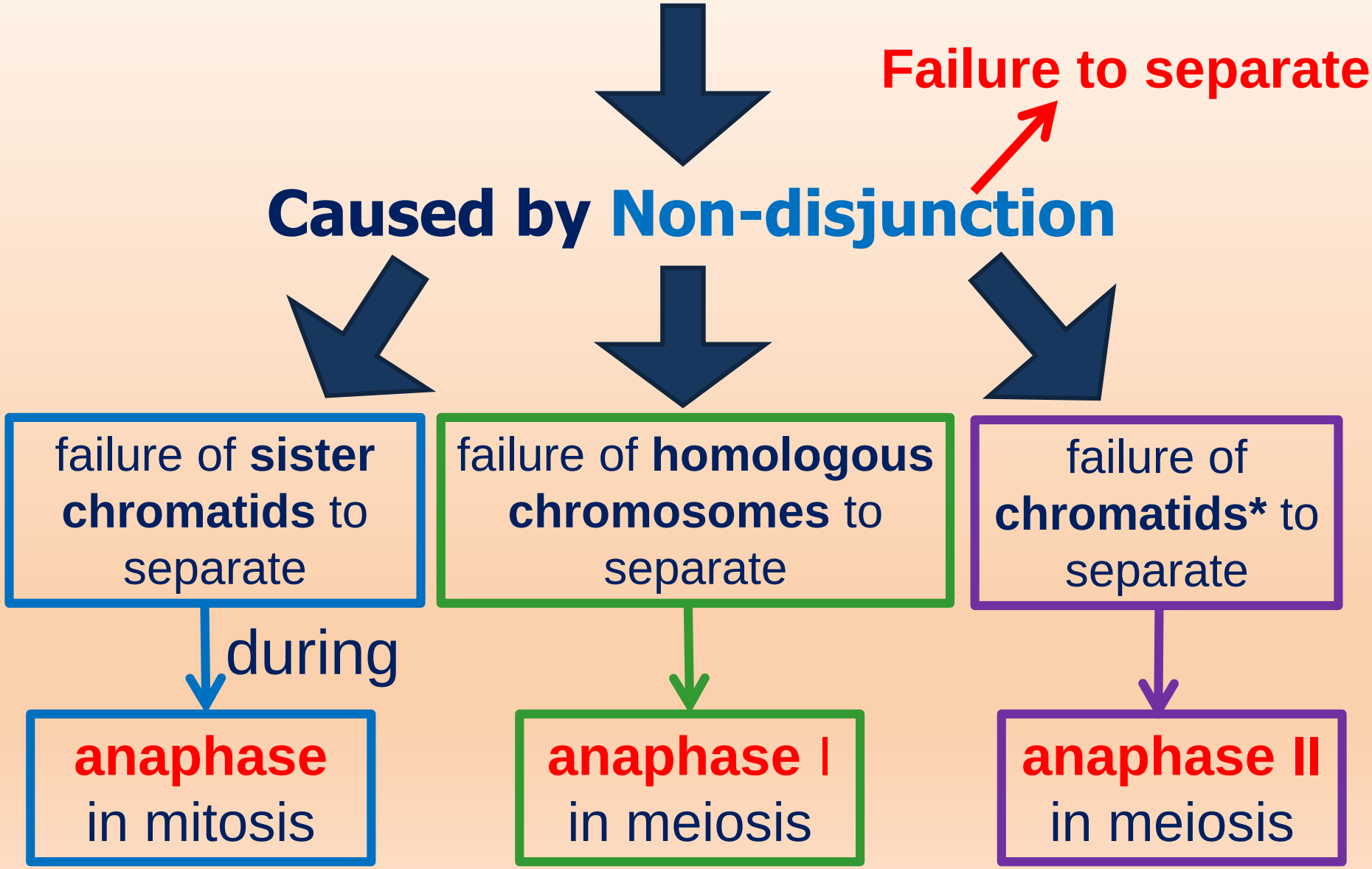
     leads to a change in the structure of chromosome **(Structural aberration)**



