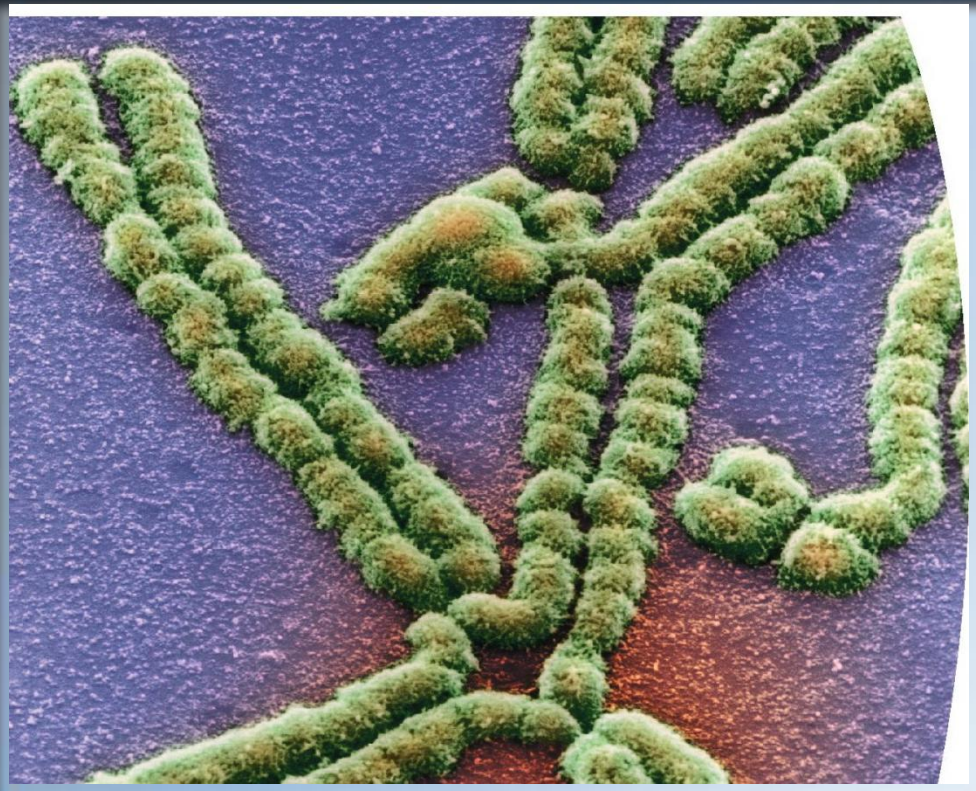


# Chromosome Mutations: Variation in Chromosome Number and Arrangement

# Chromosome Mutations: Variation in Chromosome Number and Arrangement

## Specific Terminology Describes Variations in Chromosome Number

- Although most diploid species normally contain precisely two haploid chromosome sets, there are many known variations:
  - a change in the total number of chromosomes,
  - the deletion or duplication of genes or segments of a chromosome,

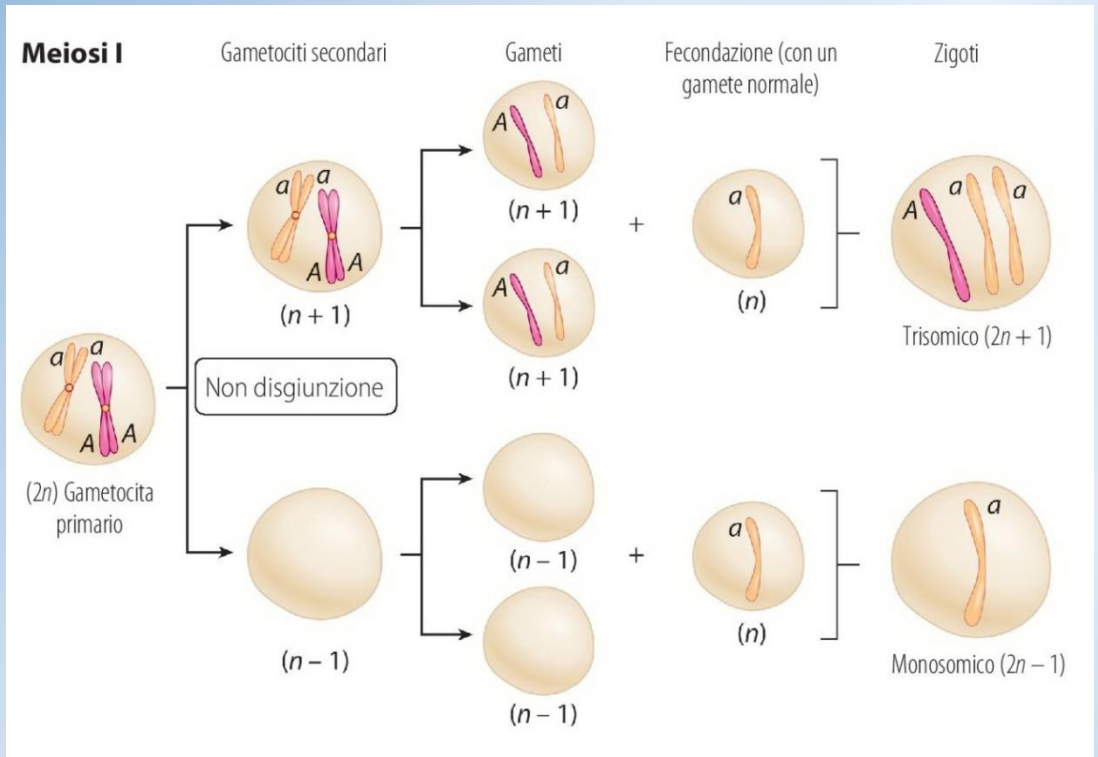
# Chromosome Mutations: Variation in Chromosome Number and Arrangement

–and rearrangements of the genetic material either within or among chromosomes.

•Such changes are called **chromosome mutations or chromosome aberrations**, to distinguish them from gene mutations.

# Chromosome Mutations: Variation in Chromosome Number and Arrangement

- Variations in chromosome number are known as **aneuploidy** when an organism gains or loses one or more chromosomes and has other than an exact multiple of the haploid set.



## TABLE 8.1 TERMINOLOGY FOR VARIATION IN CHROMOSOME NUMBERS

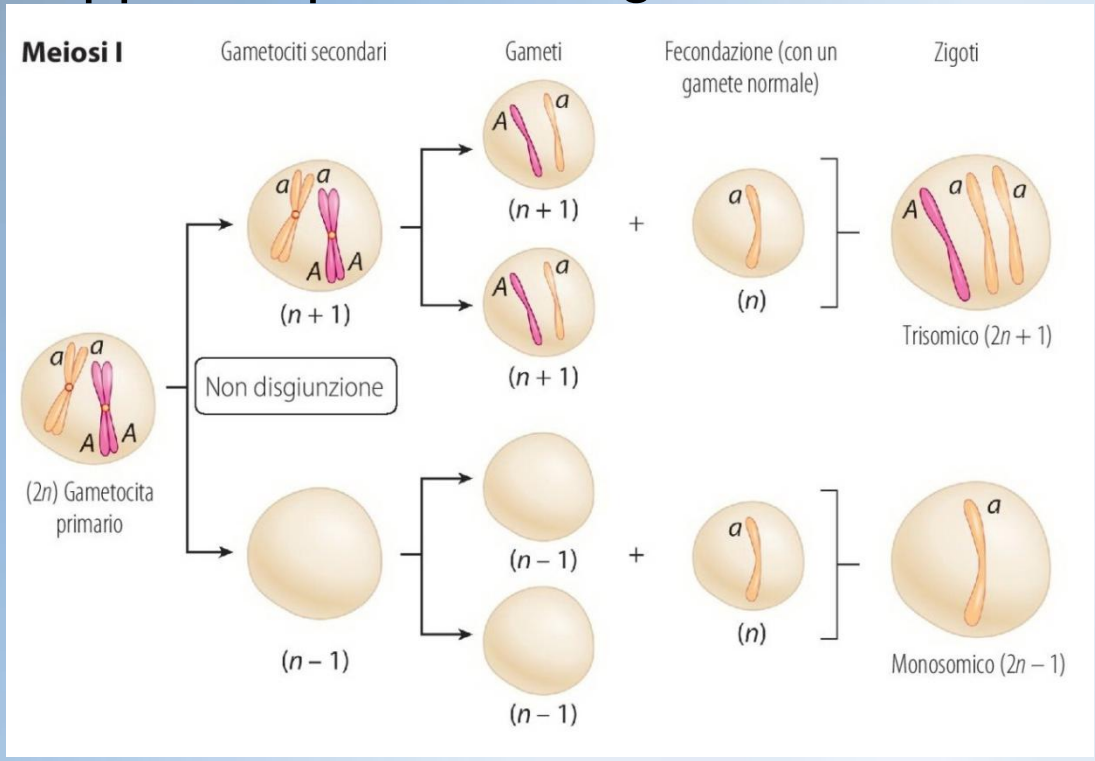
| Term | Explanation |
|---|---|
| Aneuploidy | $2n \pm x$ chromosomes |
| Monosomy | $2n - 1$ |
| Trisomy | $2n + 1$ |
| Tetrasomy, pentasomy, etc. | $2n + 2$, $2n + 3$, etc. |
| Euploidy | Multiples of $n$ |
| Diploidy | $2n$ |
| Polyploidy | $3n$, $4n$, $5n$, . . . |
| Triploidy | $3n$ |
| Tetraploidy, pentaploidy, etc. | $4n$, $5n$, etc. |
| Autopolyploidy | Multiples of the same genome |
| Allopolyploidy (Amphidiploidy) | Multiples of different genomes |

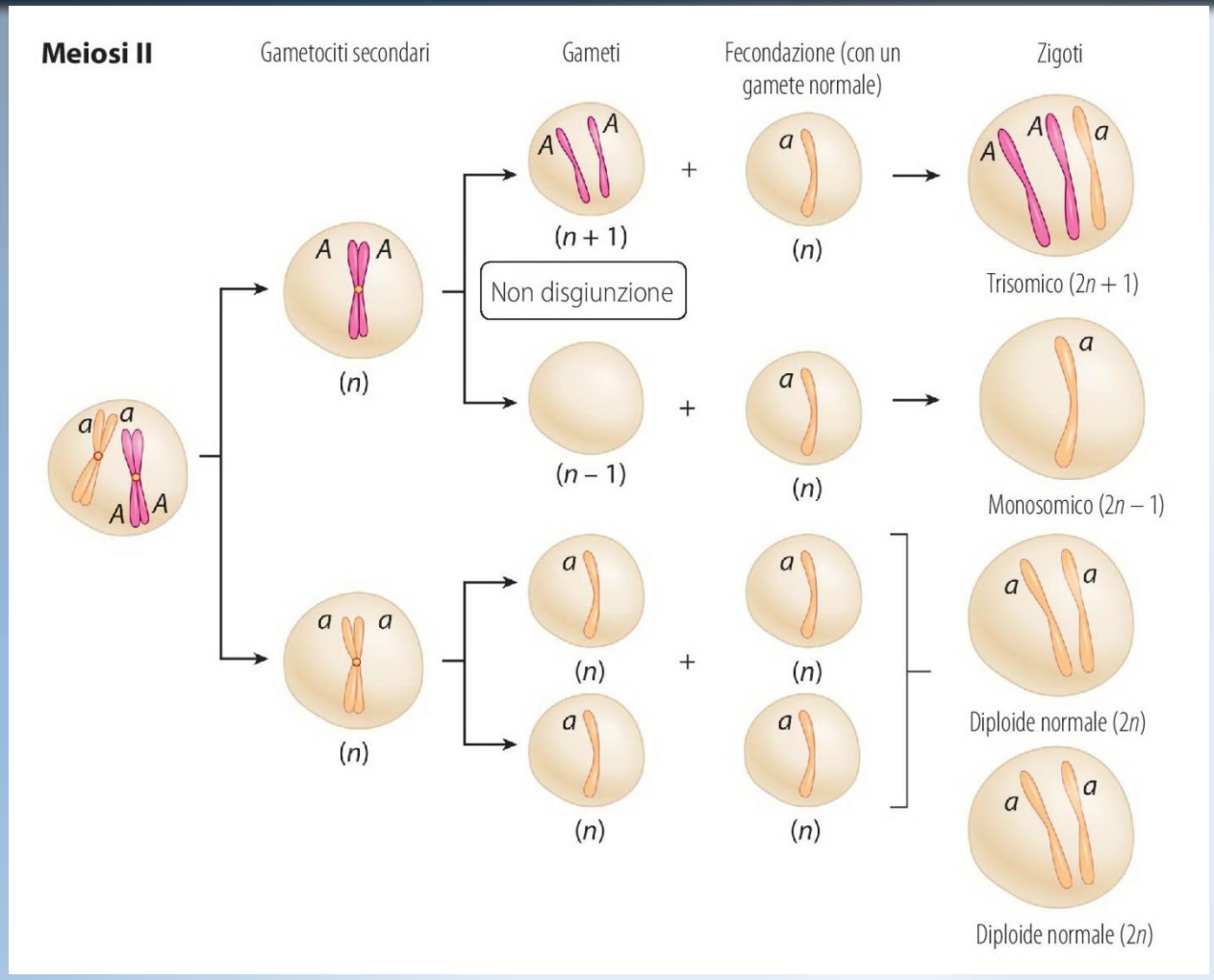
In euploidy, complete haploid sets of chromosomes are present.

**Polyploidy** occurs when more than two sets of chromosomes are present.

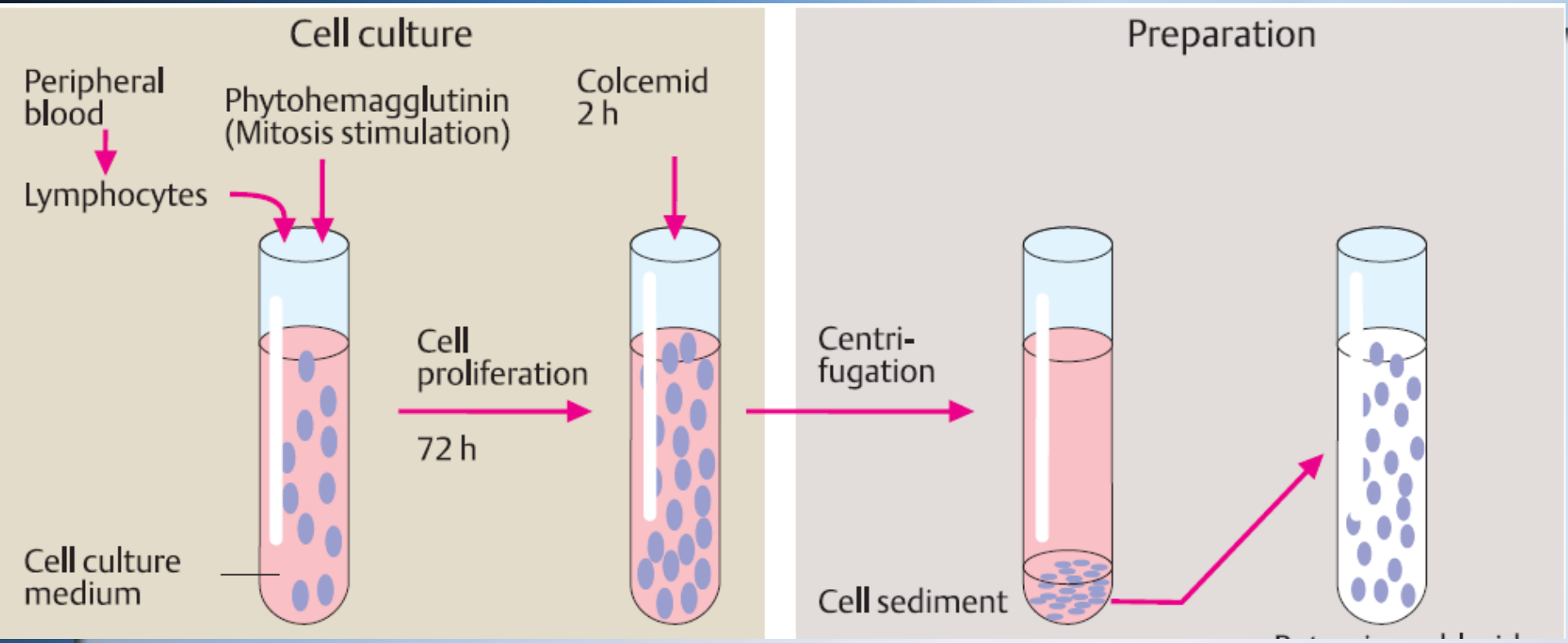
# Variation in the Number of Chromosomes Results from Nondisjunction

- Chromosomal variation can arise from nondisjunction, in which chromosomes or chromatids fail to disjoin and move to opposite poles during meiosis I or II.

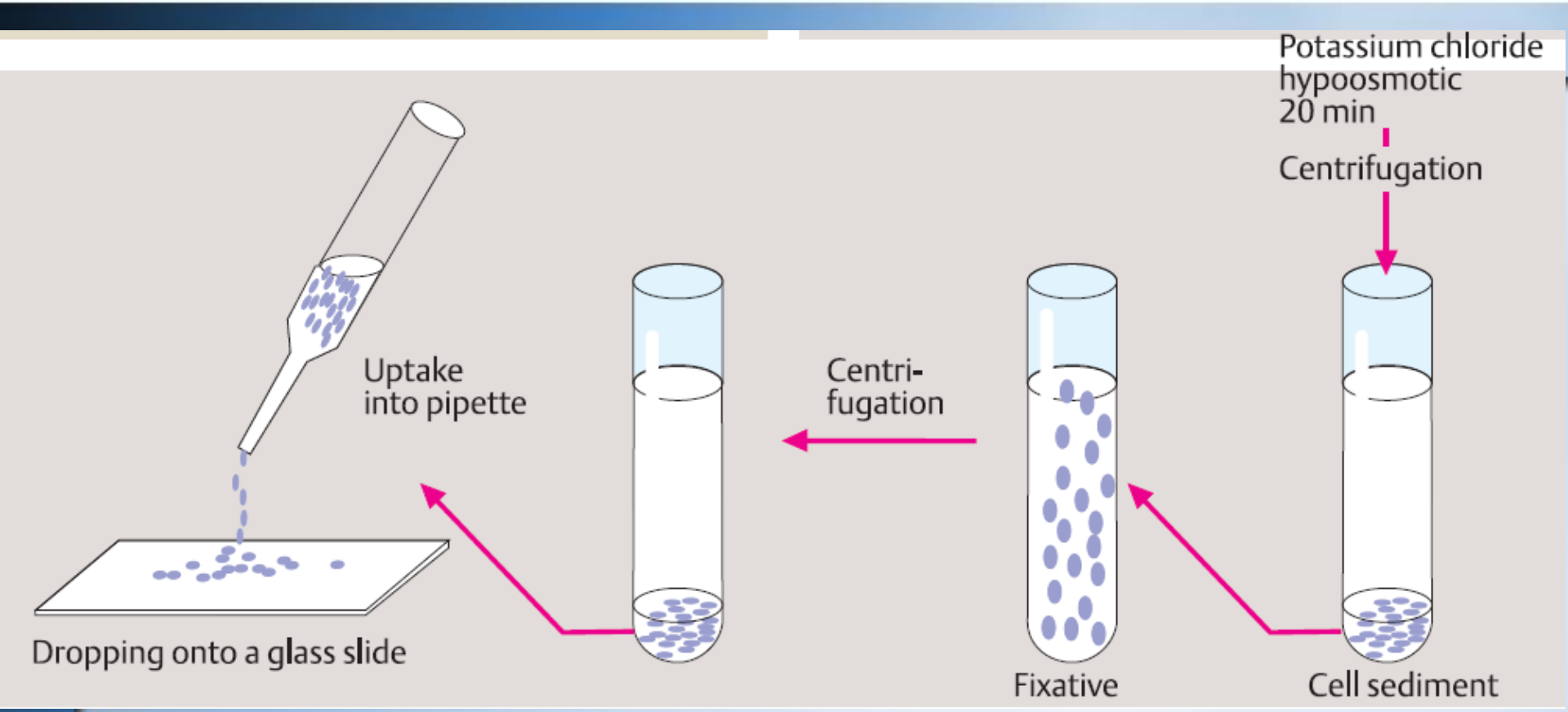



Meiosi II
Gametociti secondari
Gameti
Fecondazione (con un gamete normale)
Zigoti
A A
(n)
a a A A
A A
(n + 1)
Non disgiunzione
(n − 1)
a a
(n)
a a
(n)
a
(n)
a
(n)
a
(n)
a
(n)
A A a
Trisomico (2n + 1)
a
Monosomico (2n − 1)
a a
Diploide normale (2n)
a a
Diploide normale (2n)

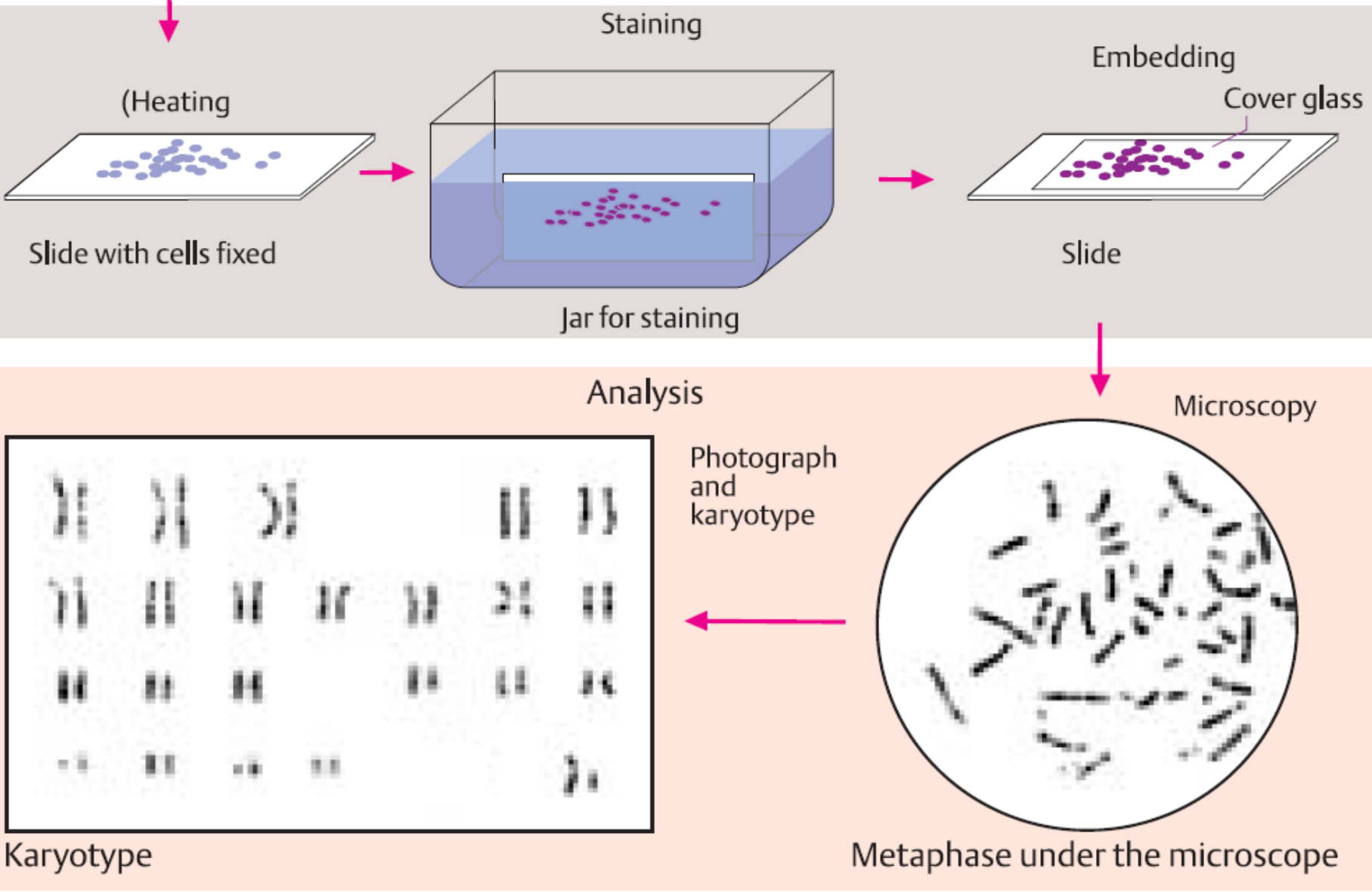
# Preparation of Metaphase Chromosomes for Analysis



# Preparation of Metaphase Chromosomes for Analysis



# Preparation of Metaphase Chromosomes for Analysis

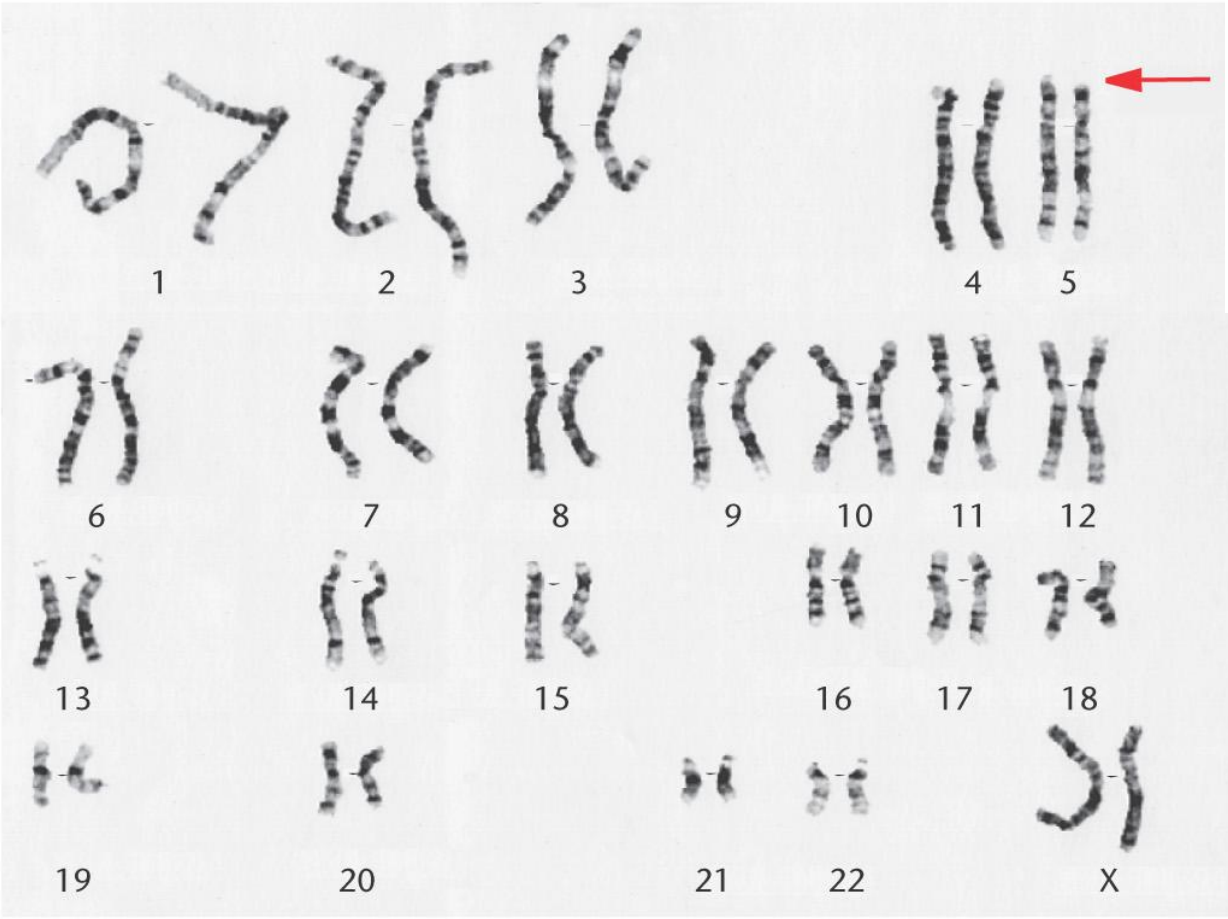


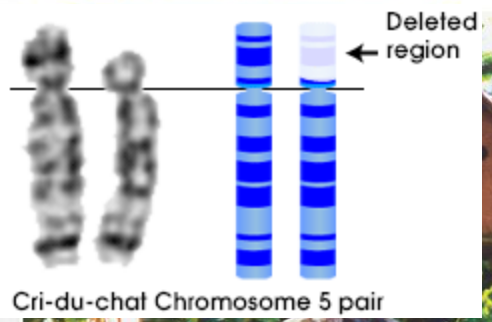
# Monosomy, the Loss of a Single Chromosome, May Have Severe Phenotypic Effects

- The loss of one chromosome to produce a $2n - 1$ complement is called **monosomy**.
- Although monosomy for the X chromosome occurs in humans, monosomy for any of the autosomes is usually not tolerated in humans and other animals.

# Monosomy, the Loss of a Single Chromosome, May Have Severe Phenotypic Effects

- In **partial monosomy or segmental deletion**, only a section of a chromosome is lost. One example is cri-du-chat syndrome, in which a small part of the short arm of chromosome 5 is lost.

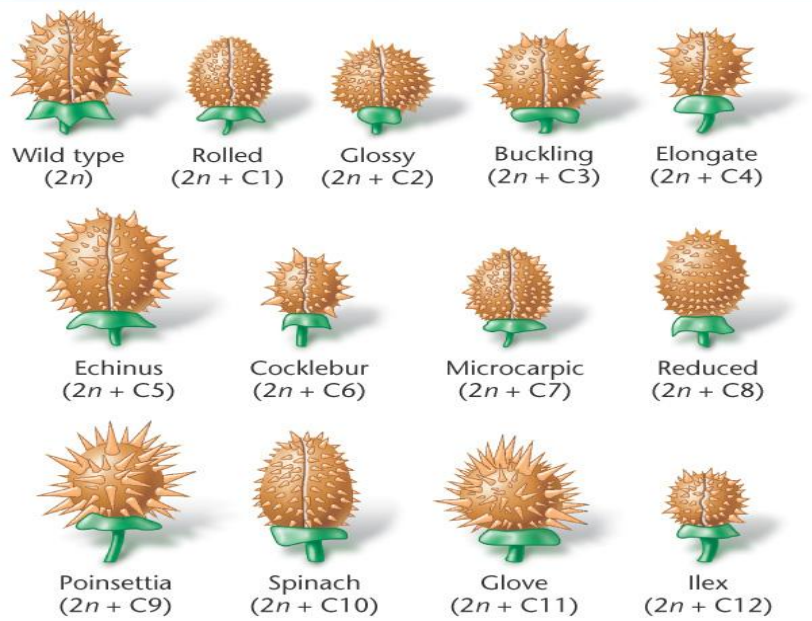



incidenza di un caso ogni 50 000 nati vivi

# Trisomy Involves the Addition of a Chromosome to a Diploid Genome

- Trisomy ($2n + 1$ chromosomes) for the sex chromosomes has a less dramatic phenotype than trisomies for autosomes, which are often lethal.