Types of Chromosomal Aberration

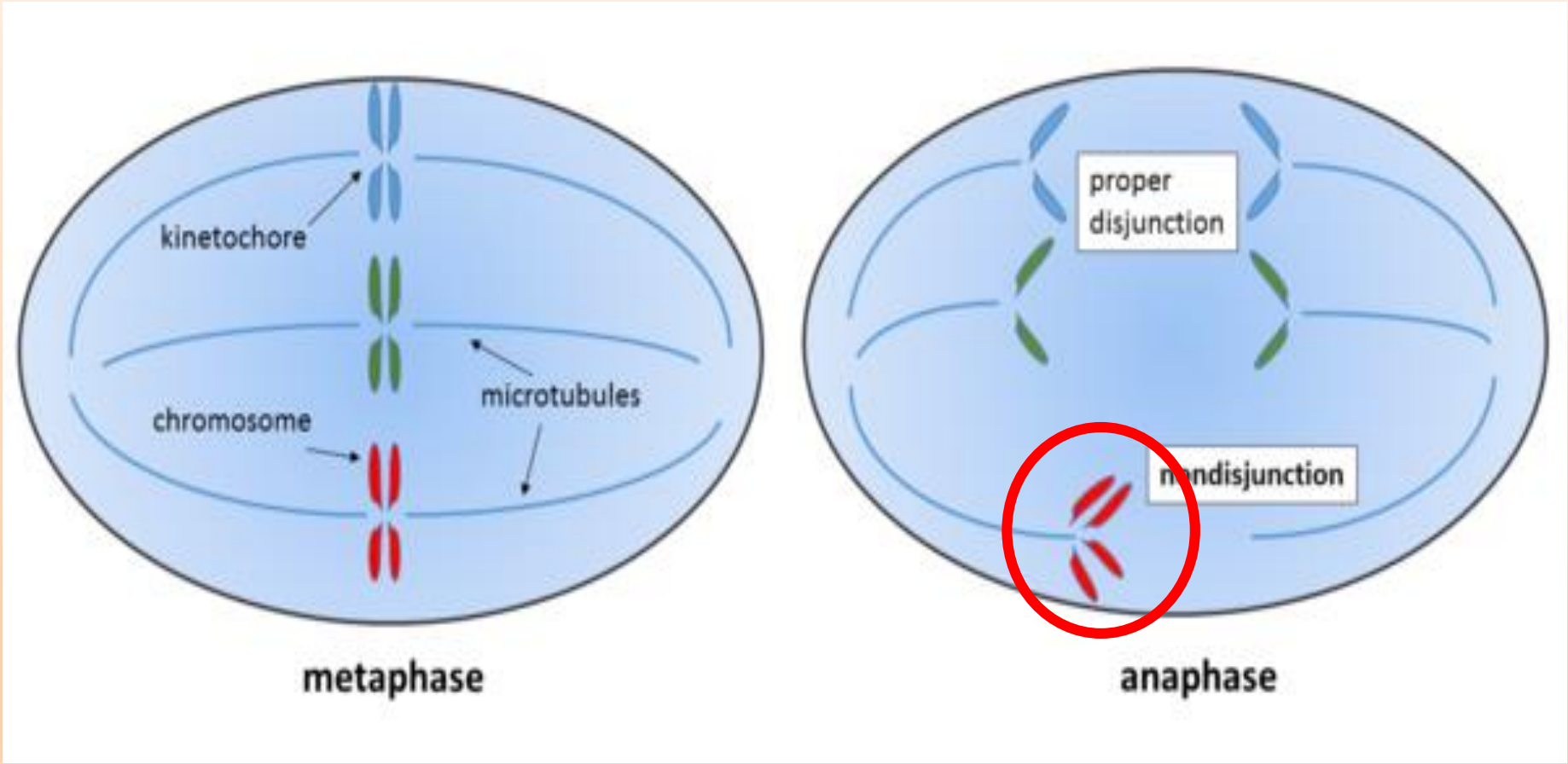


[A] Change in number of chromosomes



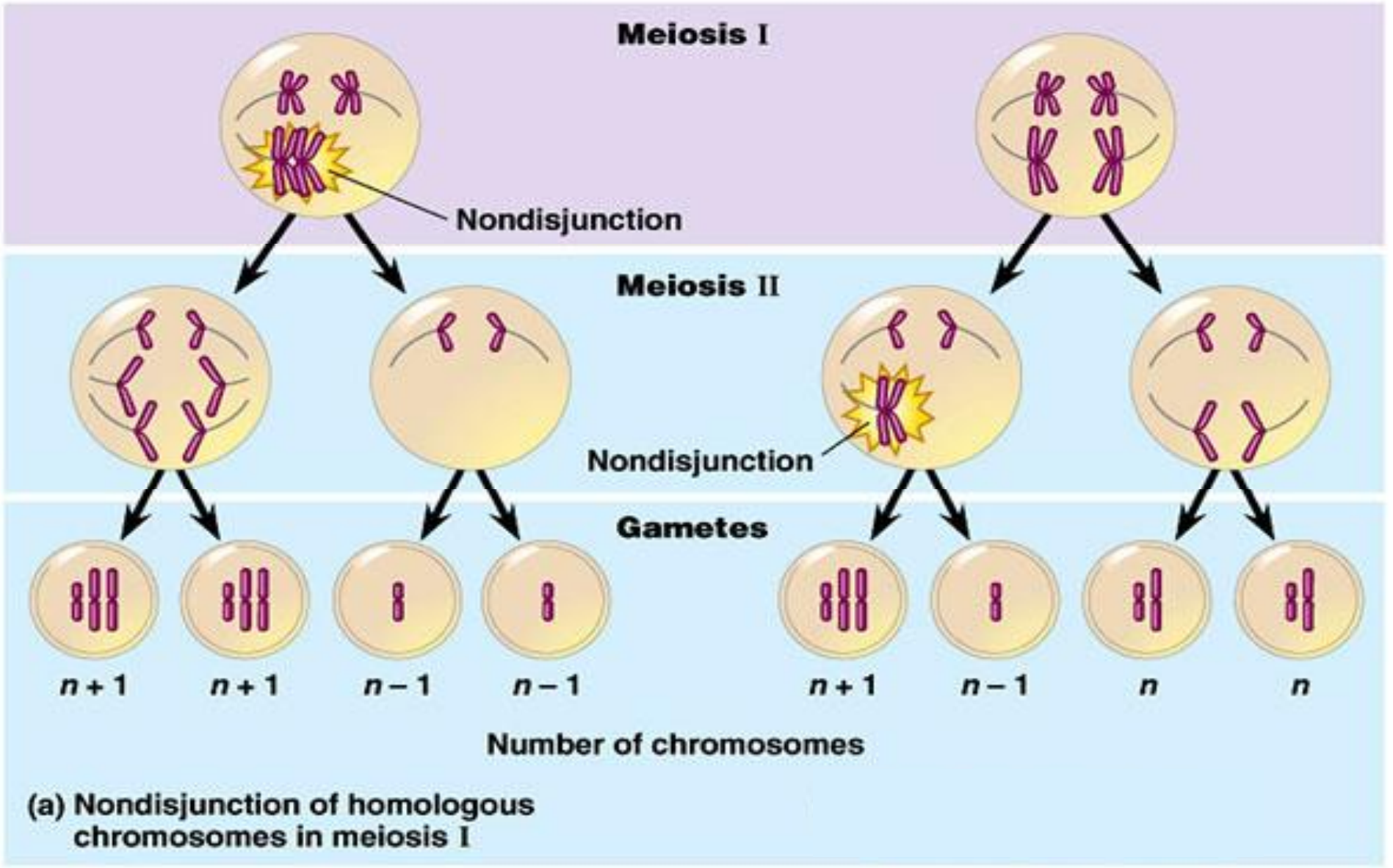
Not in notes

Nondisjunction in Mitosis



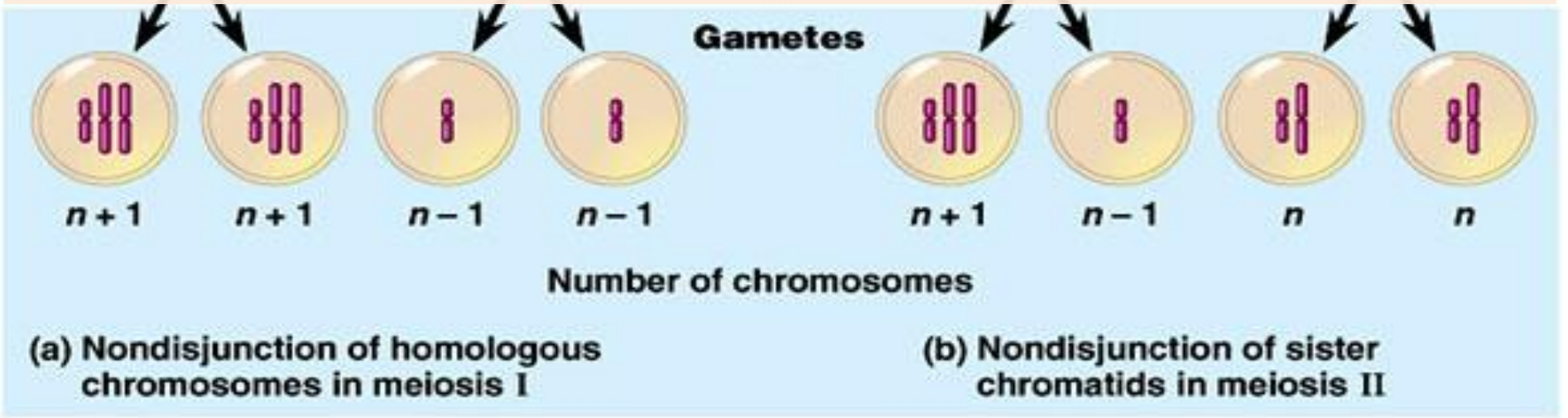
PG 40

Nondisjunction in Meiosis

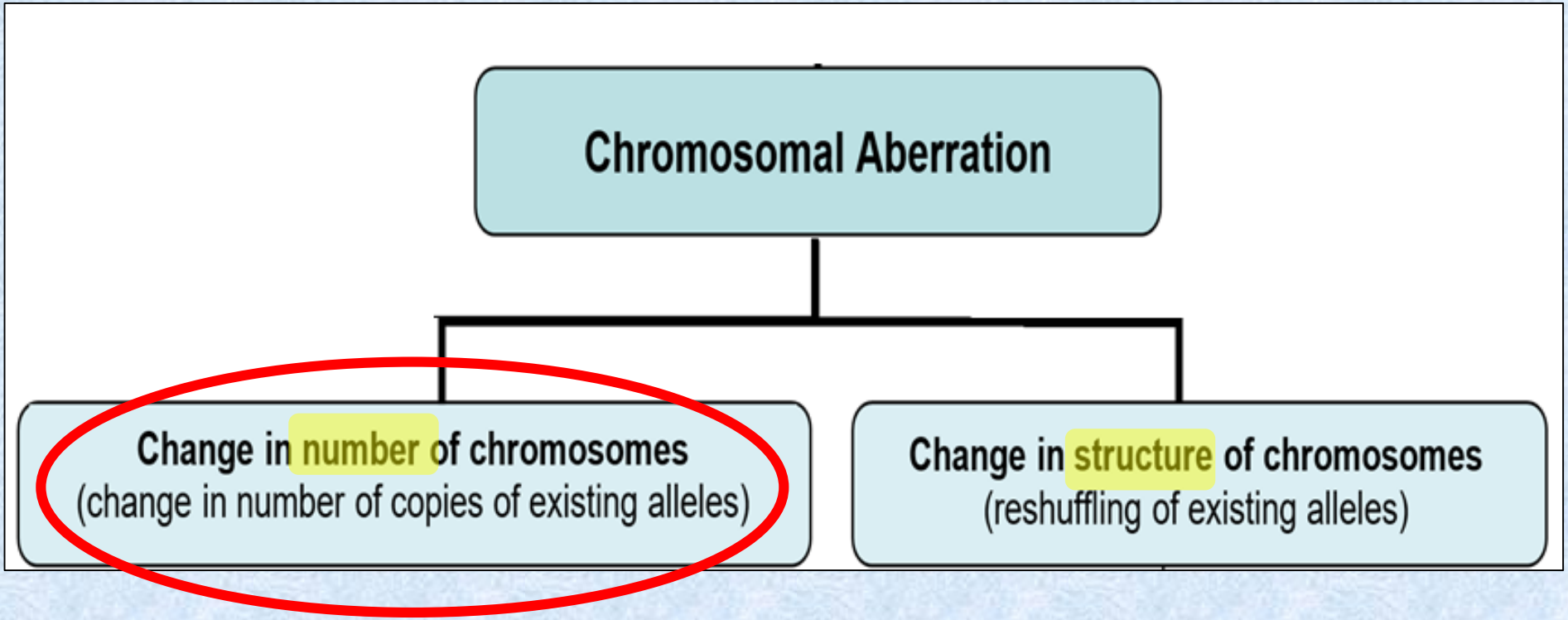


Nondisjunction in Meiosis

- Can affect one, several or all the chromosomes in a nucleus
- Changes the number of copies of existing alleles



Types of Chromosomal Aberration



I. Aneuploidy

II. Polyploidy

I) Aneuploidy

- is a condition when there is / are **one or several chromosomes** **less or more than the diploid number of chromosomes** in the nucleus of a **somatic cell**.
- denoted as :
  2n – 1 (1 chromosome less than diploid number),
  2n + 1 (1 chromosome more than diploid number)

  2n – 2 (2 chromosomes less than diploid number)

  2n + 2 (2 chromosomes more than diploid number) etc…

Note: '**±2**' = 2 non-disjunction events had occurred simultaneously for different chromosomes

I) Aneuploidy

- Occurs when there is **loss or gain** **of <u>one or several chromosome(s)</u>** in cells after non-disjunction events

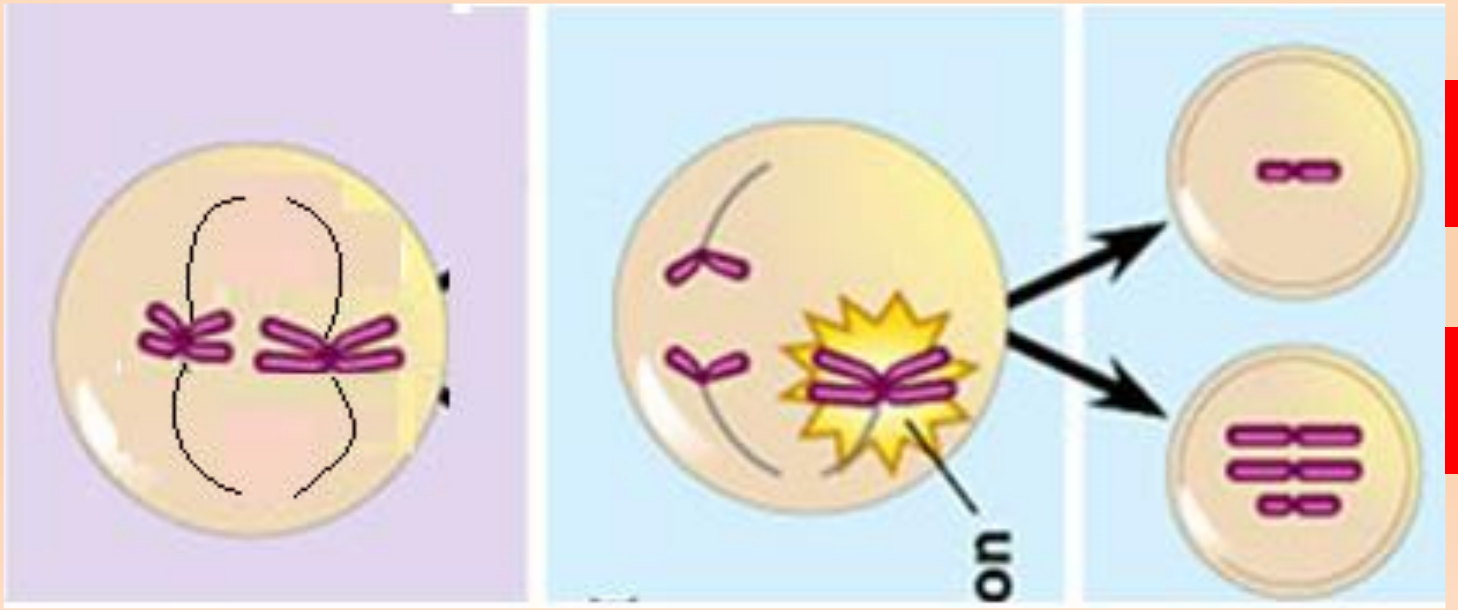
I) Aneuploidy

- *Non-disjunction events that result in aneuploidy are:*
  1. Failure of sister chromatids of **one** or **several** chromosomes to separate during **anaphase in mitosis**
  2. Failure of **one** or **several** pairs of homologous chromosomes to separate during **anaphase I in meiosis**
  3. Failure of chromatids of **one** or **several** chromosomes to separate during **anaphase II in meiosis**

I) Aneuploidy

- *For (1):*
  1. Aneuploid daughter cells end up with (2n+1) and (2n-1) chromosomes.