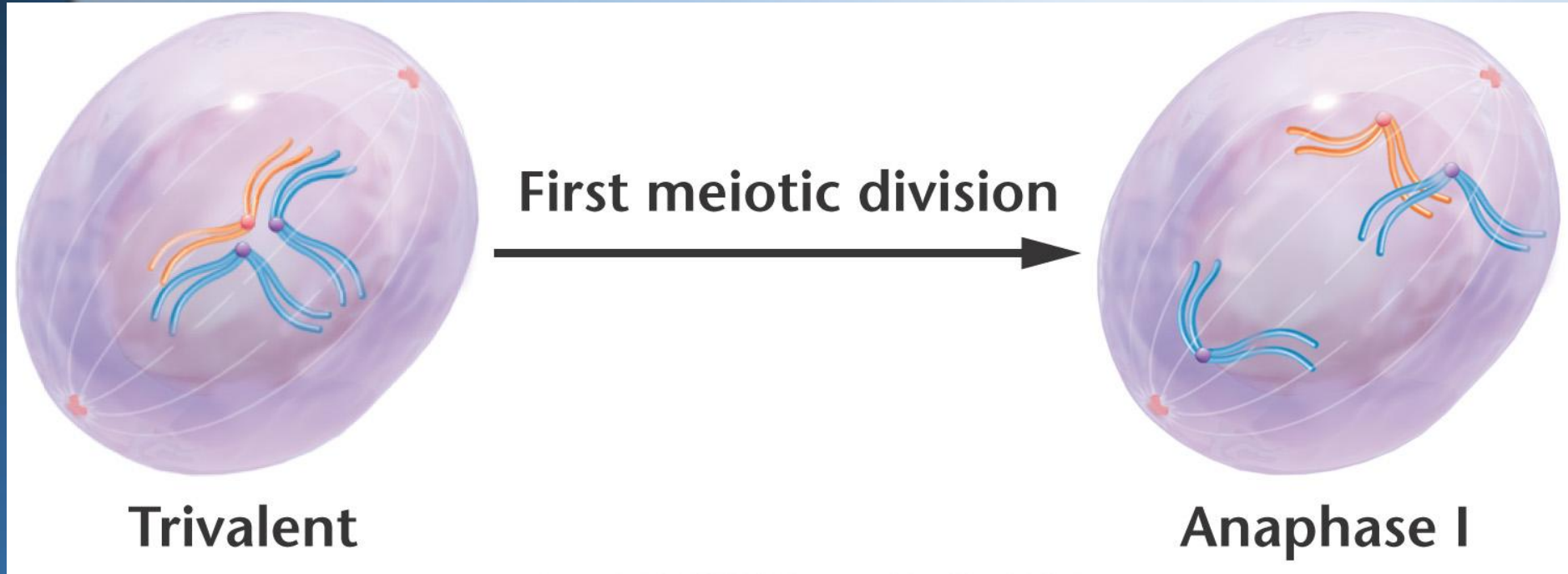


Datura stramonium

# Trisomy Involves the Addition of a Chromosome to a Diploid Genome

- In trisomy, three copies of one chromosome are present, **so pairing configurations are usually irregular**. At any particular region along the chromosome length, only two of the three homologs may synapse, though different regions of the trio may be paired.

• When three copies of a chromosome are synapsed, the configuration is called a trivalent. In some cases, prior to the first meiotic division, one bivalent and one univalent (an unpaired chromosome) may be present instead of a trivalent.



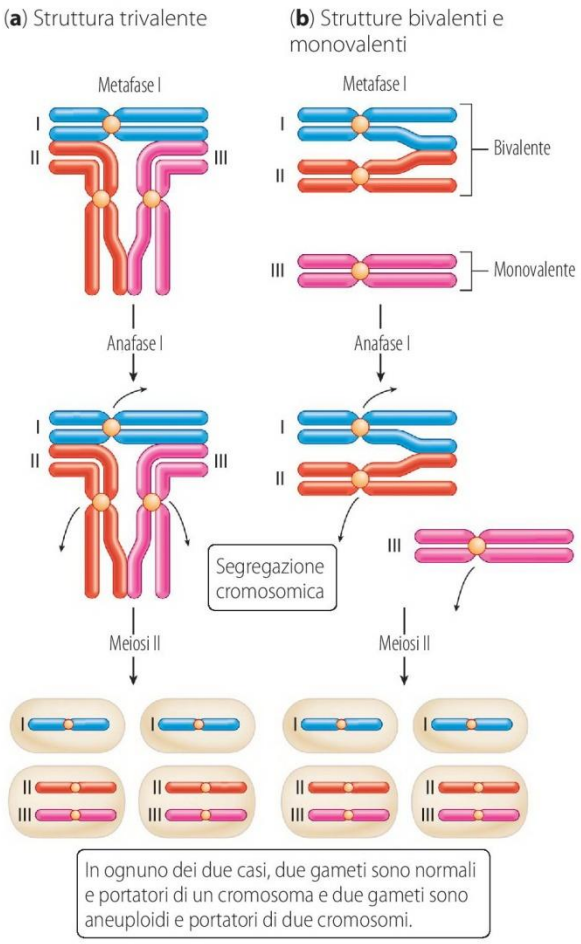
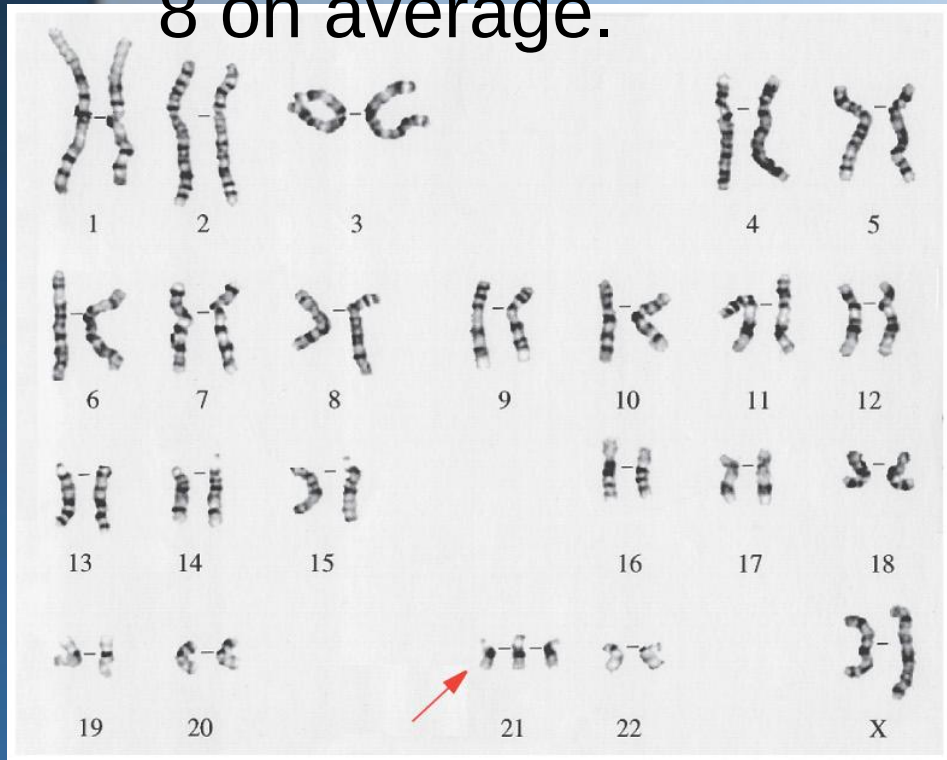
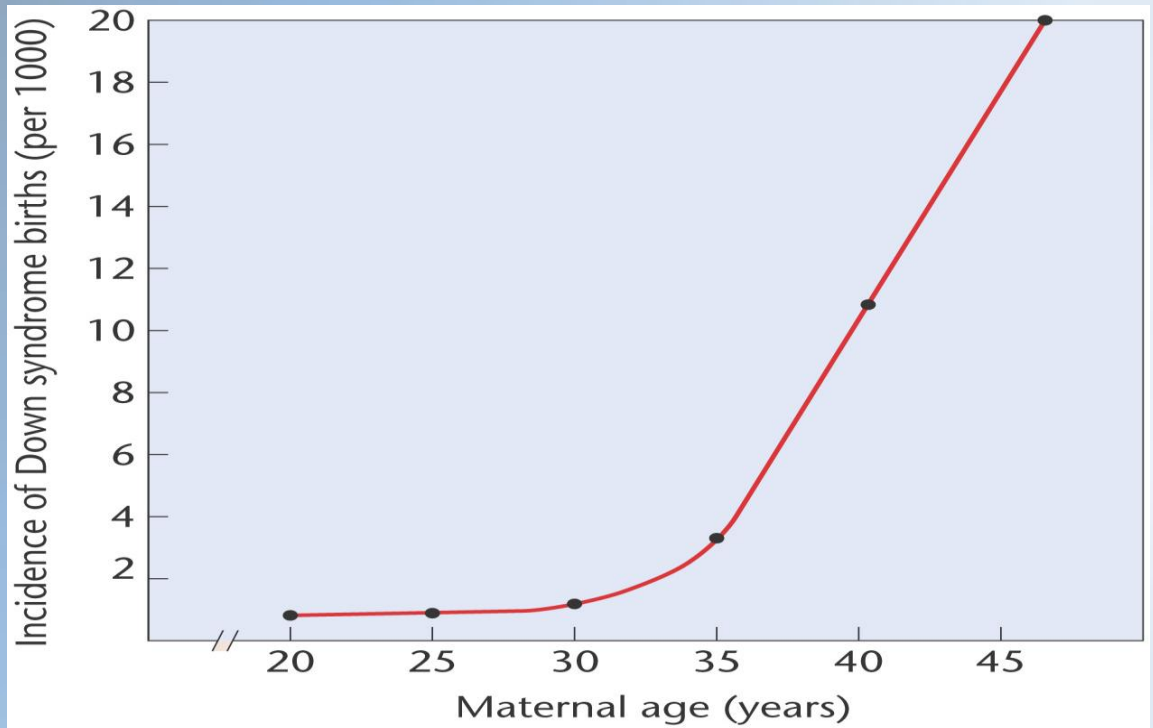



**Figura 13.4 Due modelli di segregazione meiotica nella trisomia.** (**a**) Tre cromosomi formano una struttura trivalente durante l'appaiamento e generano solo due gameti aploidi normali su quattro. (**b**) Anche un arrangiamento bivalente e uno monovalente dei tre cromosomi determina la formazione di soli due gameti aploidi normali.

- **<u>Down syndrome</u>** results from trisomy of chromosome 21. Down syndrome has 12 to 14 characteristics, and affected individuals express 6 to 8 on average.

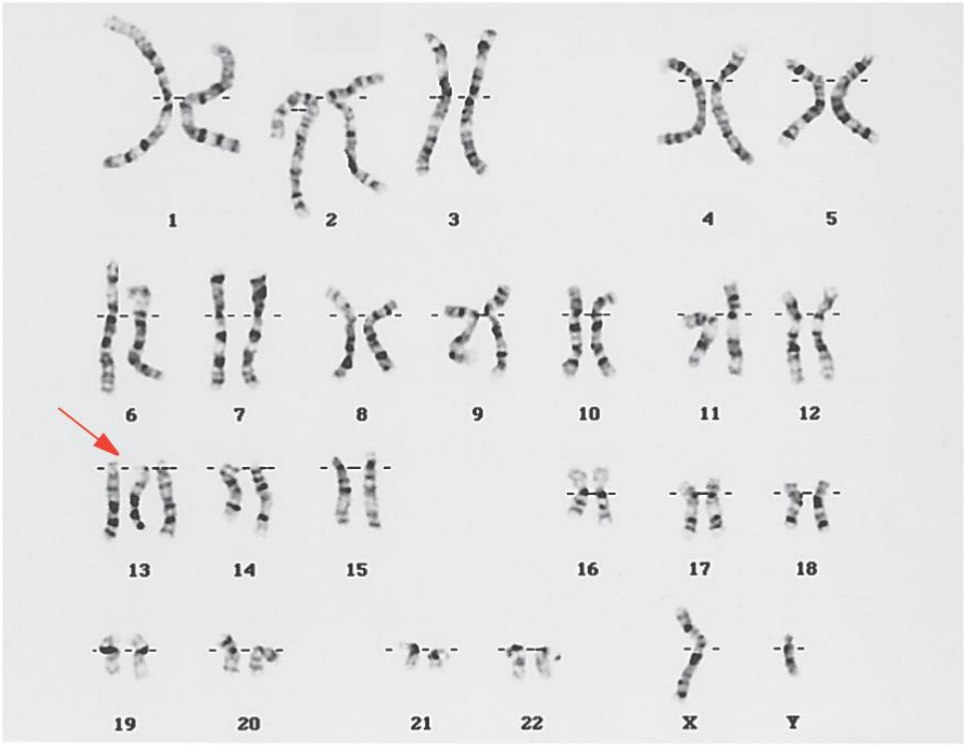



- Down syndrome is **usually a result of nondisjunction of the maternal chromosome 21** during meiosis and shows an increased incidence with increasing maternal age.



- Down syndrome occasionally runs in families. These instances, referred to as familial Down syndrome, involve a **translocation** of chromosome 21.
- Genetic counseling is recommended for women who become pregnant late in their reproductive years. Diagnostic testing—amniocentesis or chorionic villus sampling (CVS)—may be recommended.

- Other examples of trisomy syndromes are Patau syndrome (trisomy 13) and Edwards syndrome (trisomy 18).

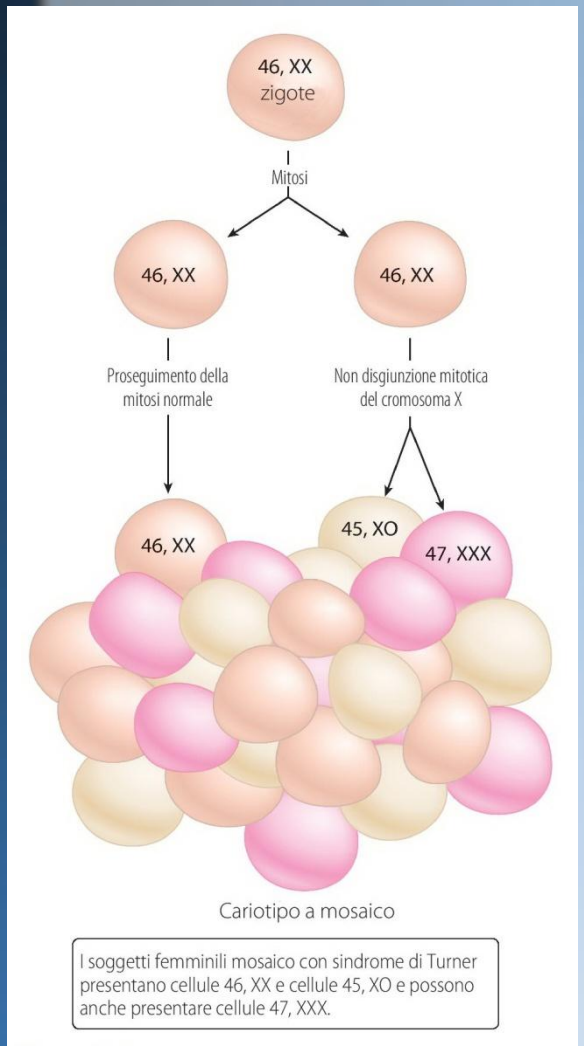



Mental retardation
Growth failure
Low set deformed ears
Deafness
Atrial septal defect
Ventricular septal defect
Abnormal polymorphonuclear granulocytes

Microcephaly
Cleft lip and palate
Polydactyly
Deformed finger nails
Kidney cysts
Double ureter
Umbilical hernia
Developmental uterine abnormalities
Cryptorchidism

- Trisomies are often found in spontaneously aborted fetuses, but monosomies are not, which suggests that monosomic gametes may be very functionally impaired.