Aneuploid daughter cells

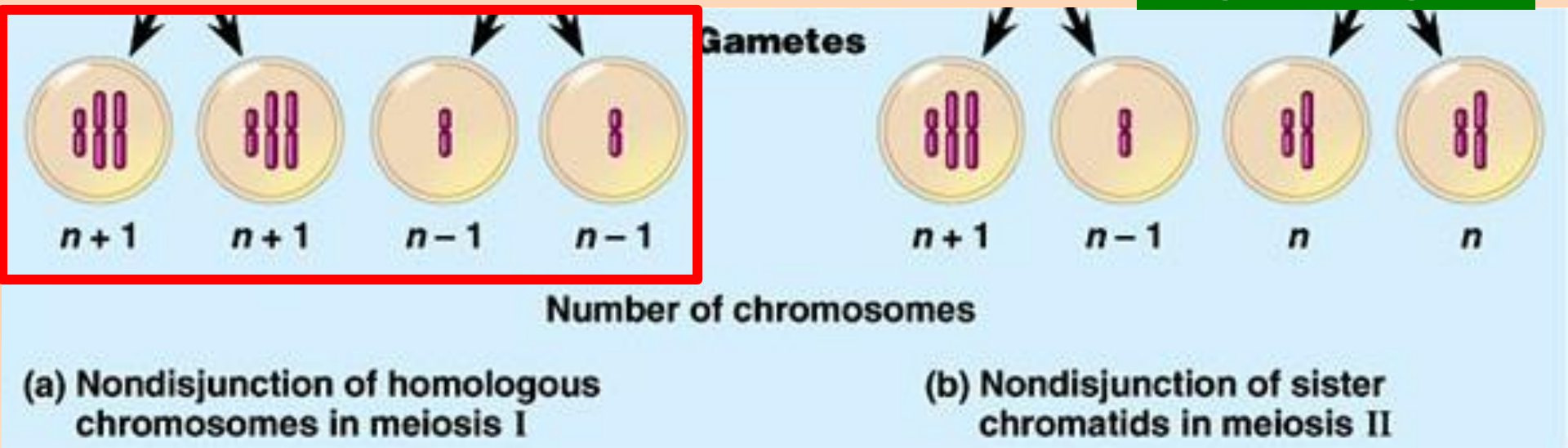


COPY THIS

I) Aneuploidy

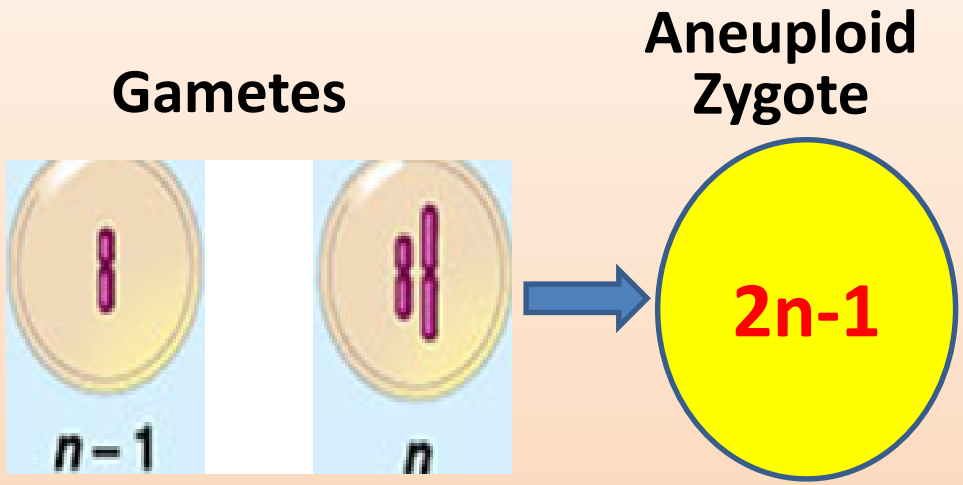
- *For (2) & (3):*
  2. 50% of gametes formed have (n+1) & 50% of gametes have (n-1)
  3. 25% of gametes have (n+1), 25% have (n-1), 50% has (n)

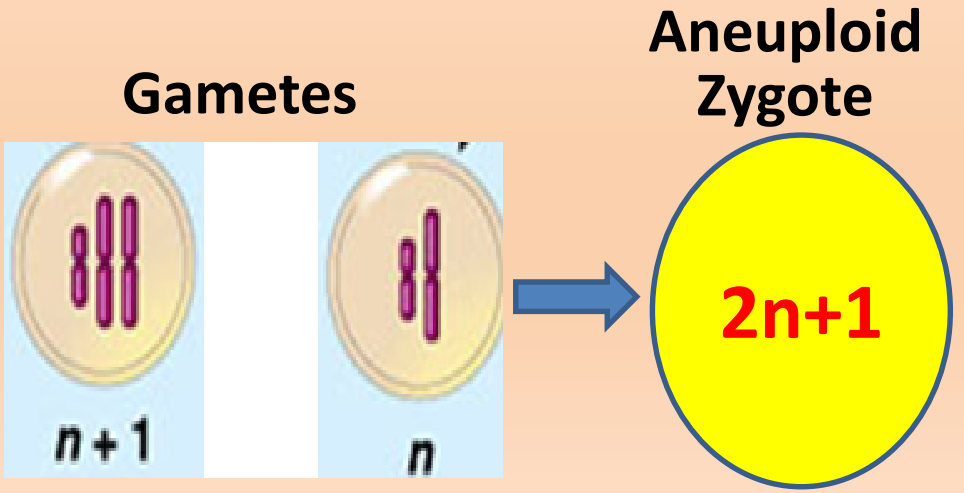
Fig on Pg 41



I) Aneuploidy

Subsequent **fusion** of a **normal** haploid gamete with a gamete carrying (n – 1) OR (n + 1) chromosomes would lead to **all the cells** in the offspring being **aneuploid**.





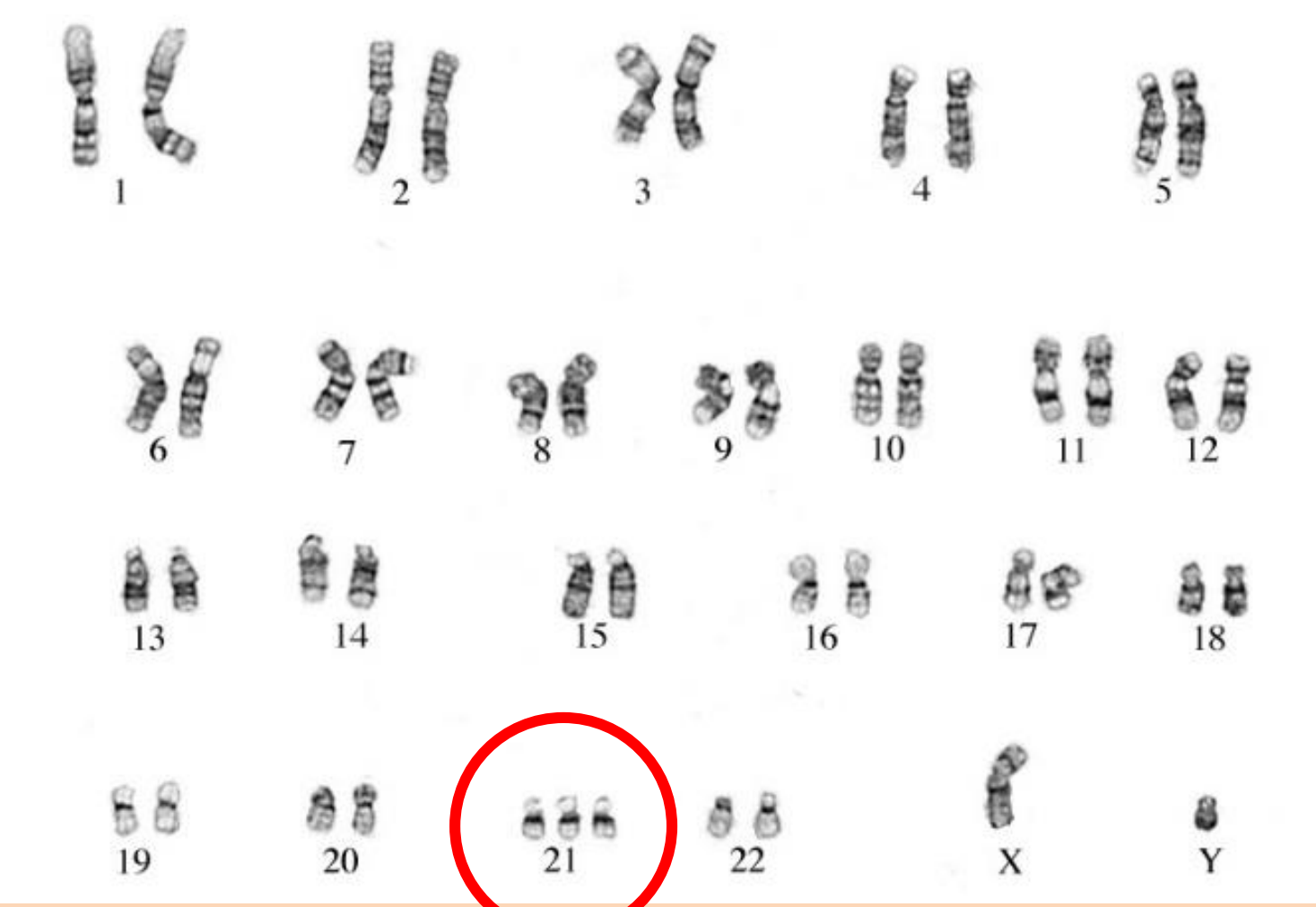
E.g. of abnormalities due to aneuploidy

Down's syndrome (Trisomy 21)