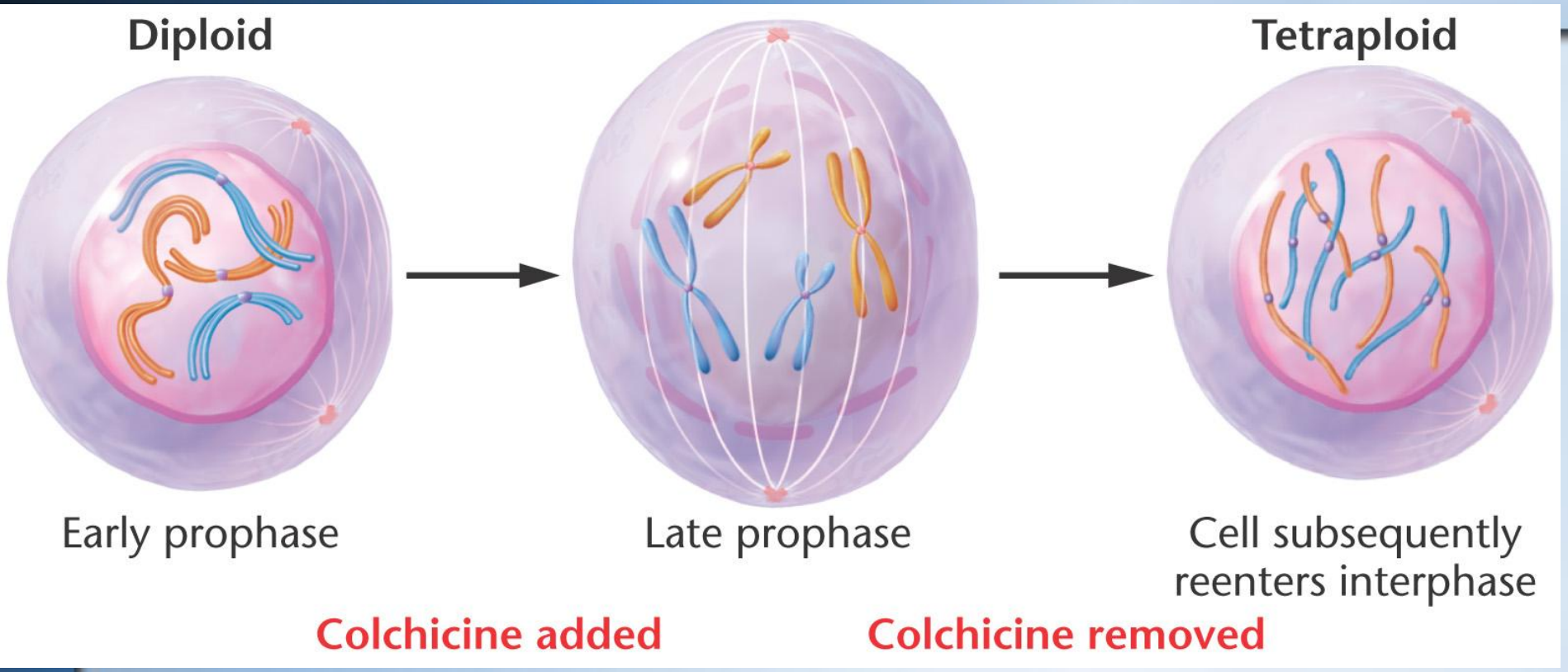
# Mosaicism



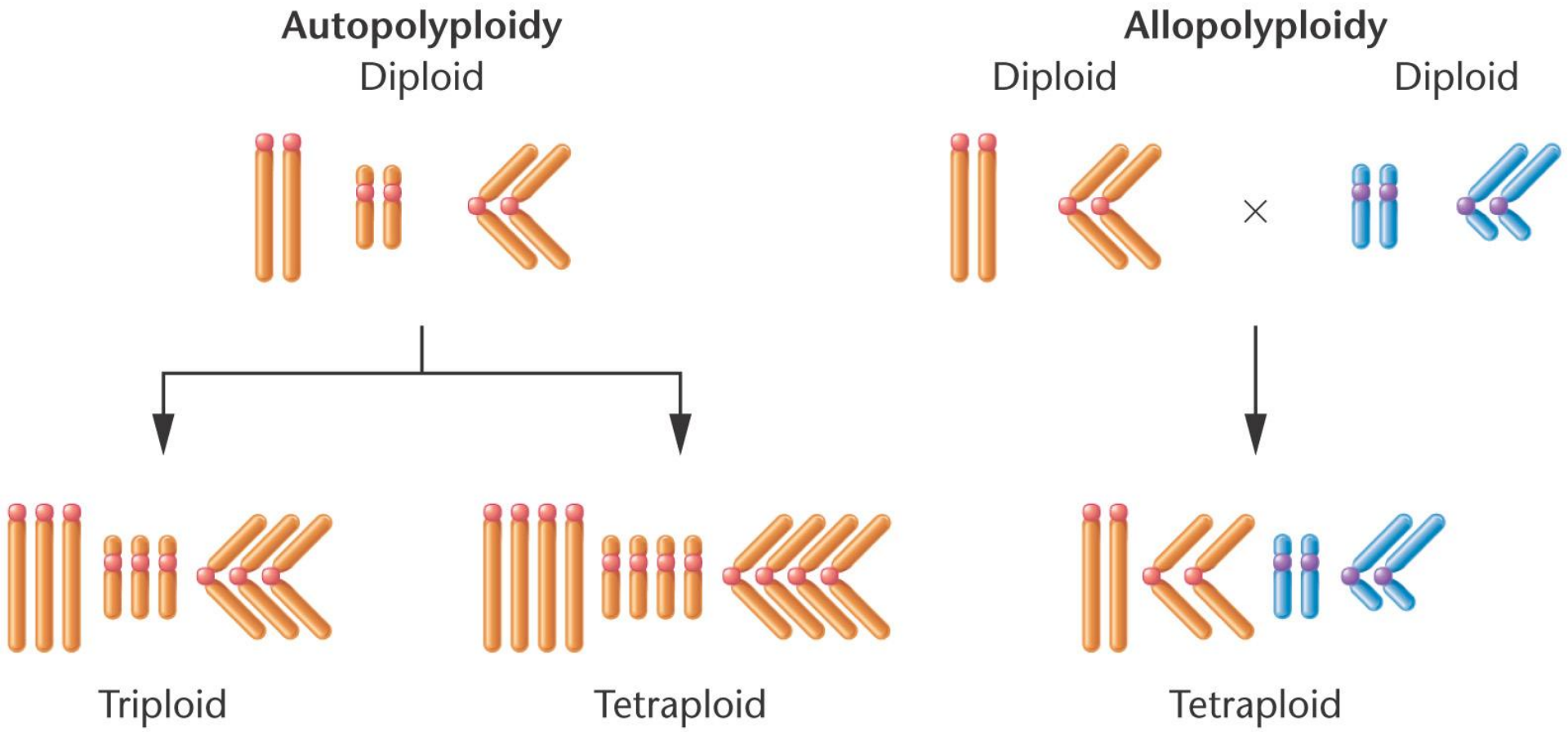

25/30% of Turner syndrome is due to mitotic non disjunction.

# Polyploidy Is Prevalent in Plants

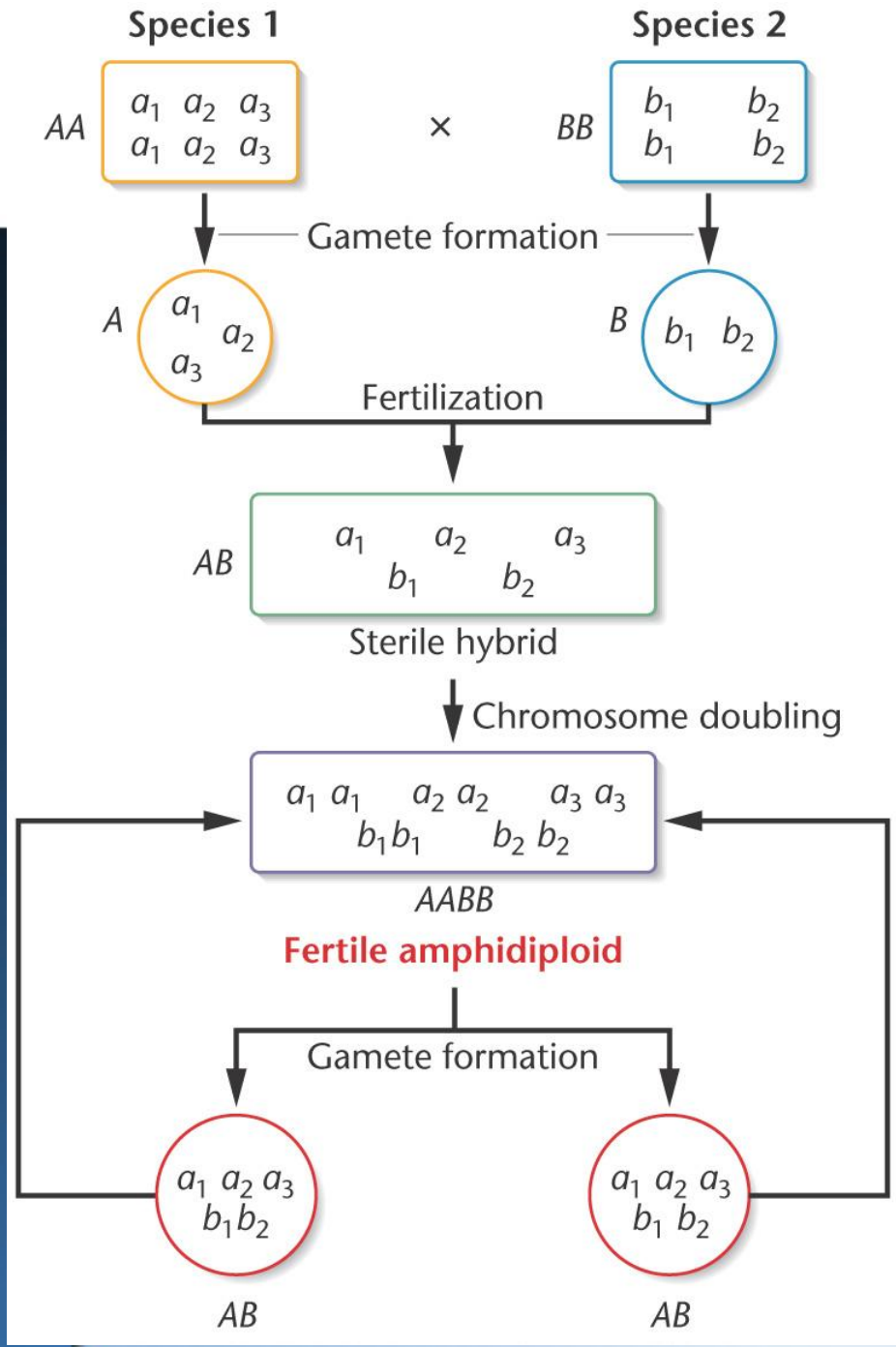
- The naming of polyploids is based on the number of sets of chromosomes found: a triploid has 3*n* chromosomes; a tetraploid has 4*n*; a pentaploid, 5*n*; and so forth.


Diploid
Tetraploid
Early prophase
Late prophase
Cell subsequently reenters interphase
Colchicine added
Colchicine removed

- Polyploidy can originate by the addition of one or more sets of chromosomes identical to the haploid complement of the same species (**autopolyploidy**) or by the combination of chromosome sets from different species as a consequence of interspecific matings (**allopolyploidy**).

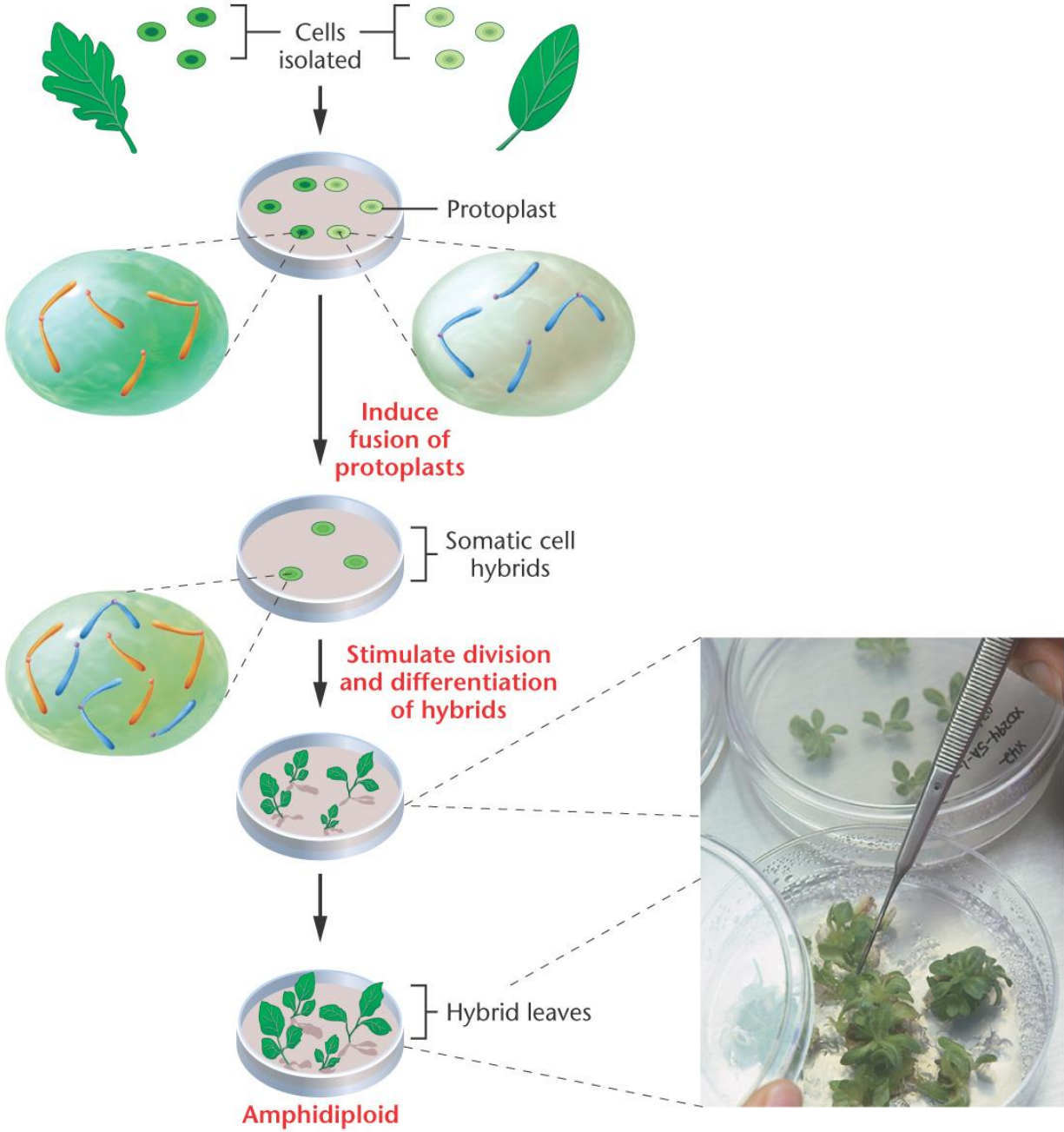

Autopolyploidy
Diploid
Allopolyploidy
Diploid
Diploid
×
Triploid
Tetraploid
Tetraploid

- An allotetraploid arises from **hybridization of two closely related species**. If the sterile hybrid undergoes a natural chromosomal doubling, a fertile **amphidiploid** is produced.




- Gossypium ricostruito sperimentalmente
- Esperimenti falliti: Raphanus X Brassica
- Triticum X Secale
- Il caffè

- Amphidiploid plants can be produced by somatic cell hybridization.