For additional information

- Klinefelter's syndrome
- Turner's syndrome

Down's syndrome

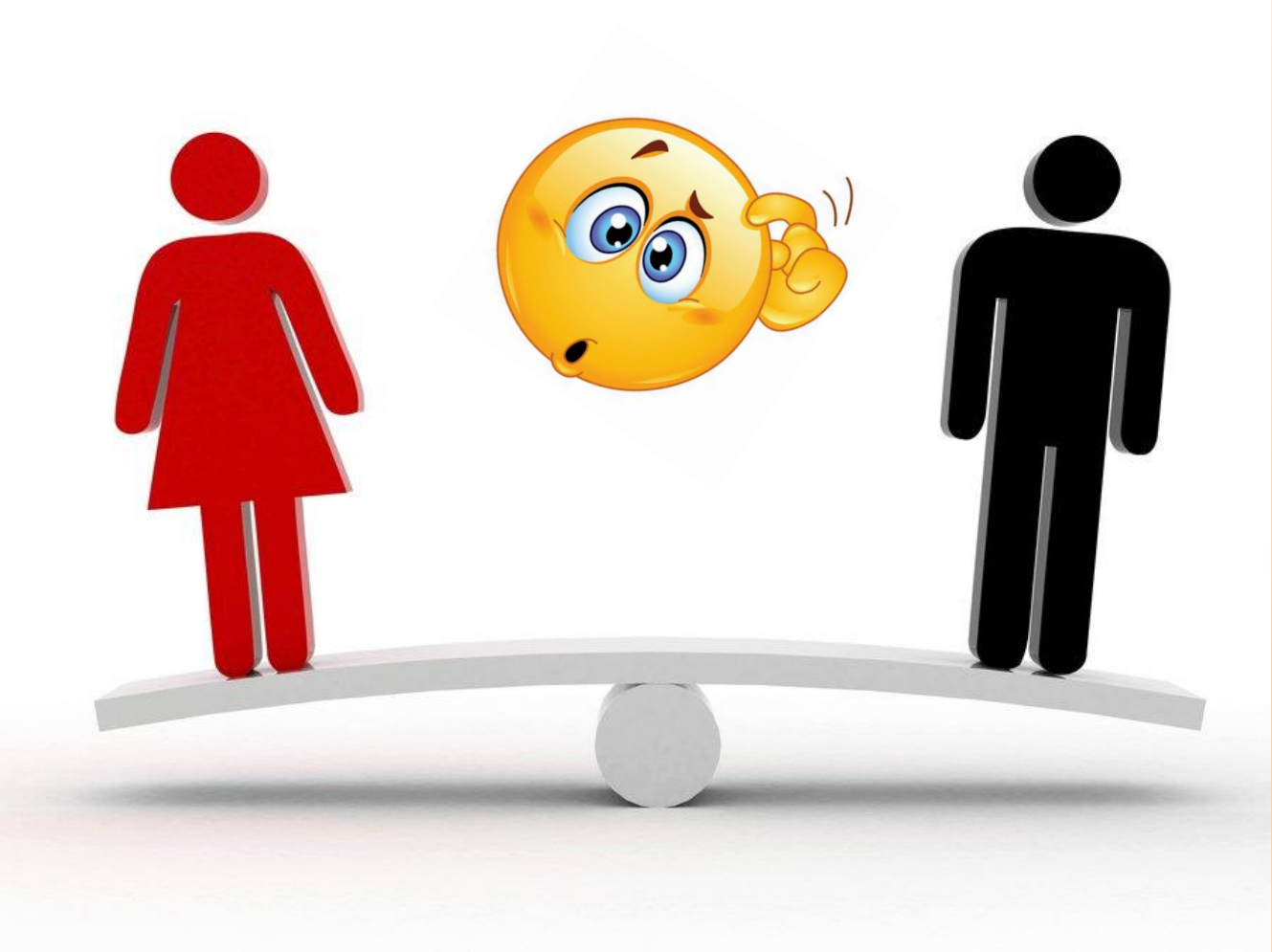


Down's syndrome

- Extra chromosome 21 (trisomy = three chromosome 21)
- Total number of chromosomes in a somatic cell of this affected person is **2n+1 = 47**
- Commonly due to non-disjunction in Anaphase of **Meiosis I**

Antonarakis, S. E., Petersen, M. B., McInnis, M. G., Adelsberger, P. A., Schinzel, A. A., Binkert, F., … Chakravarti, A. (1992). stage of nondisjunction in trisomy The meiotic 21 : Determination by using DNA polymorphisms. *American Journal of Human Genetics*, *50*(3), 544–550.

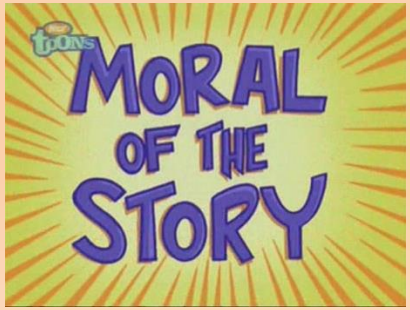
Cause: Mom or Dad?



Down's syndrome

- Occurrence of trisomy 21 is highly correlated with the **age** of the **mother**.
- The probability of bearing a child with trisomy 21 **increases exponentially** with age.

Age of mother	Risk of baby with Down Syndrome
20	1 in 1667
25	1 in 1250
30	1 in 952
35	1 in 250
37	1 in 224
39	1 in 136
40	1 in 100
42	1 in 63
45	1 in 30



https://www.healthhub.sg/live-healthy/945/pregnancy-down-syndrome-tests

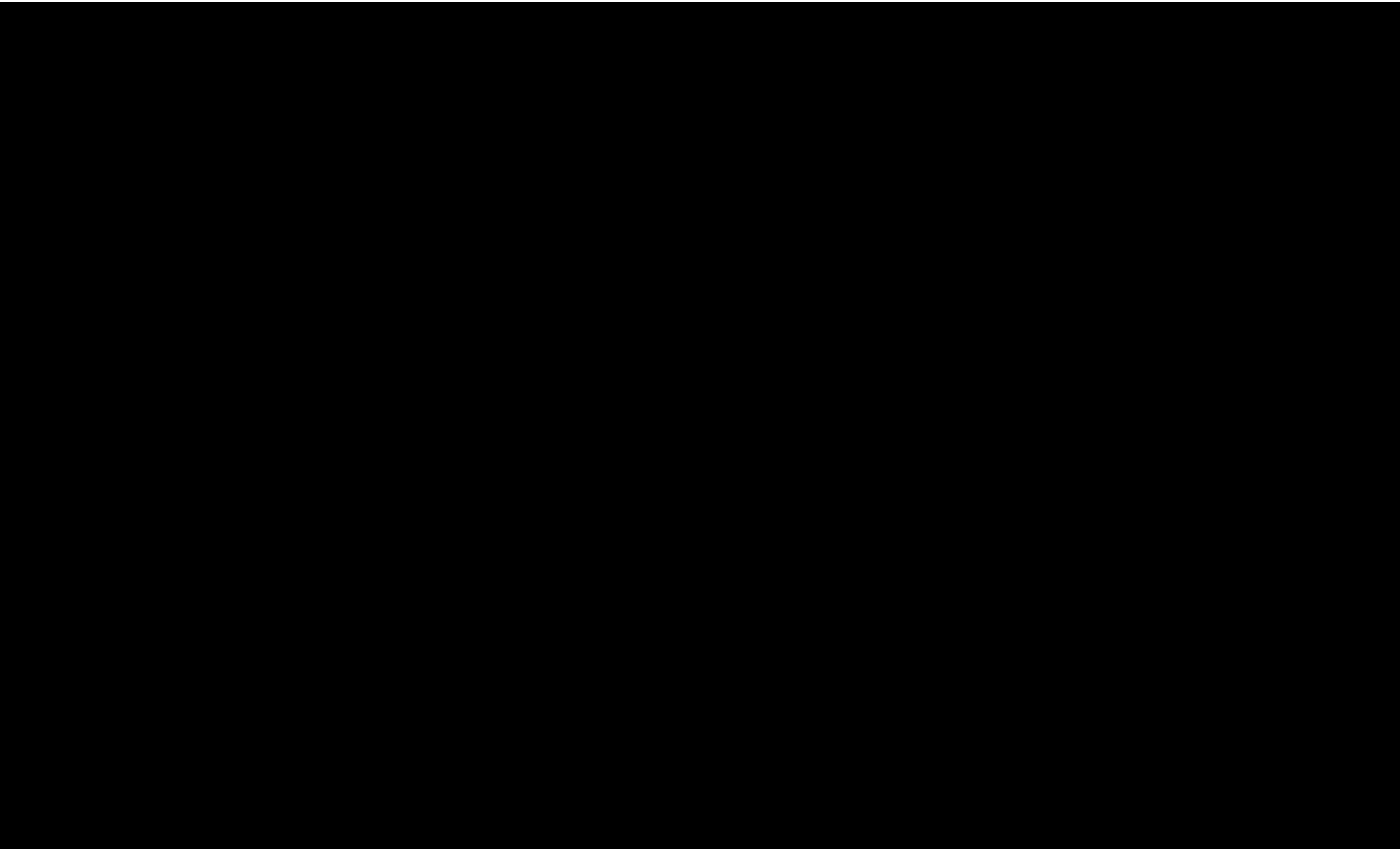
Down's syndrome

- Characteristic facial features, short stature, heart defects
- **Susceptibility to respiratory infection, and mental retardation**
- Greater risk of developing Alzheimer's disease and leukaemia

DOWN SYNDROME ASSOCIATION
(SINGAPORE)

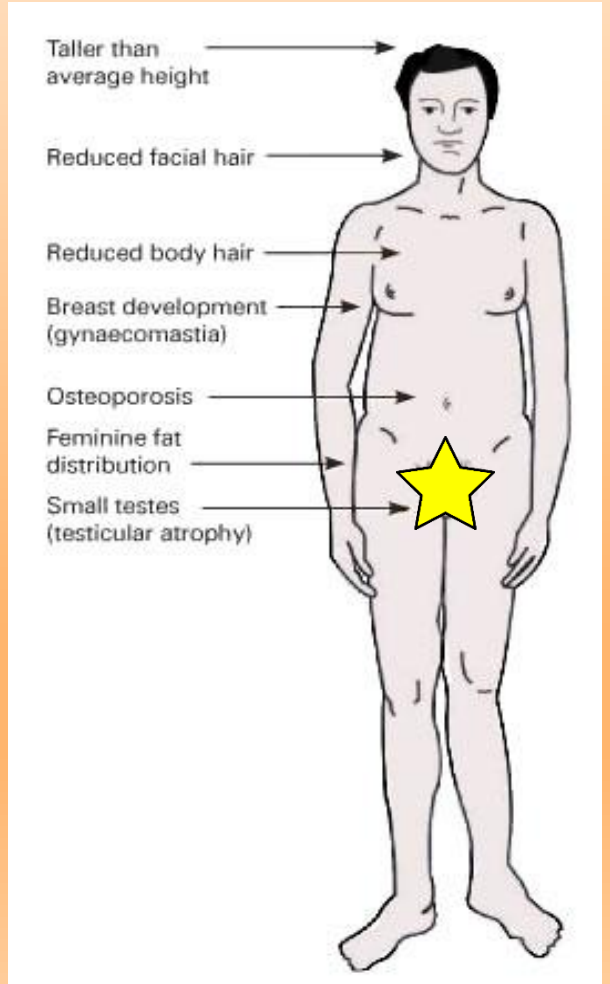
Video: Down Syndrome

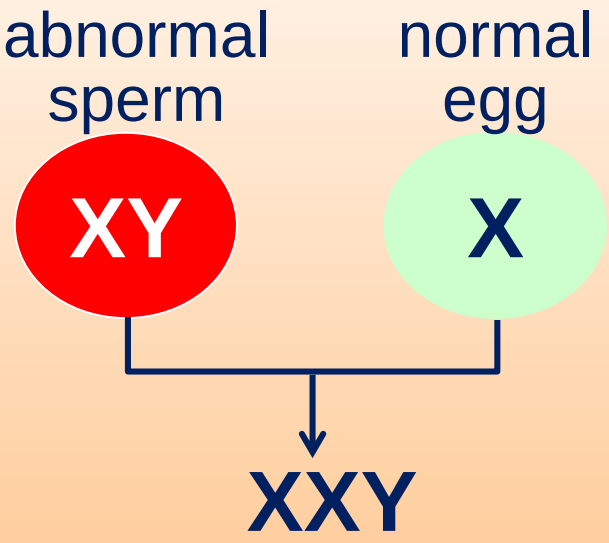
https://www.youtube.com/watch?v=EA0qxhR2oOk