# Polyploidy and evolution

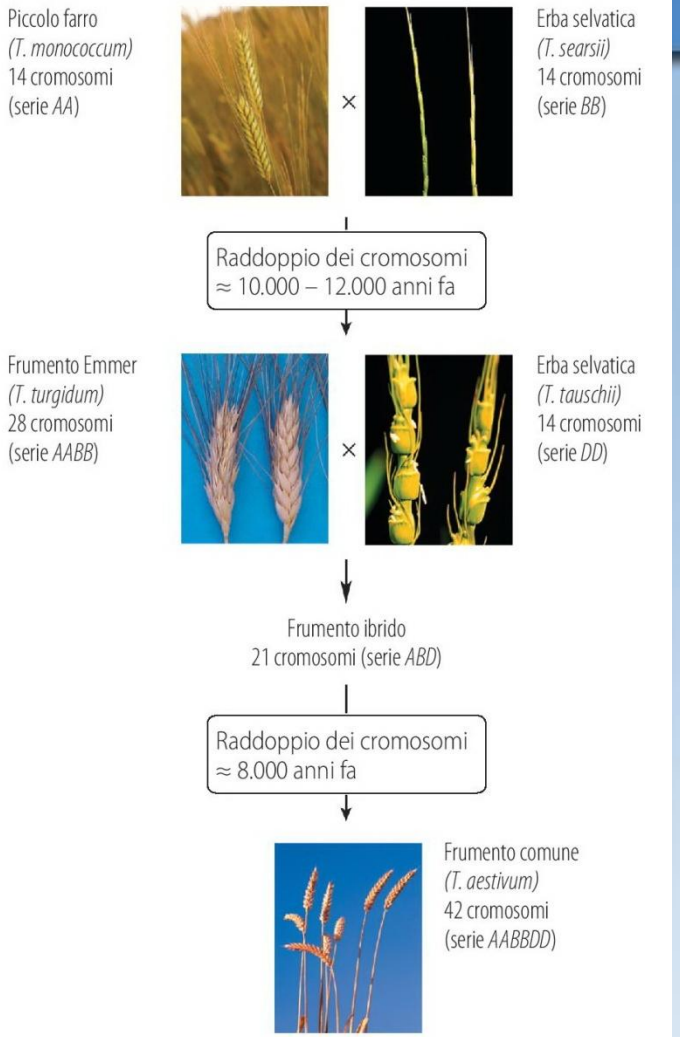
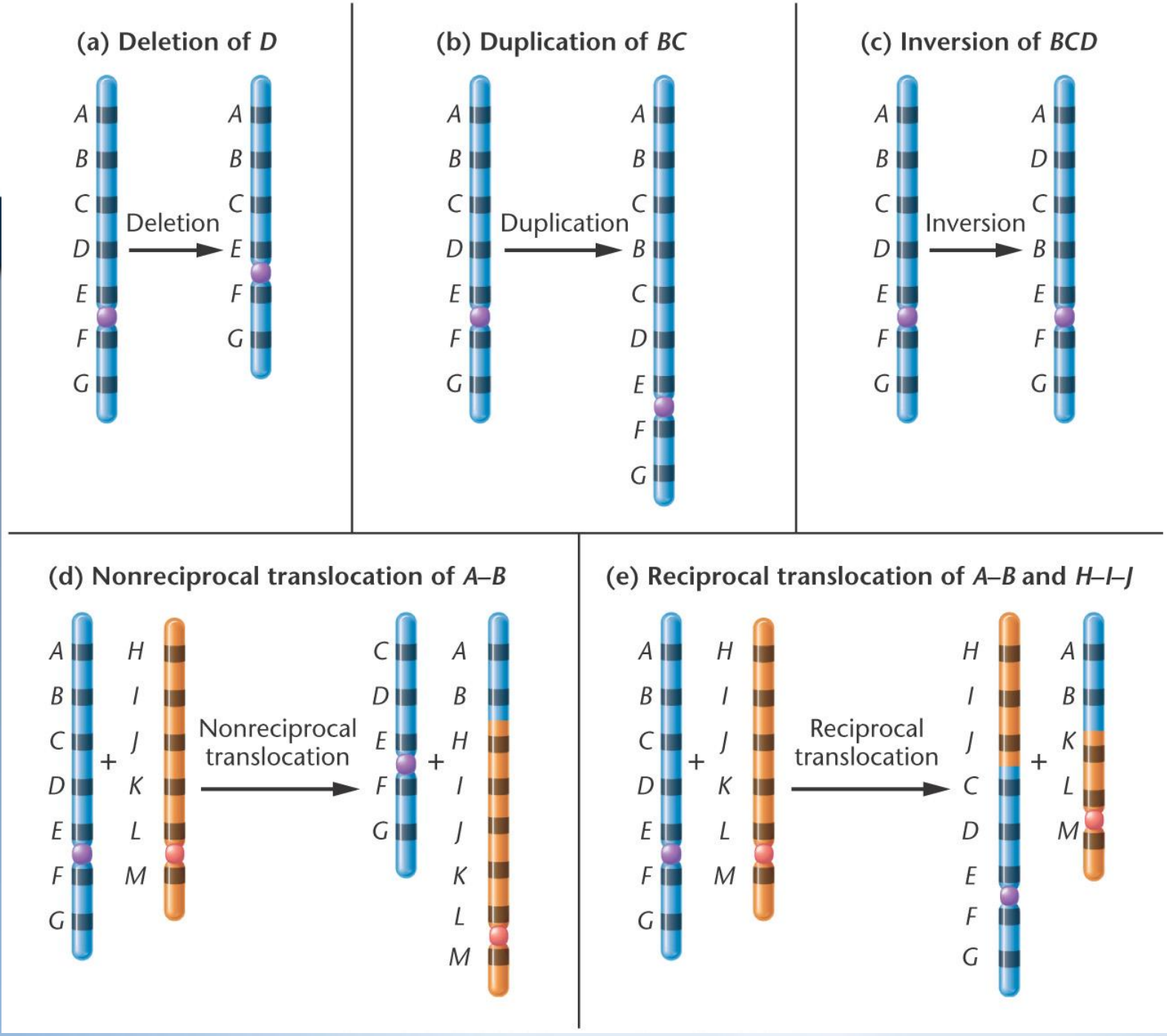



**Figura 13.9 Evoluzione del frumento moderno (*Triticum aestivum*).**

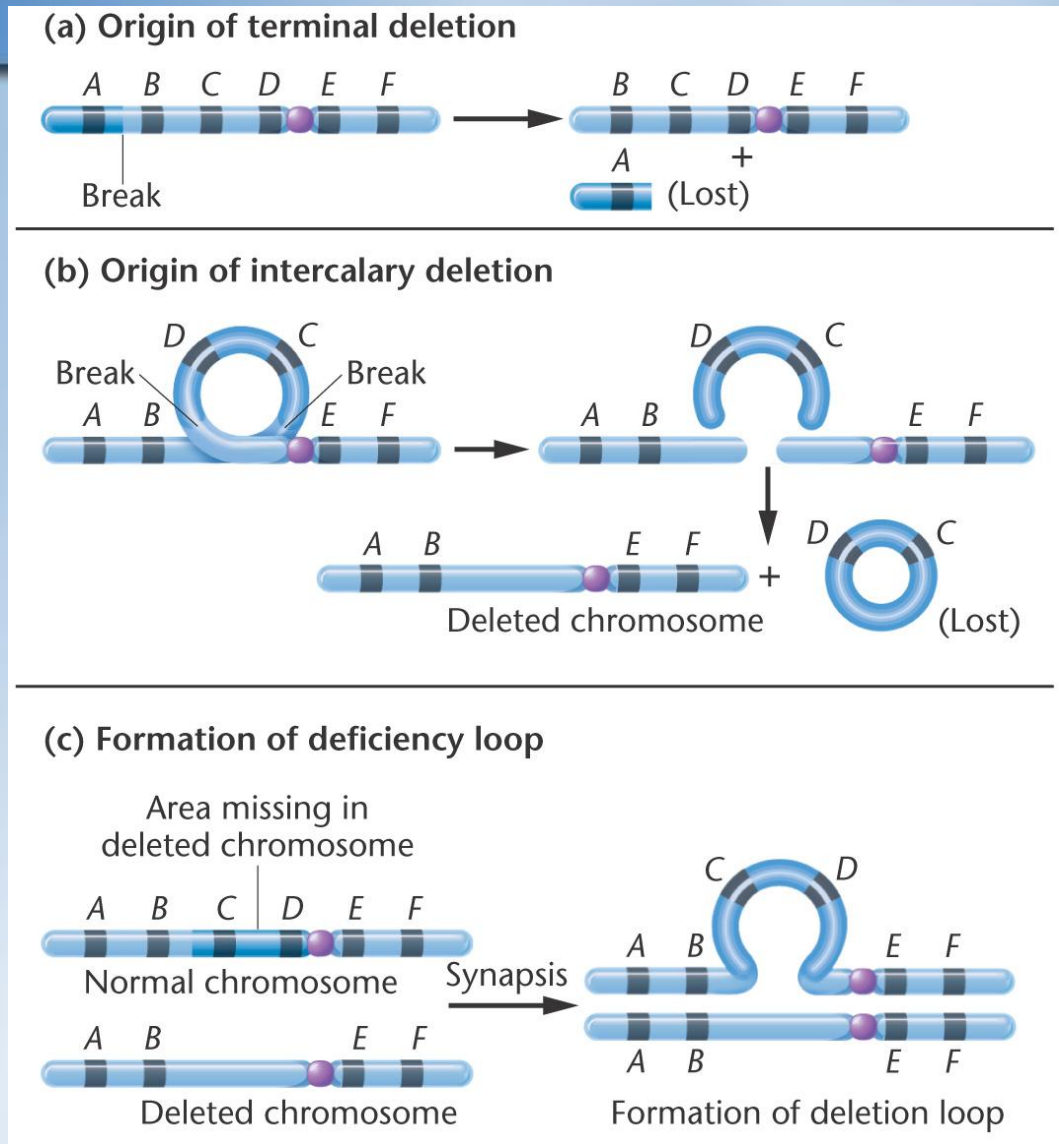
# Variation Occurs in the Structure and Arrangement of Chromosomes

- Rearrangements of chromosome segments include
  - Deletions,
  - duplications,
  - inversions,
  - nonreciprocal translocations, and
  - reciprocal translocations.

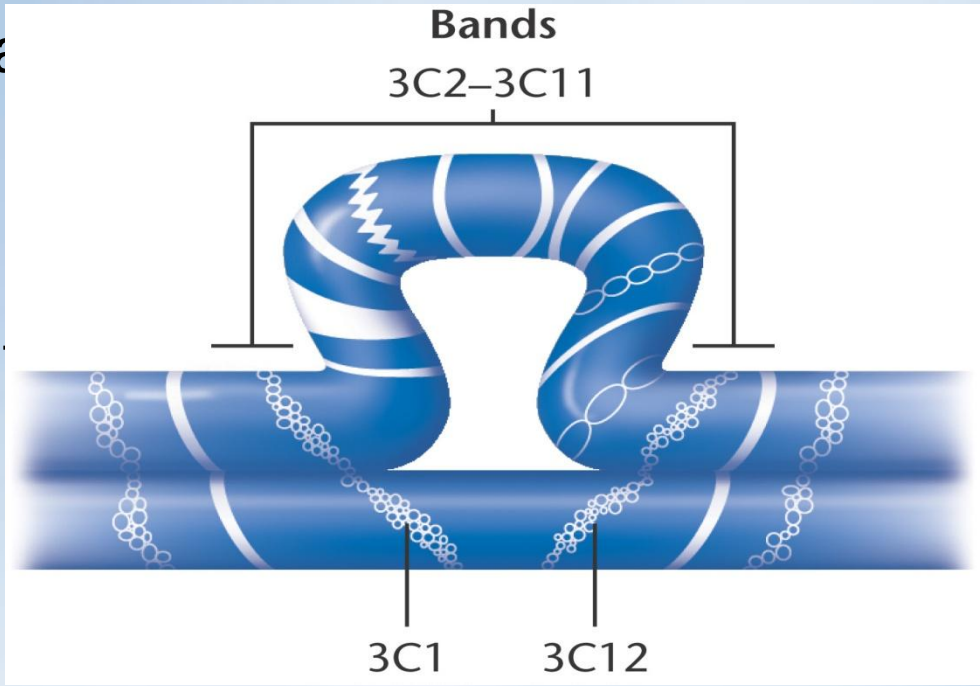

(a) Deletion of D
A B C D E F G
Deletion
A B C E F G
(b) Duplication of BC
A B C D E F G
Duplication
A B C B C D E F G
(c) Inversion of BCD
A B C D E F G
Inversion
A B D C B E F G
(d) Nonreciprocal translocation of A–B
A B C D E F G
+
H I J K L M
Nonreciprocal translocation
C D E F G
+
A B H I J K L M
(e) Reciprocal translocation of A–B and H–I–J
A B C D E F G
+
H I J K L M
Reciprocal translocation
H I J C D E F G
+
A B K L M

# A Deletion Is a Missing Region of a Chromosome

- When a chromosome breaks in one or more places and a portion of it is lost, the missing piece is referred to as a deletion (or a deficiency). The deletion can occur near one end (terminal deletion) or from the interior of the chromosome (intercalary deletion).

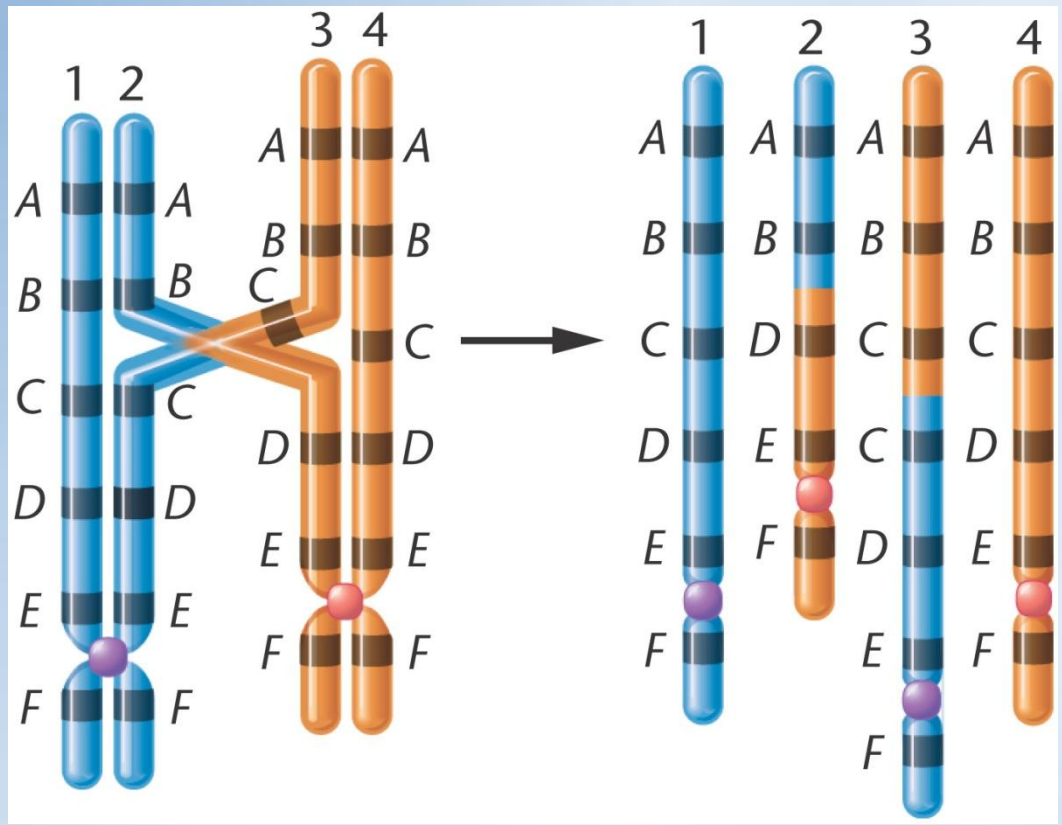


• For synapsis to occur between a chromosome with a large intercalary deletion and a normal complete homolog, the unpaired region of the normal homolog must loop out of the linear structure into a **deletion or compensation loop**.



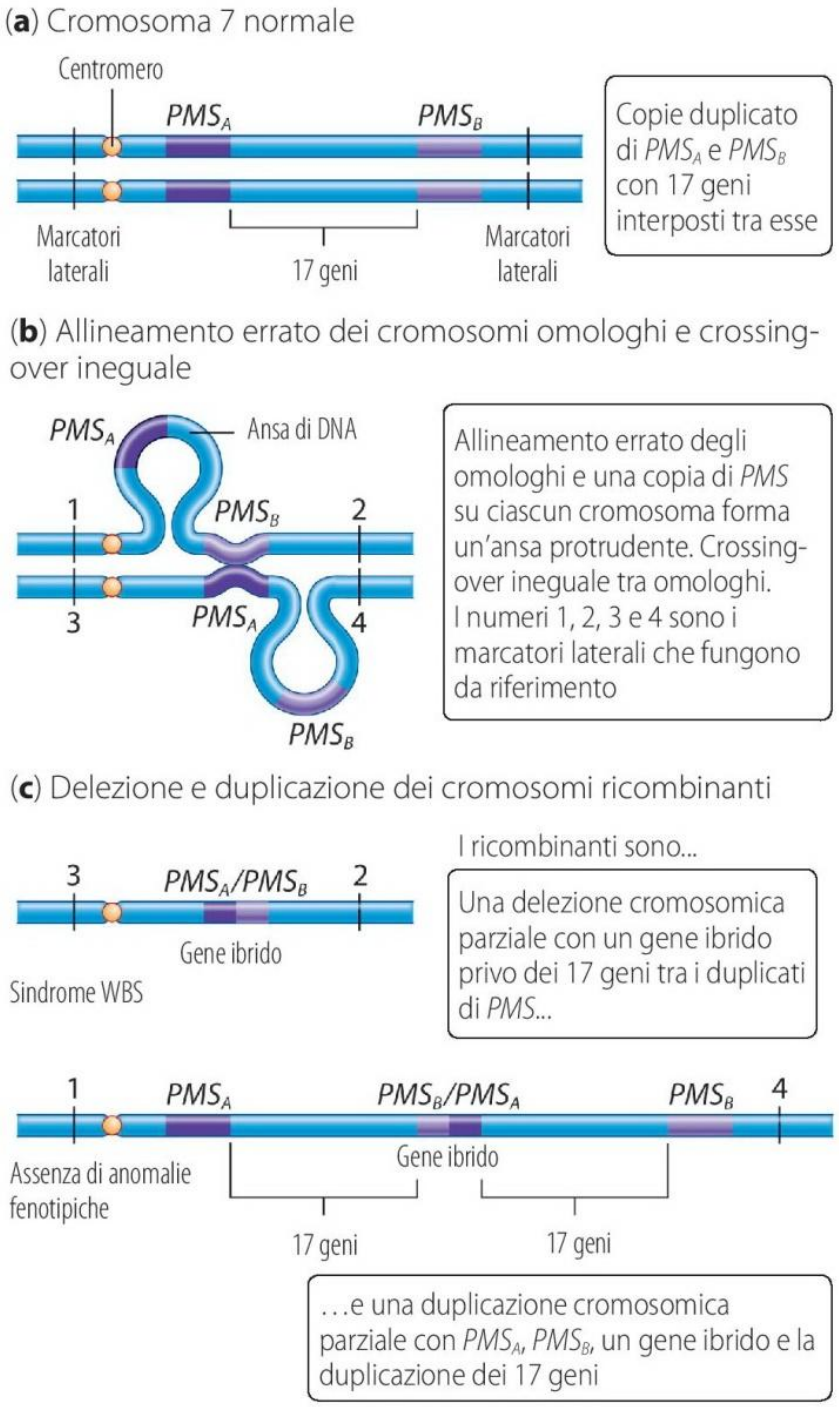
# A Duplication Is a Repeated Segment of the Genetic Material

- Duplications arise as the result of unequal crossing over during meiosis or through a replication error prior to meiosis.

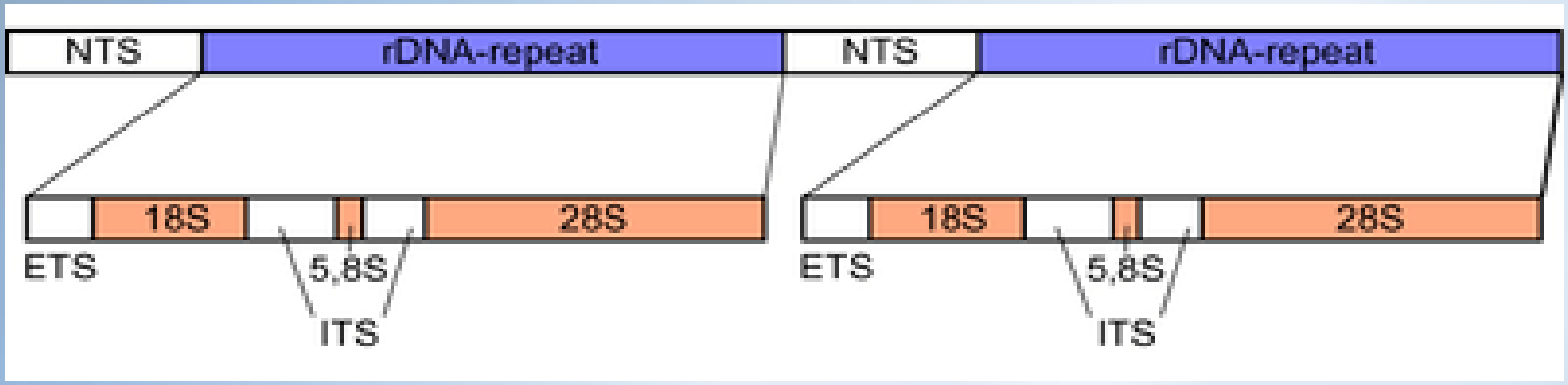


# Patologia di Williams-Beuren

OMIM 194050

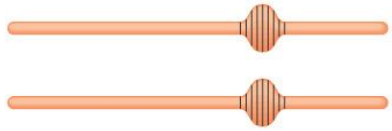
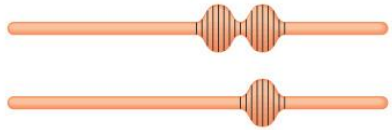
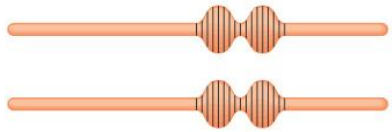
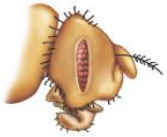
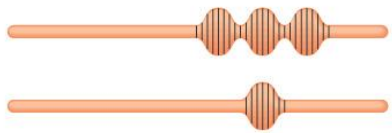


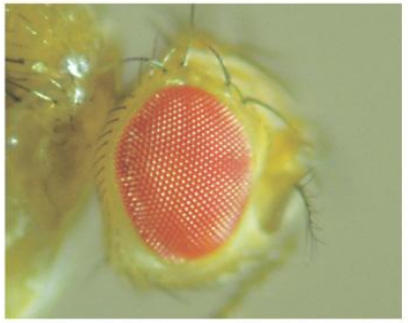
- Organisms have multiple copies of the ribosomal RNA genes (rDNA). This is an example of gene redundancy. **Gene amplification is another mechanism to increase the rDNA.**



# The Bar-eye phenotype in Drosophila results from duplication and is a case of semidominance.

(a) Genotypes and Phenotypes

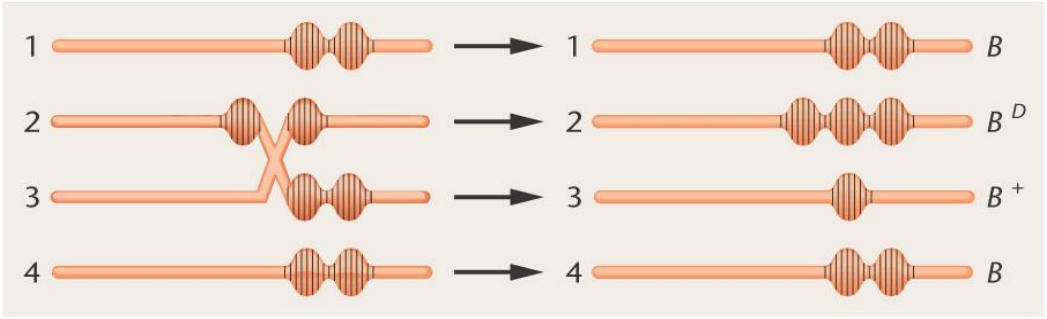
| Genotype | Facet Number | Phenotype | = 16A segments |
|---|---|---|---|
| $B^+/B^+$ | 779 |  |  |
| $B/B^+$ | 358 |  |  |
| $B/B$ | 68 |  |  |
| $B^D/B^+$ | 45 |  |  |



$B^+/B^+$

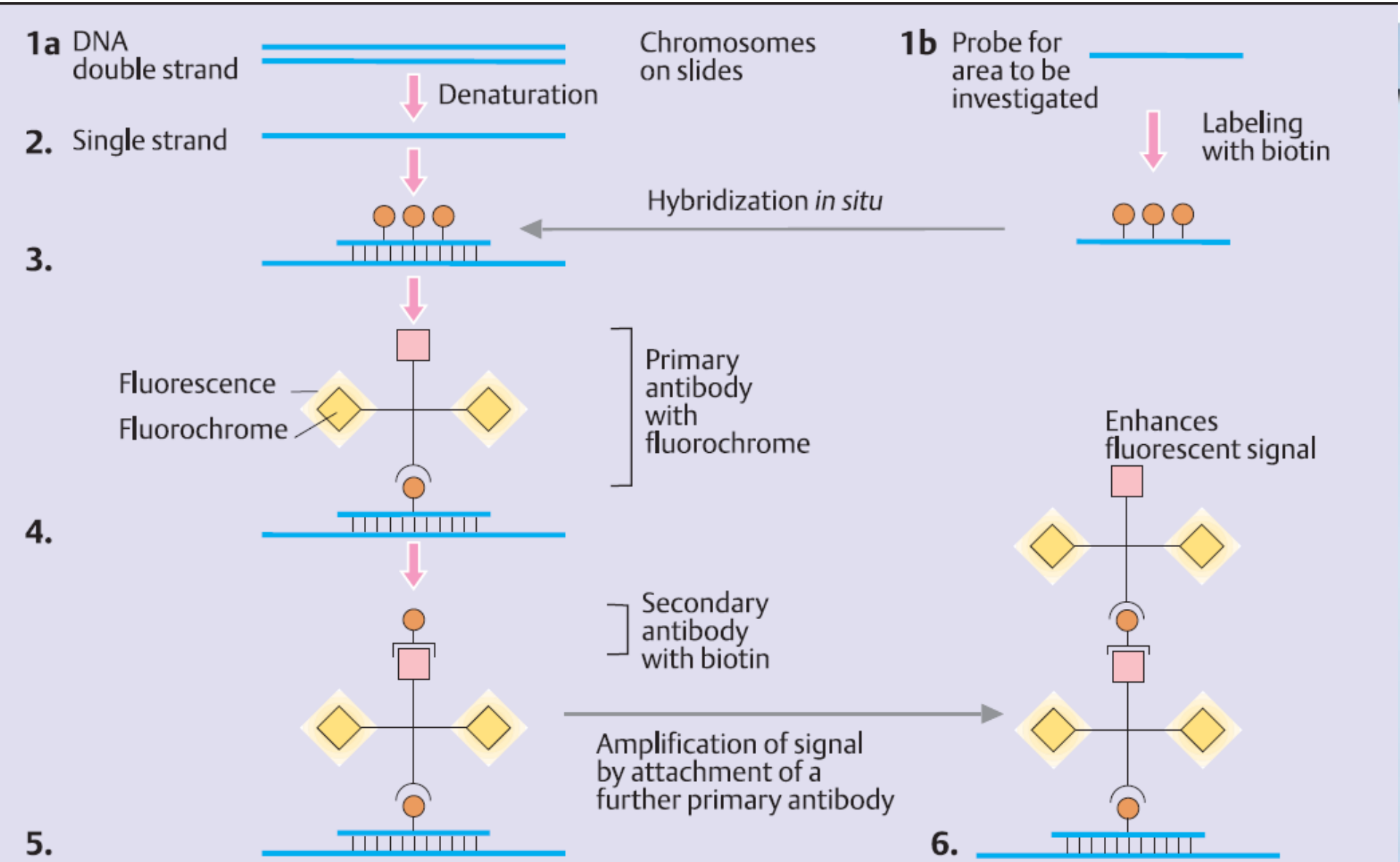
$B/B^+$

(b) Origin of $B^D$ allele as a result of unequal crossing over

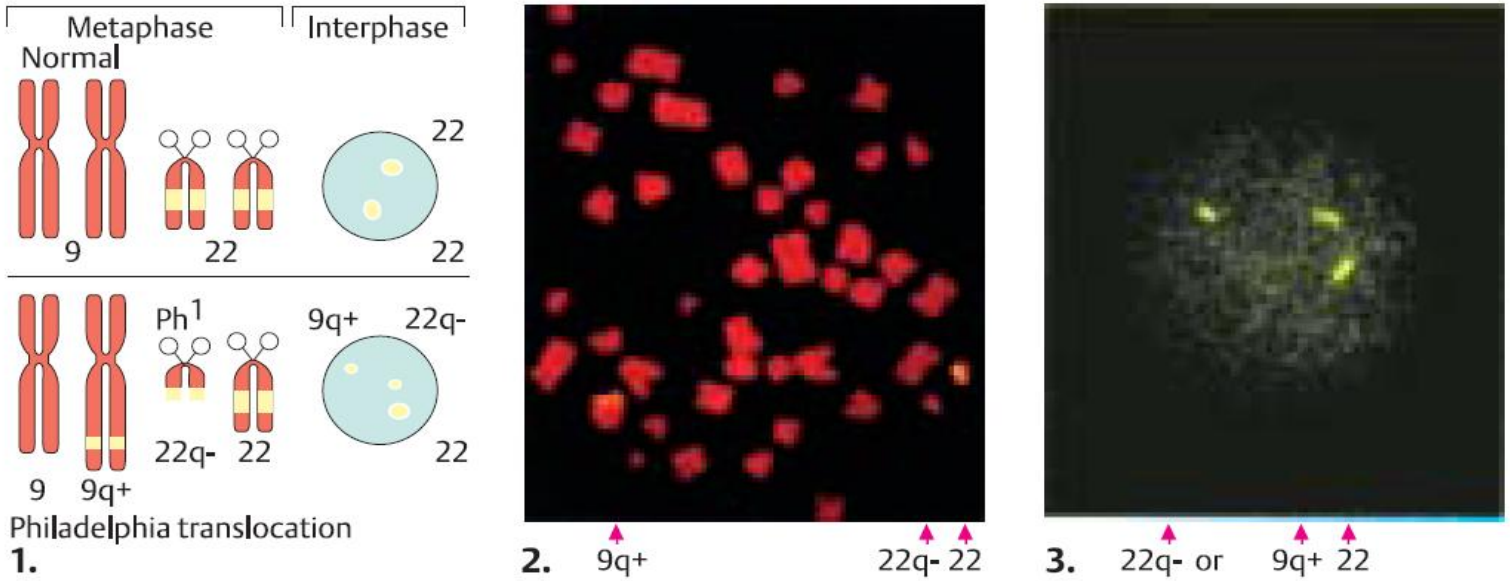



$B/B$

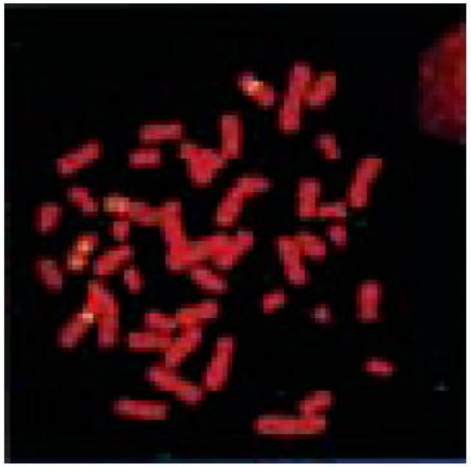
# FISH: In Situ Hybridization in Metaphase and Interphase