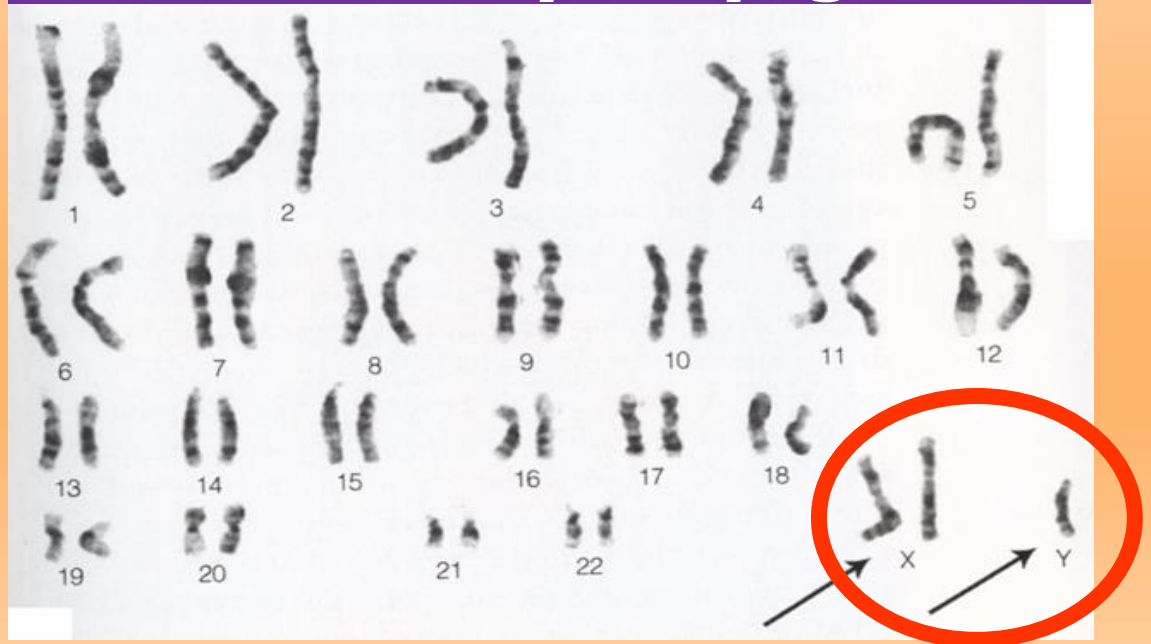
Klinefelter's syndrome

- **MALE** with extra X chromosome (**XXY**)
- rare cases – XXXY, XXXXY



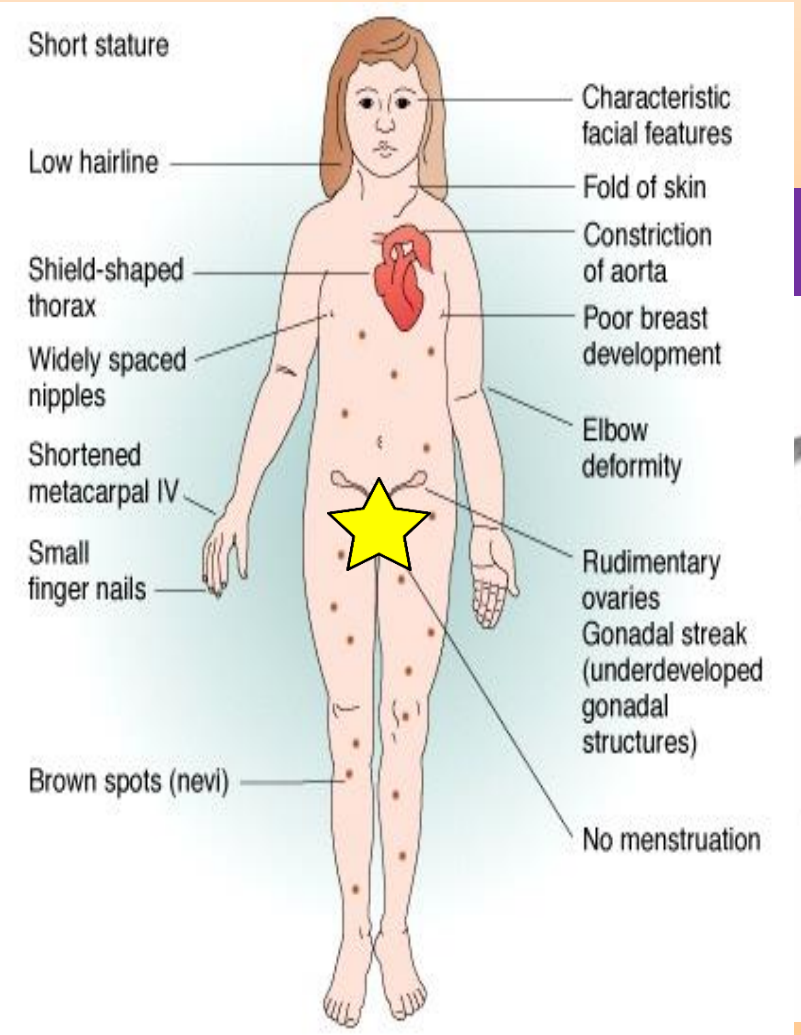


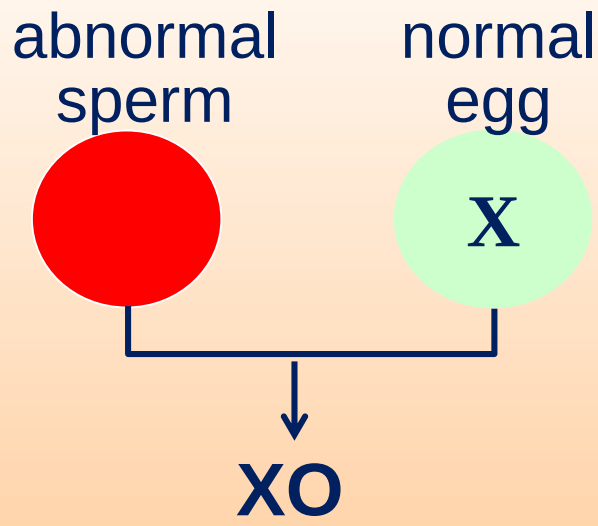
Detection by karyogram



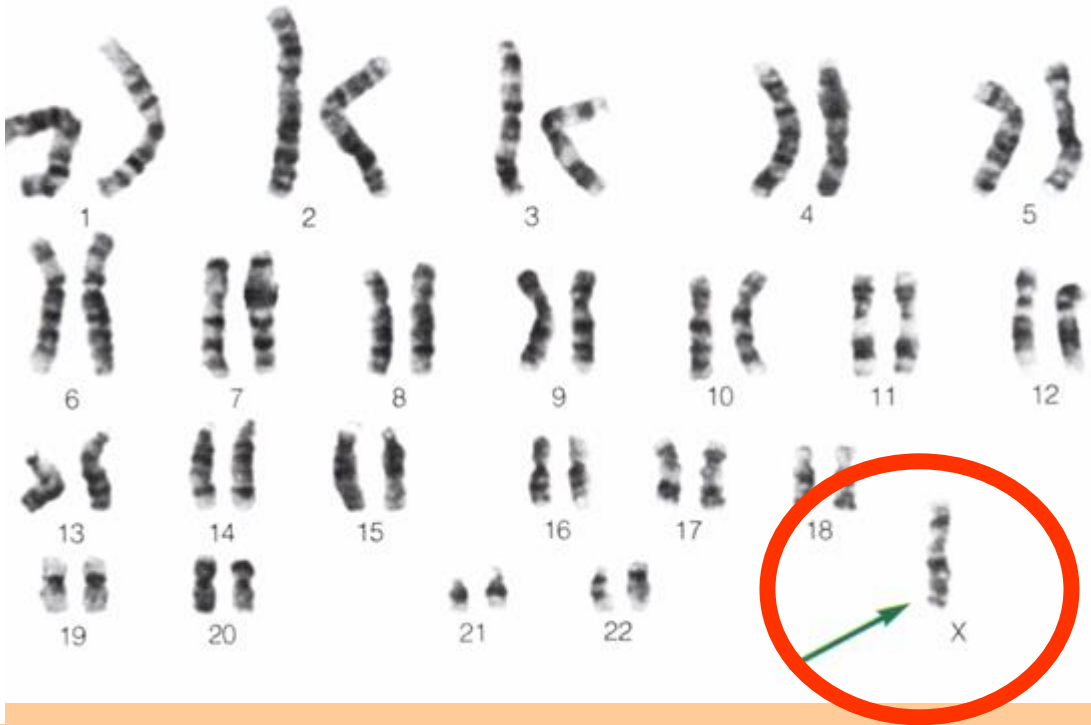
Turner's syndrome

FEMALE with one fewer X chromosome (XO)

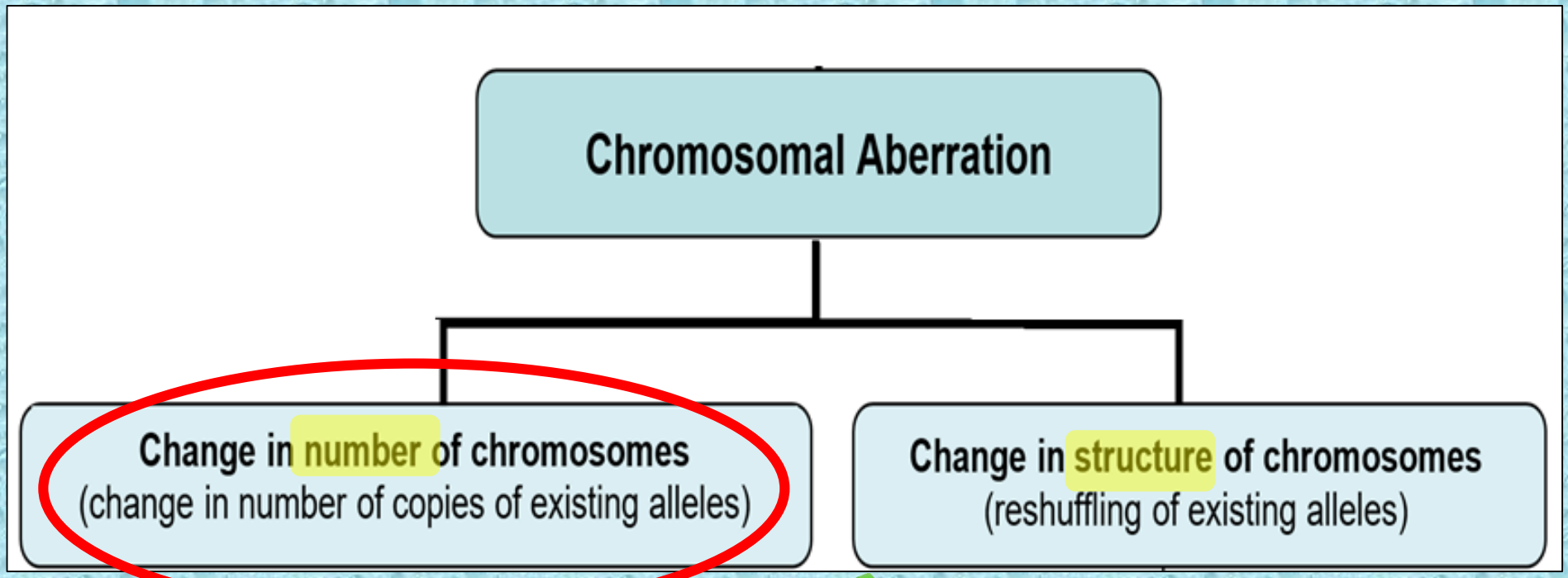




Detection by karyogram



Types of Chromosomal Aberration



I. Aneuploidy ✓

II. Polyploidy

II) Polyploidy

- is a condition when there are **three or more times** the haploid number (n) of chromosomes in a nucleus.
- **denoted as :**
  3n (three times haploid number),
  4n (four times haploid number) or
  5n (five times haploid number) etc.
- occurs when there is **increase in the number of sets of chromosomes** during non-disjunction events.

II) Polyploidy

Aneuploidy

1 extra chr

Polyploidy

1 extra set

????

1 extra section of chromosome

II) Polyploidy

Non-disjunction events that result in polyploidy are:

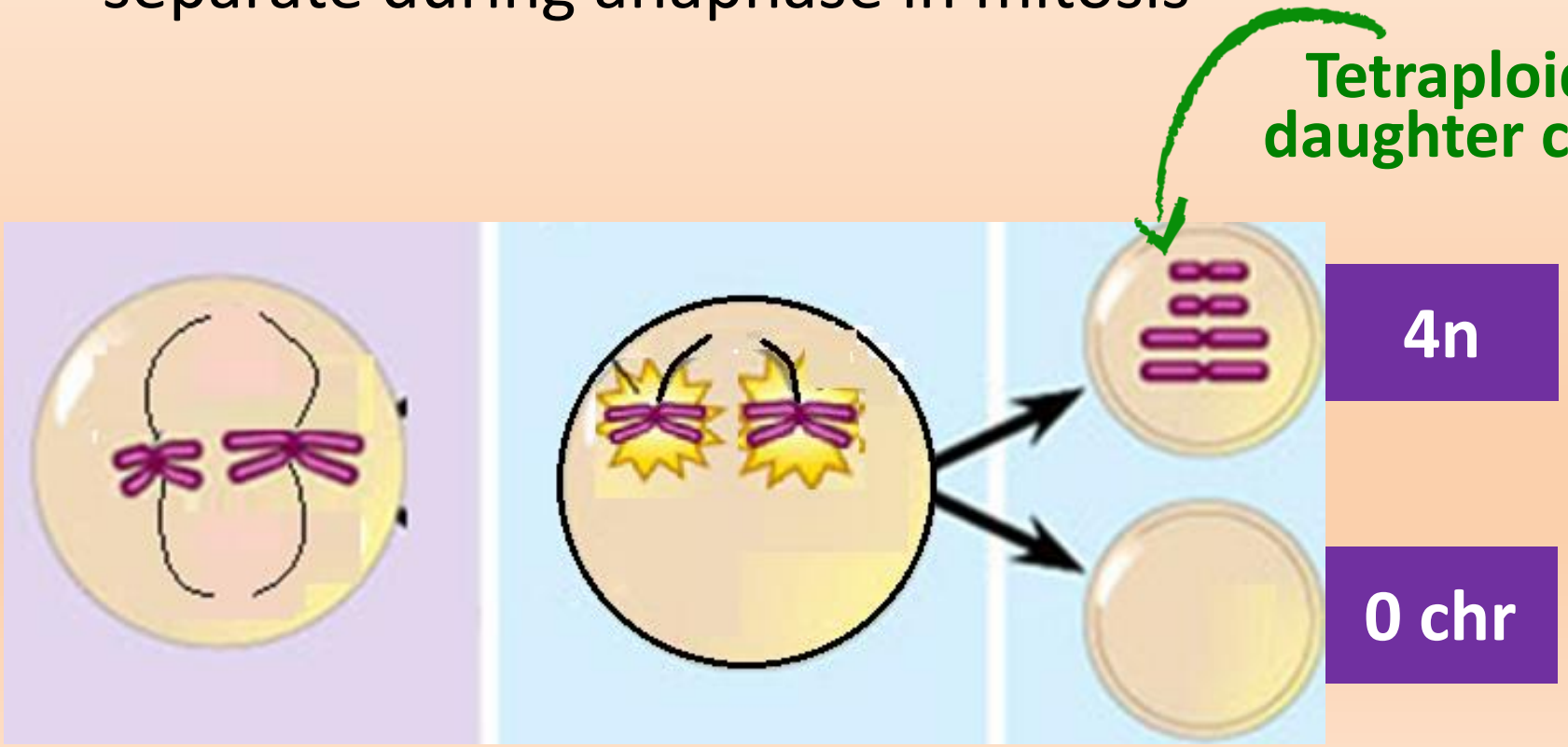
1. Failure of sister chromatids of **all** the chromosomes to separate during anaphase in mitosis
2. Failure of **all** homologous pairs of chromosomes to separate during anaphase I in meiosis
3. Failure of chromatids of **all** the chromosomes during anaphase II in meiosis.

Compare with pg 48, paragraph 2
'one or several' vs 'all

II) Polyploidy

For (1), daughter cells formed will have 4n

1. sister chromatids of **ALL** chromosomes fail to separate during anaphase in mitosis



II) Polyploidy

For (2) & (3): diploid gametes are formed

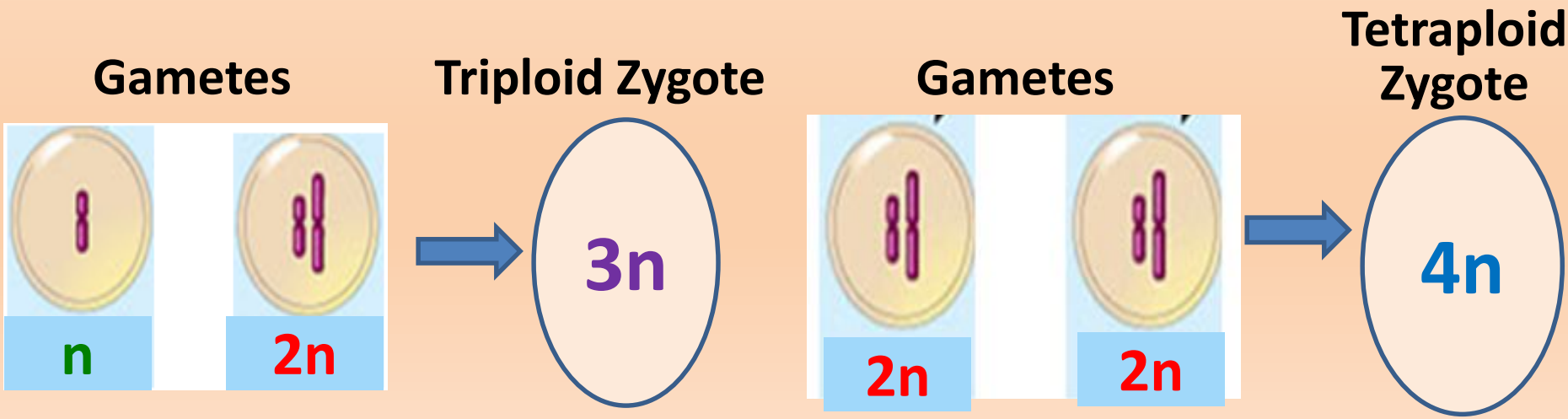
2. **ALL** homologous pairs of chromosomes failed to separate during **anaphase I in meiosis**
3. chromatids of **ALL** chromosomes fail to separate during **anaphase II in meiosis**.

Normal Gamete

Diploid Gamete (abnormal)

II) Polyploidy

- Subsequent fusion of a **diploid gamete (2n)** with a **normal haploid gamete (n)** results in a **triploid nucleus (3n)**
  OR
- Fusion of **two diploid gametes (2n)** results in a **tetraploid nucleus (4n)**.



Polyploidy is more common in plants than animals

Problem:

Increased number of sets of chromosomes makes normal gamete formation during **meiosis** much **more prone to error**.

Special Note:

Since most plants are **capable of vegetative propagation** (asexual reproduction), they are able to reproduce (asexually) despite being polyploid.

Polyploidy in plants

Advantage:

Polyploidy is often associated with **advantageous features** such as increased size, **HARDINESS** and resistance to disease.

This is called **hybrid vigour**.

Polyploidy

Examples of Polyploid Plants	
Name	**Number**
Common wheat	**6N** = 42
Tobacco	**4N** = 48
Potato	**4N** = 48
Banana	**3N** = 27
Boysenberry	**7N** = 49
Strawberry	**8N** = 56

Many **ferns** are polyploid with chromosome number up to 400N

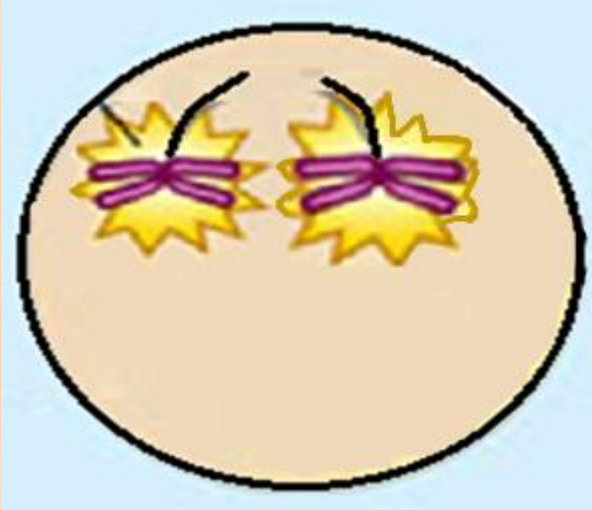
Most of our domestic plants are polyploids, producing large fruits, storage organs, flowers or leaves.