# In Situ Hybridization in Metaphase and Interphase




B. Demonstration of the Philadelphia translocation in chronic myelogenous leukemia



C. Translocation 4;8

D. Telomere sequences in metaphase chromosomes

# FISH

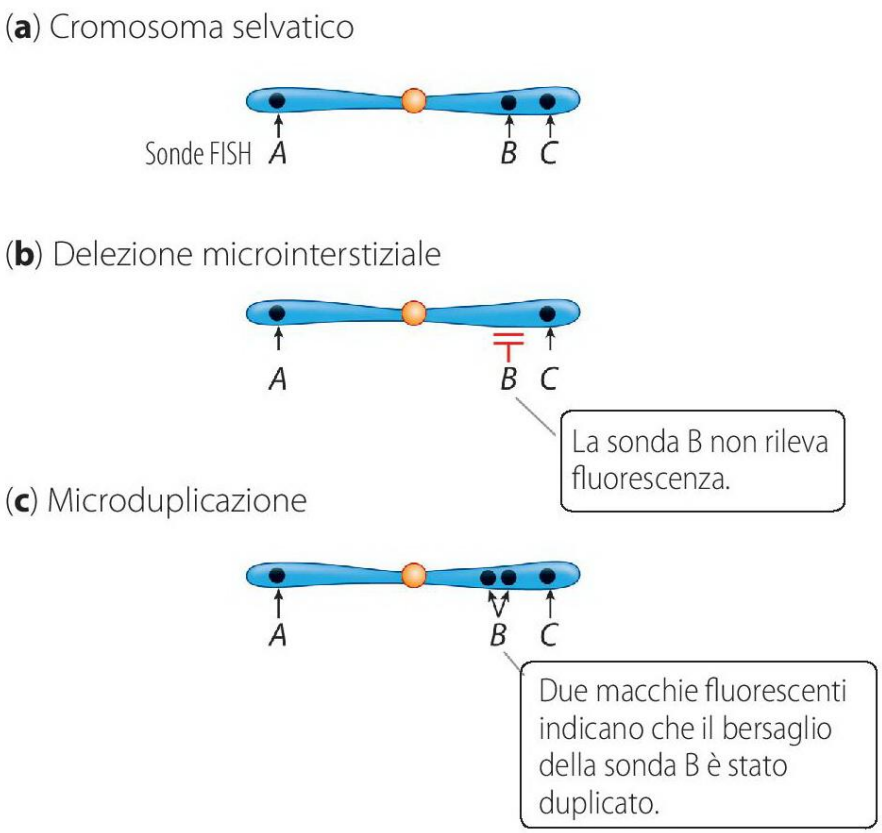


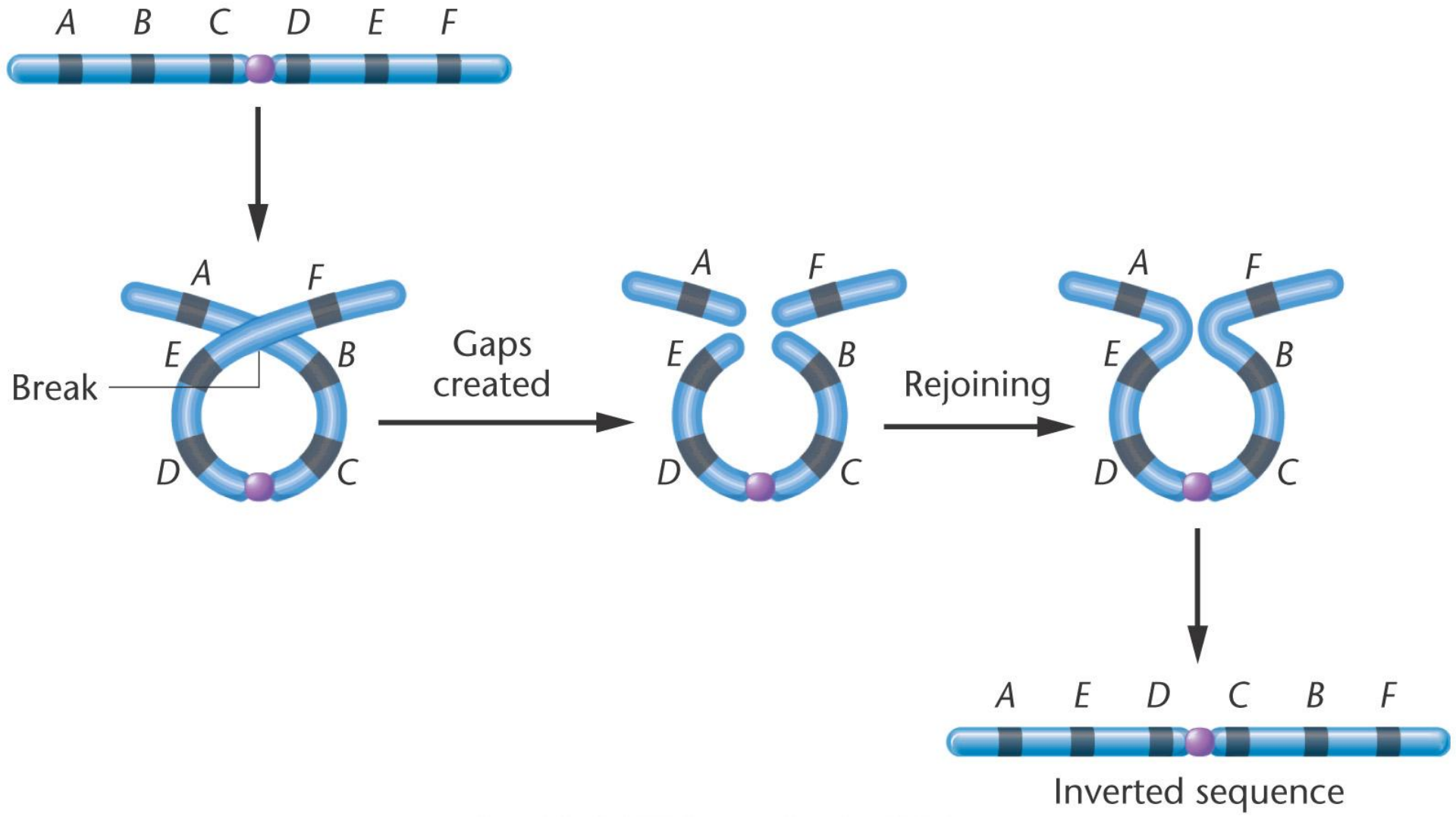

**Figura 13.13 Identificazione di microdelezioni e microduplicazioni cromosomiche mediante FISH.** (**a**) Tre sonde FISH identificano i geni A, B e C. (**b**) La microdelezione di un segmento cromosomico contenente B impedisce l'ibridazione della sonda. (**c**) La microduplicazione causa l'ibridazione della sonda B ai geni duplicati.

Minimum size 100-200kbp to be analysed by chromosomal bands

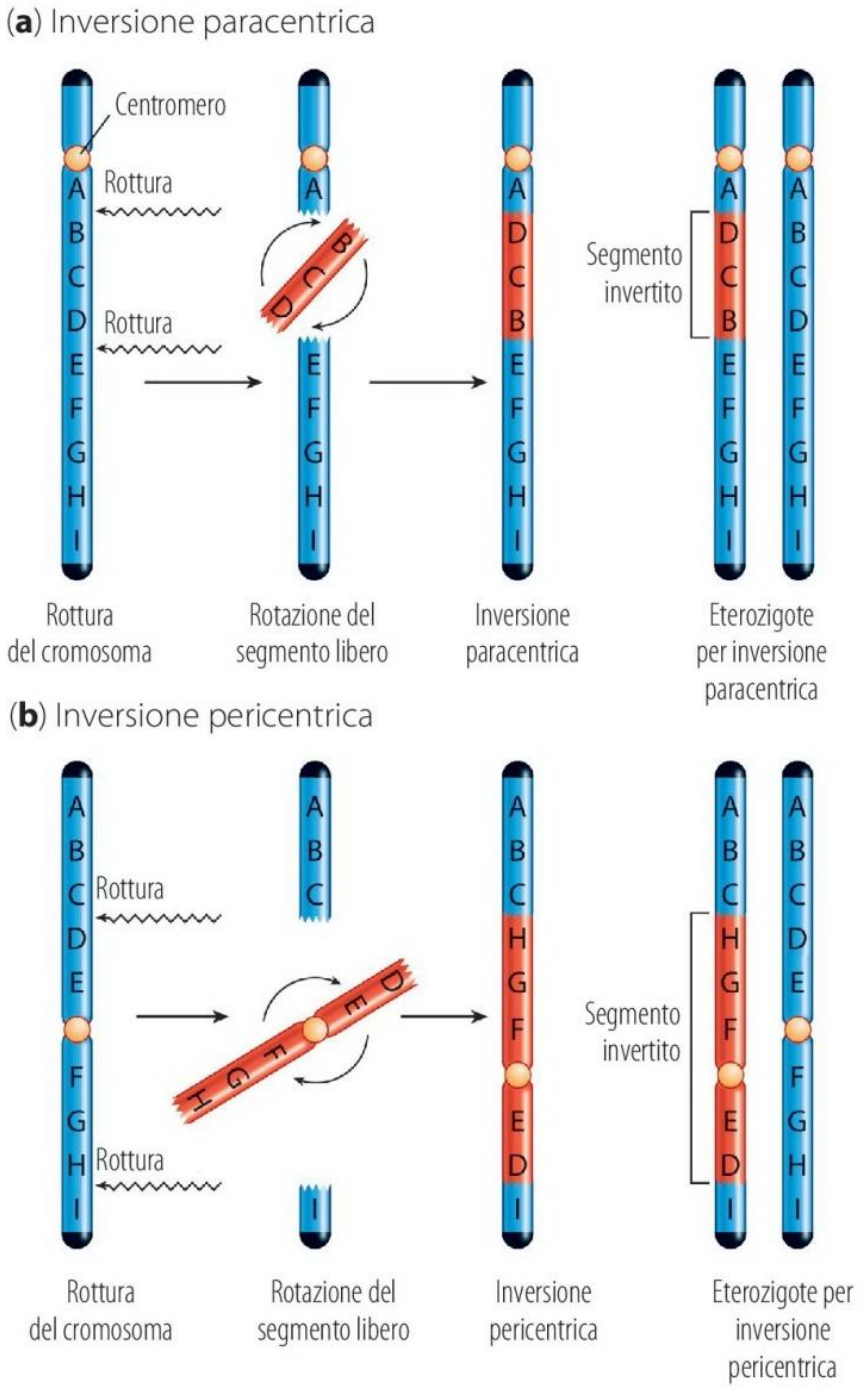
# Inversions Rearrange the Linear Gene Sequence

• An inversion involves a rearrangement of the linear gene sequence rather than the loss of genetic information. In an inversion, a segment of a chromosome is turned around 180  within a chromosome.

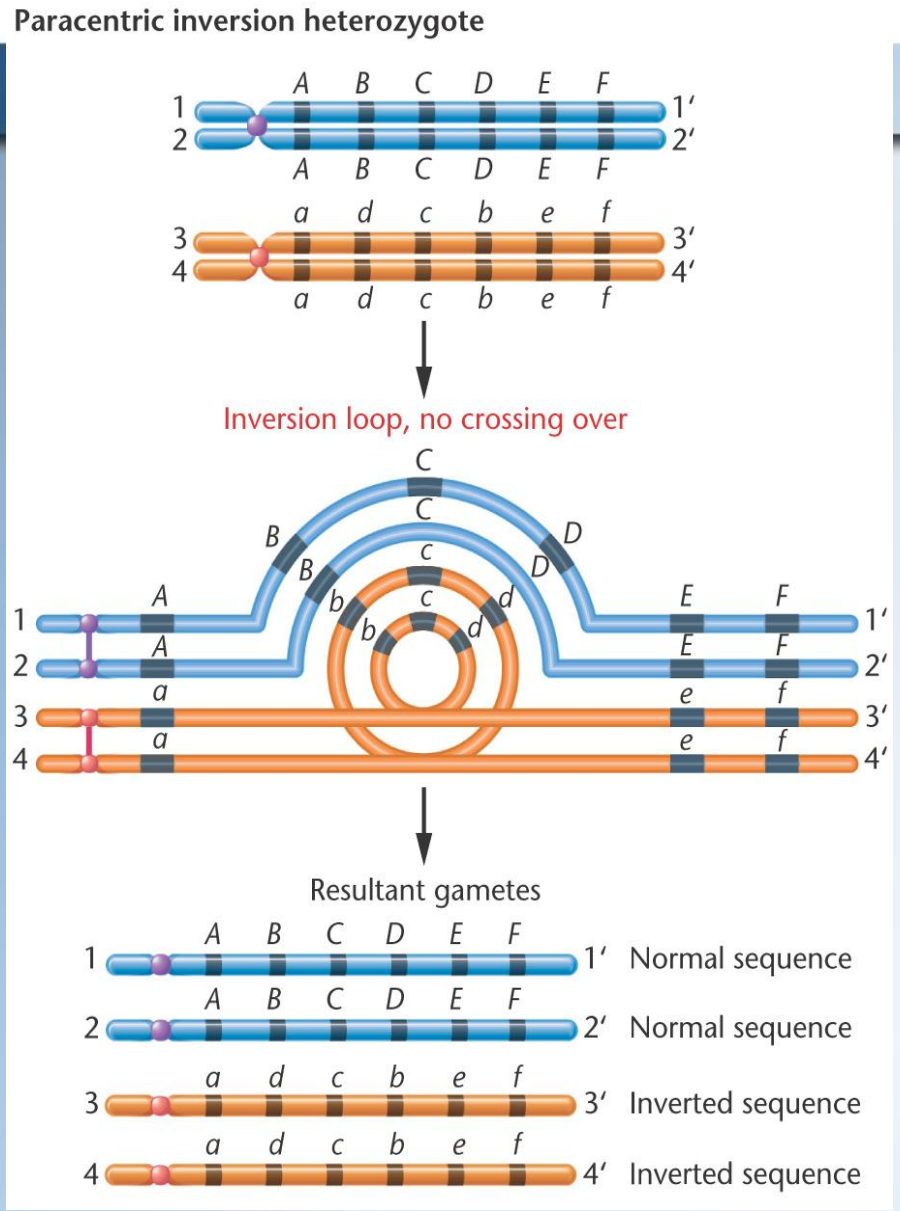
•An inversion requires two breaks in the chromosome and subsequent reinsertion of the inverted segment. **An inversion may arise from chromosomal looping**


A B C D E F
A F
E B
D C
Break
Gaps created
A F
E B
D C
Rejoining
A F
E B
D C
A E D C B F
Inverted sequence

- A **paracentric** inversion *does not* change the relative lengths of the two arms of a chromosome, whereas a **pericentric** inversion *does*.