Polyploids look more normal than aneuploids

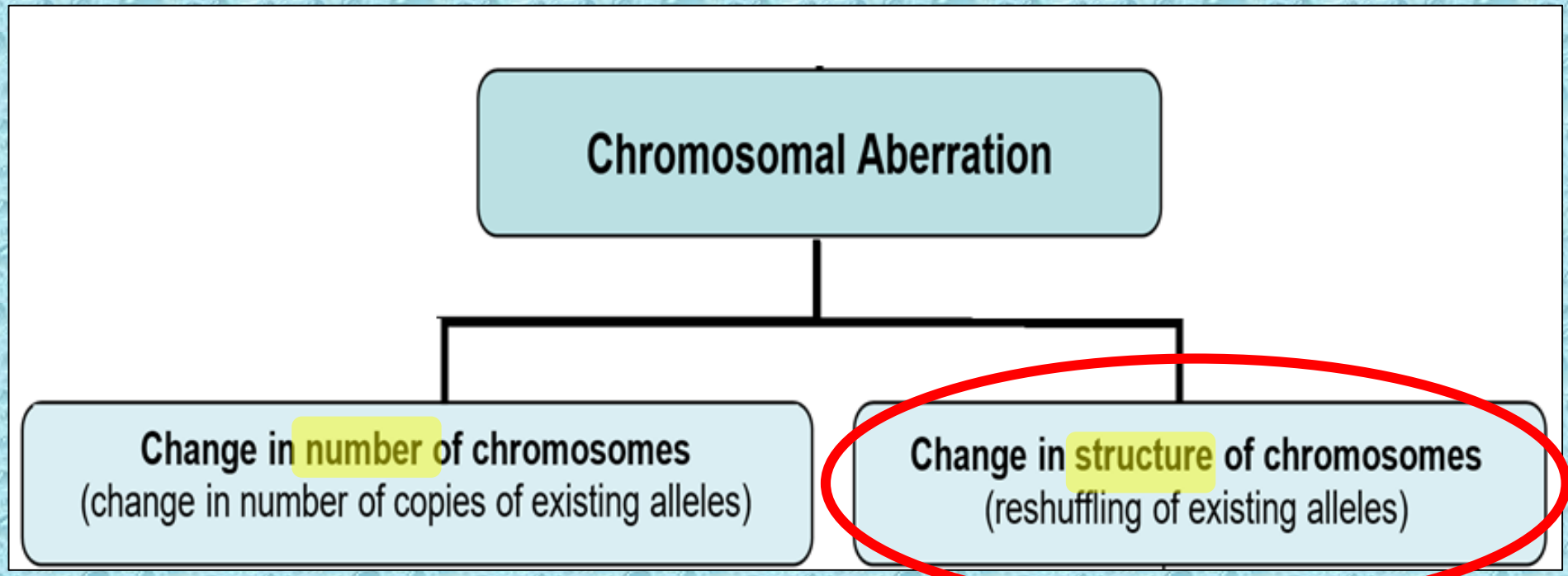
One extra (or missing) chromosomes apparently disrupts the genetic balance more than an entire extra set of chromosome.

II) Polyploidy

- **Colchicine** is a drug that can induce polyploidy
- It **inhibits spindle formation** by disrupting microtubules so that **sister chromatids fail to separate** during anaphase.



Types of Chromosomal Aberration



I. Aneuploidy ✓

II. Polyploidy ✓

1. Deletion
2. Duplication
3. Inversion
4. Translocation

[2] Change in structure of chromosomes

- Results from **chromosomal breaks** during mitosis or meiosis
- Effect: This often leads to **reshuffling** of **alleles** **on the affected chromosomes**

[2] Change in structure of chromosomes

- **4 types** of changes in chromosome structure:
  1. **Deletion**
  2. **Duplication**
  3. **Inversion**
  4. **Translocation**

General Effects

Deletion and **duplication** usually lead to an **abnormal phenotype**

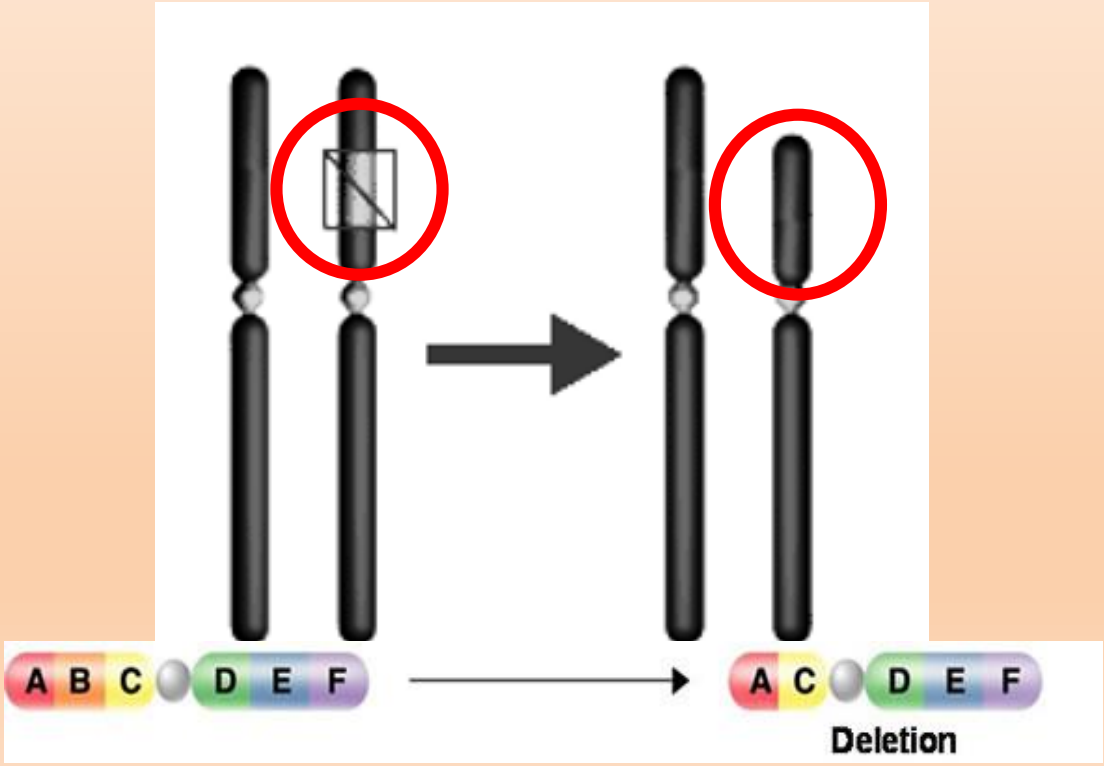
due to → **missing or increased number of genes**

However, **inversion** and **translocation** can be **balanced**. (does not manifest an abnormal phenotype)

because → **entire genome still present, only position is changed**

1) Deletion

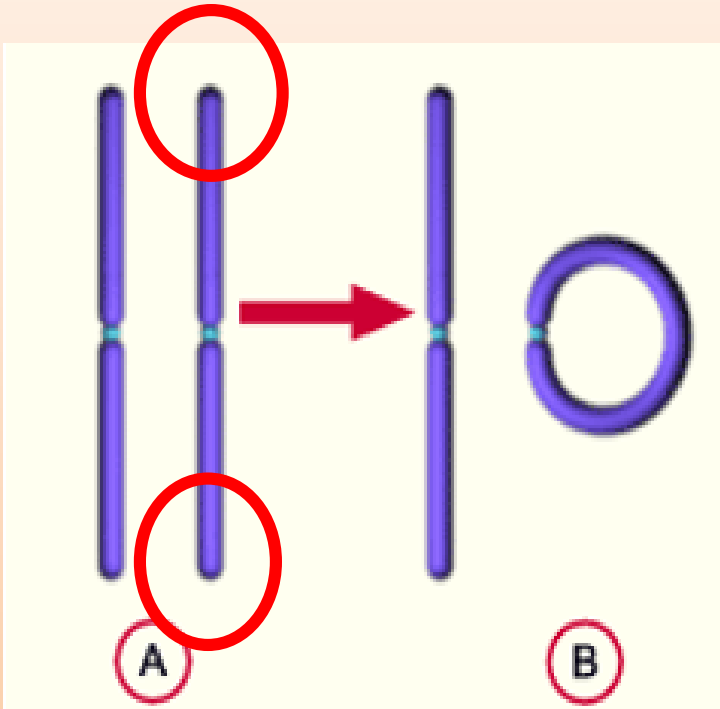
- Involves the **removal of a chromosomal segment**
- **Effect**: Consequence depends on the size of the missing segment and which genes are found on it.



1) Deletion

- Deletion of **telomeres**
- May cause the formation of **Chromosome rings** when the two ends join to each other.

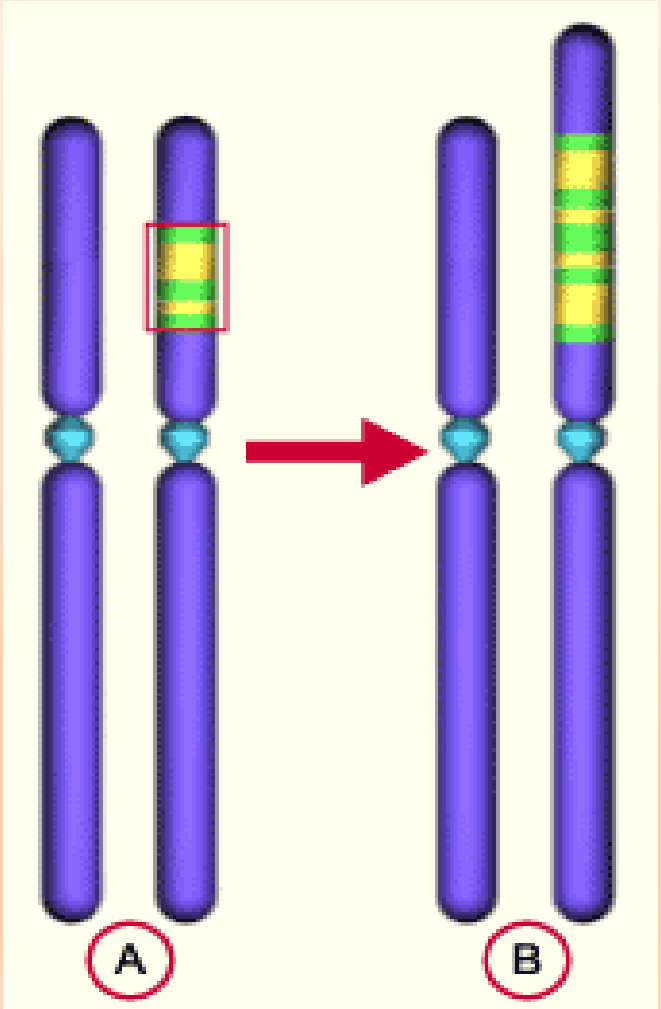
- **Effect**: If no genetic information is lost, such changes are **balanced** and the phenotype is **inconspicuous**.



A Normal chromosome pair
B Ring formation

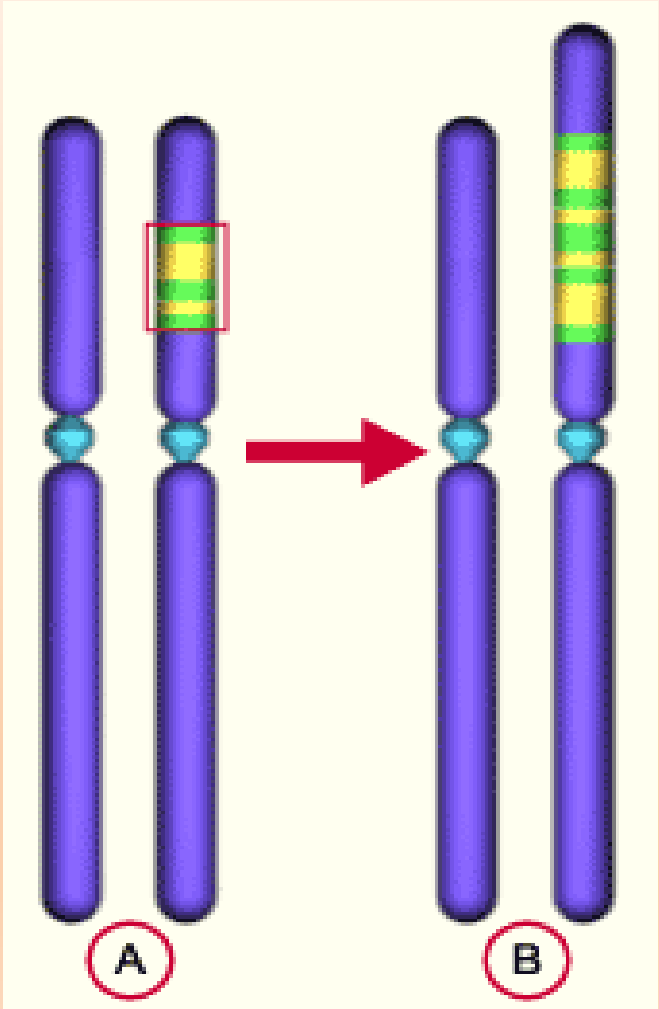
2) Duplication

- Involves the **repeat** **of a chromosomal segment**
- A duplication is sometimes termed a "**partial trisomy**"
- Affected person now has **3 copies of alleles** of a particular gene



2) Duplication

Effect: Extra copies of alleles of a particular gene may lead to **congenital abnormalities** or **developmental problems**

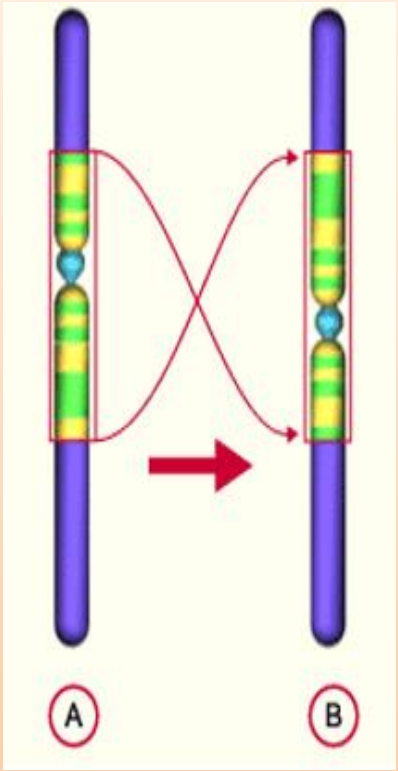


3) Inversion

- Involves the **reversal** of a chromosomal segment

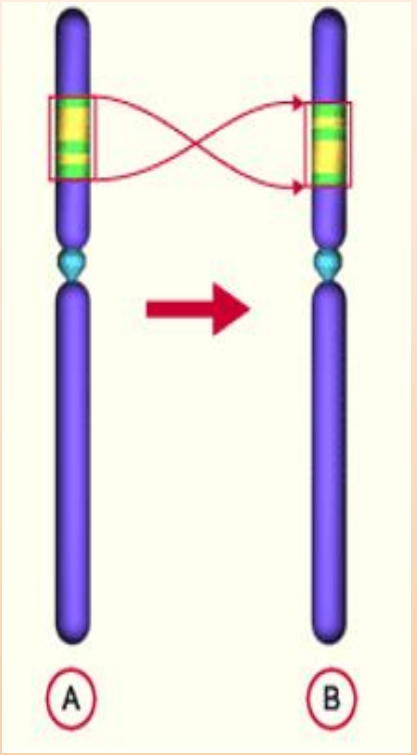
- **Effect:** The phenotype of this disorder is **usually not exhibited**, since the complete genetic information is still present.

3) Inversion



‘surrounding’

‘to the side of’



Pericentric
(includes centromere)

Paracentric
(Does not include centromere)

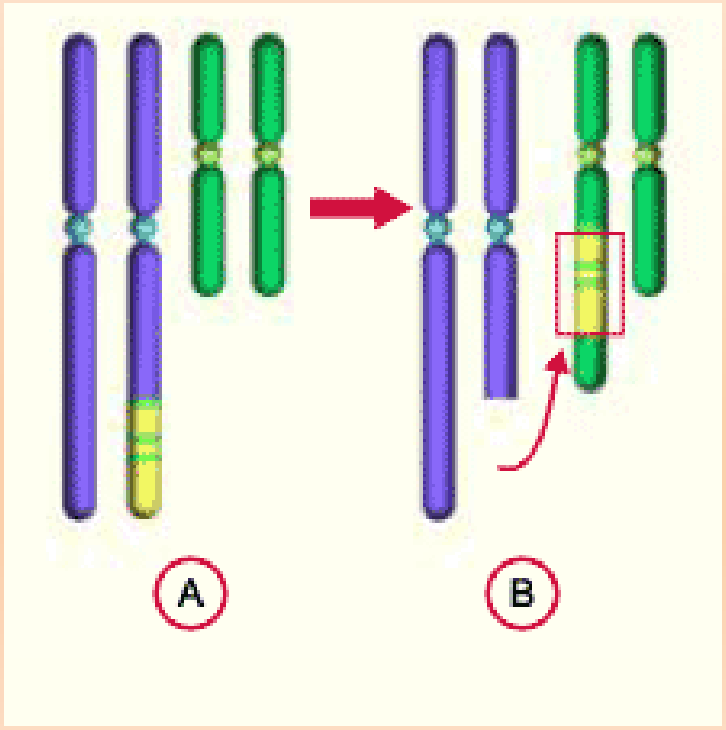
4) Translocation

- Involves segment from one chromosome being **moved** to another **non-homologous chromosome**
- **Effect:** Can result in an abnormal phenotype if an **important gene is translocated to be downstream of an active / less active promoter**
- → change in expression level of protein

4) Translocation

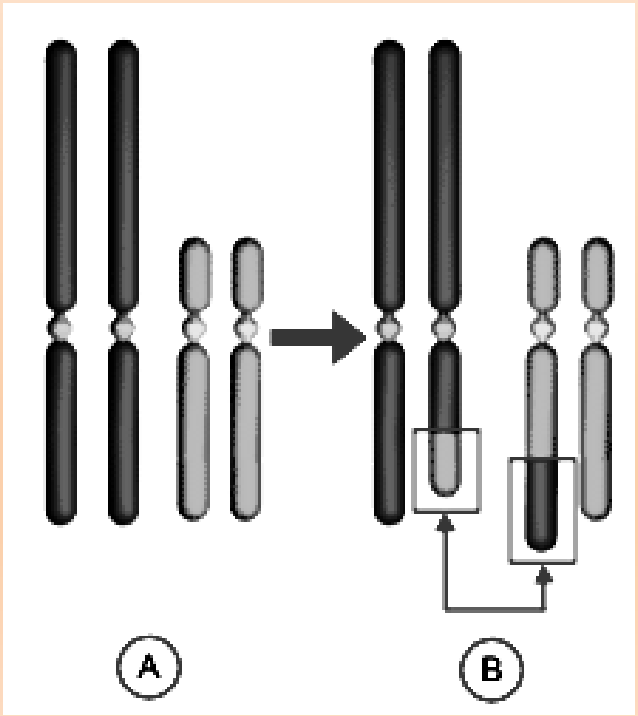
Non-reciprocal translocation

(1 way)



Reciprocal translocation

(2 way)



Not in Notes

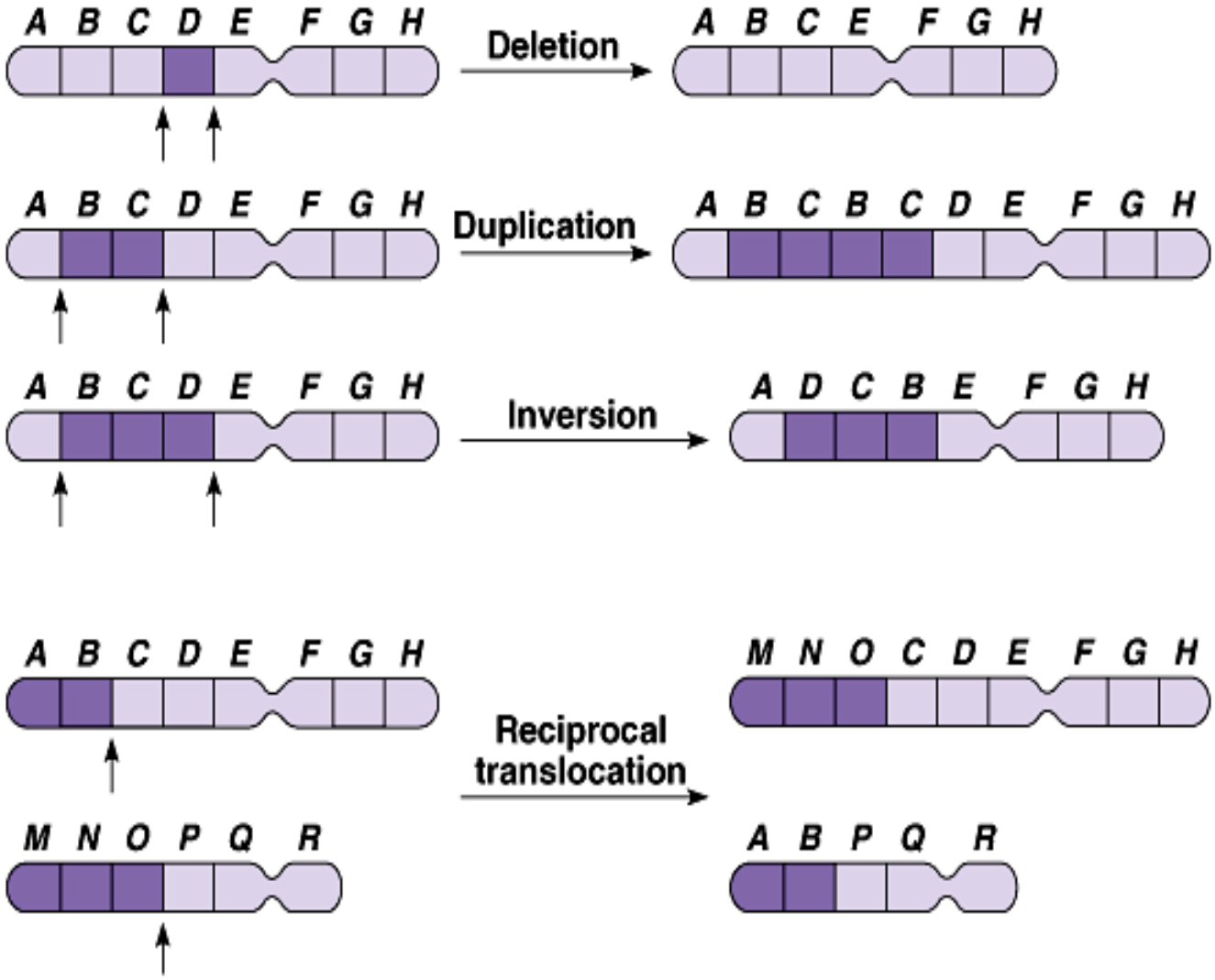
Types of chromosomal breaks

(a) A **deletion** removes a chromosomal segment.

(b) A **duplication** repeats a segment.

(c) An **inversion** reverses a segment within a chromosome.

(d) A **translocation** moves a segment from one chromosome to another, non-homologous one.



Not in Notes

Summary