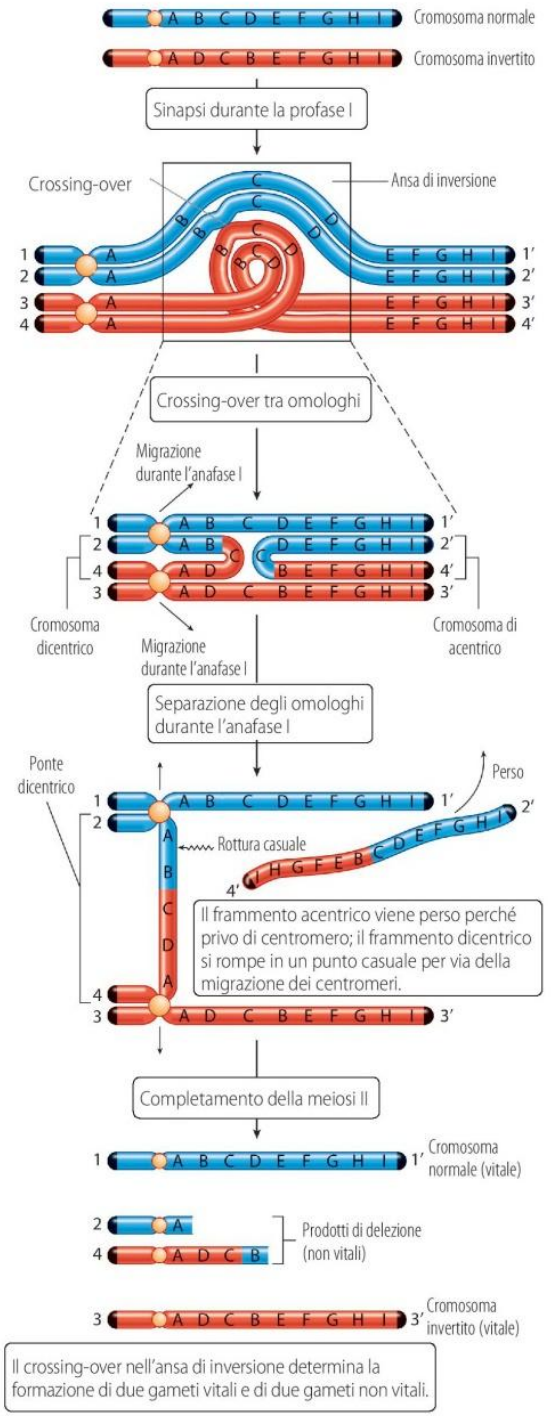
# Synapsis of inverted chromosomes requires an inversion loop



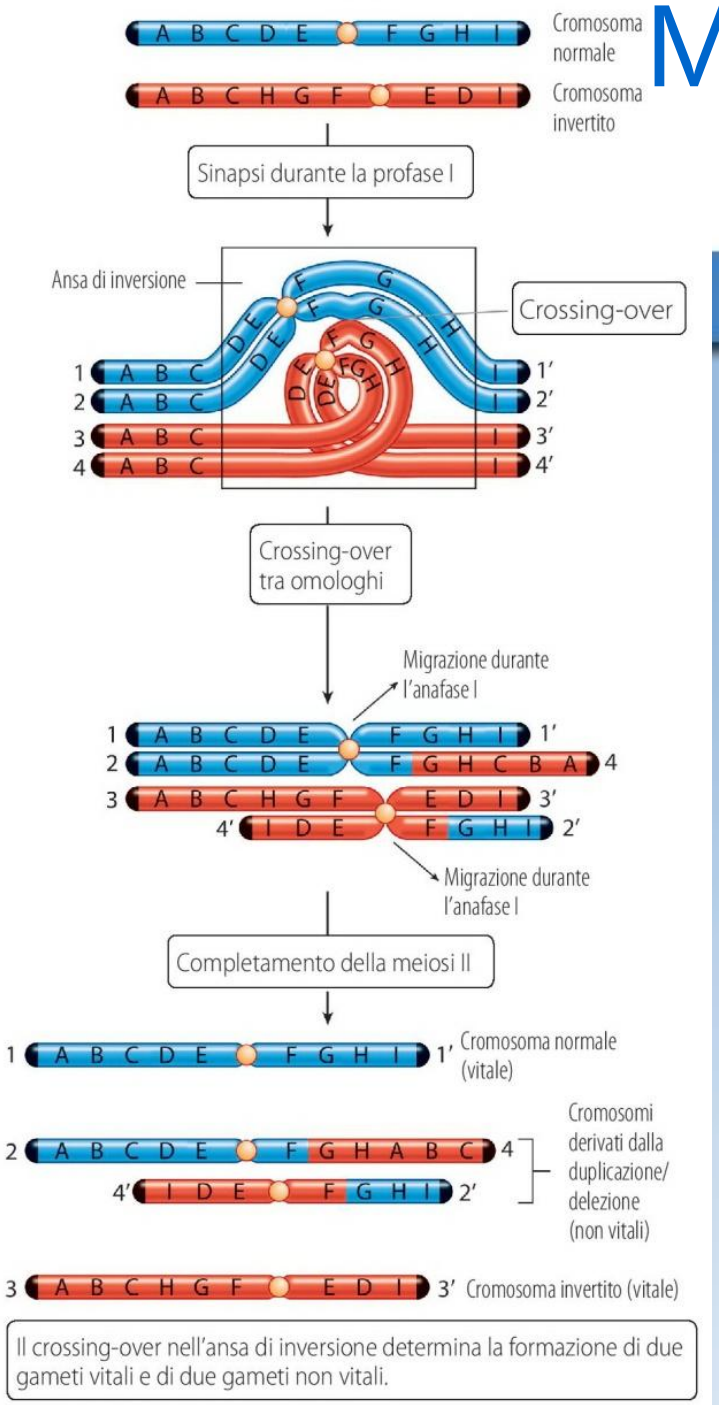
# Mitosis of parancentric chromosomes

This figure shows the effects of a single crossover within an inversion loop for **paracentric** inversion heterozygotes.

As shown, one recombinant chromatid is dicentric (two centromeres), and one is acentric (lacking a centromere).

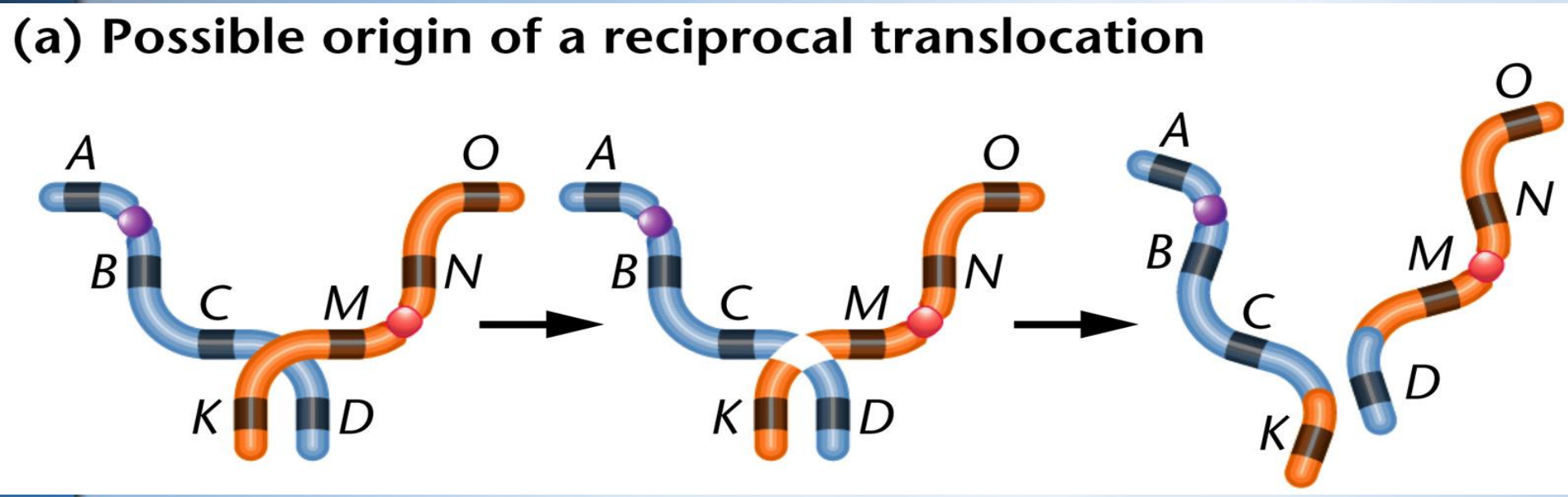


# Mitosis of perancentric chromosomes

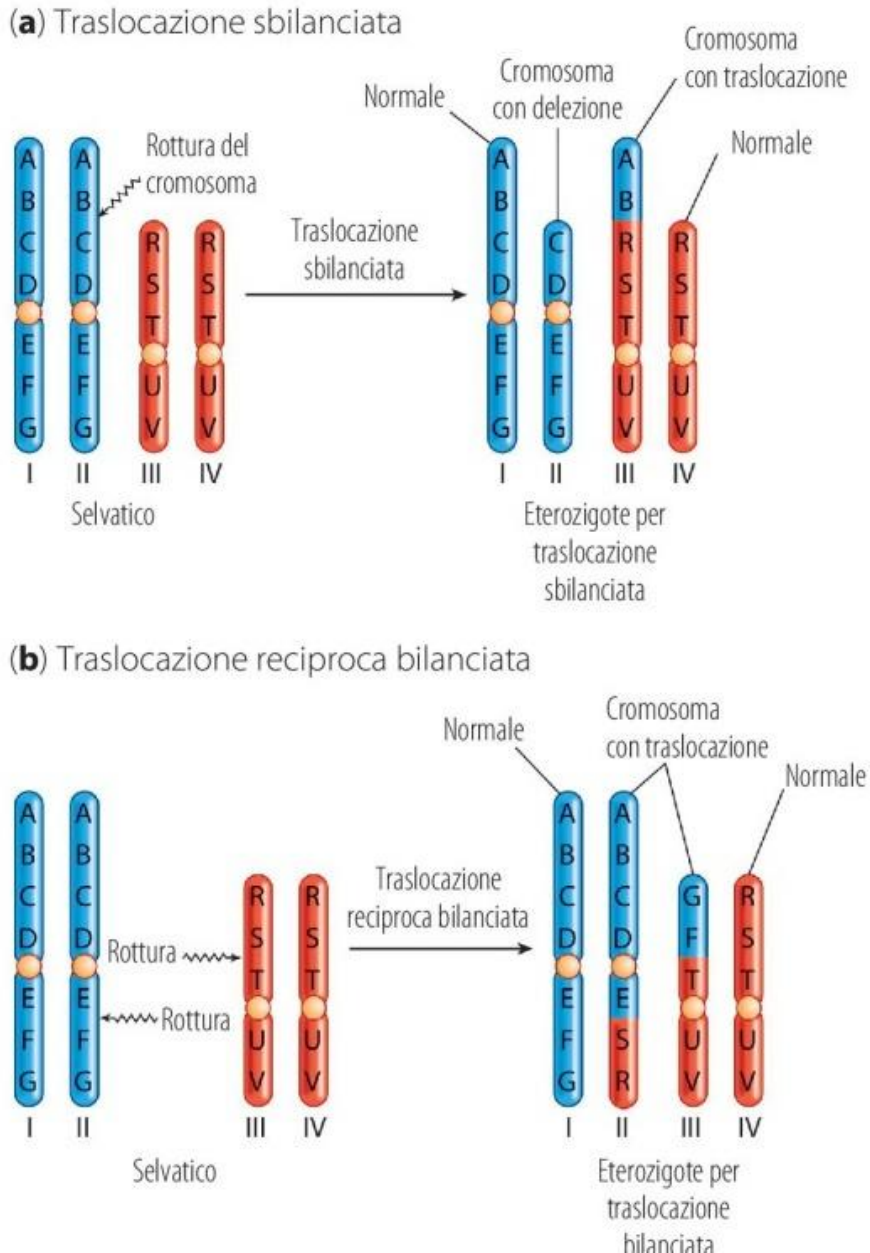


# Translocations Alter the Location of Chromosomal Segments in the Genome

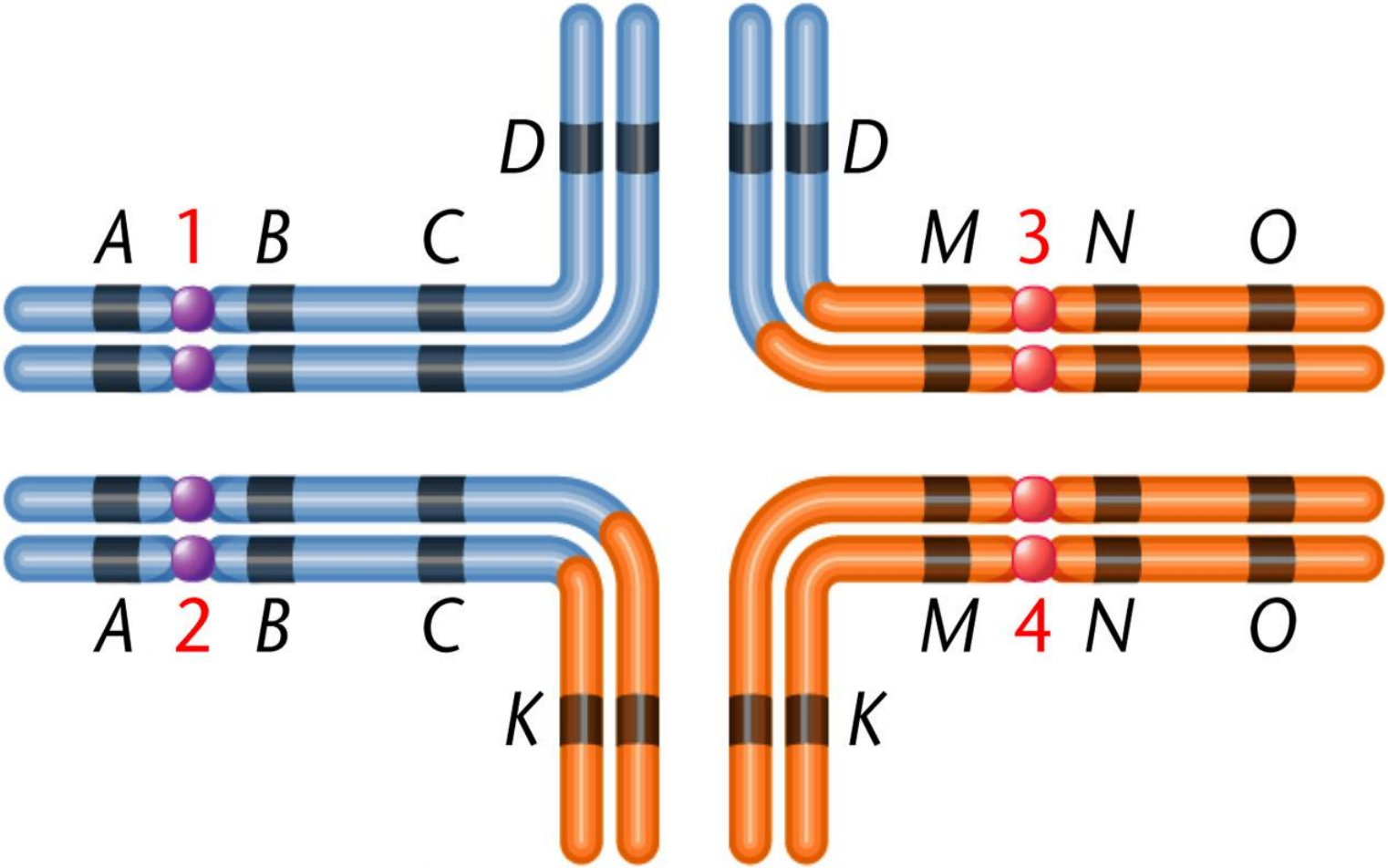
- **Translocation** is a movement of a chromosomal segment to a new location in the genome.
- A **reciprocal translocation** involves the exchange of segments between two nonhomologous chromosomes and has an unusual synapsis configuration during meiosis.

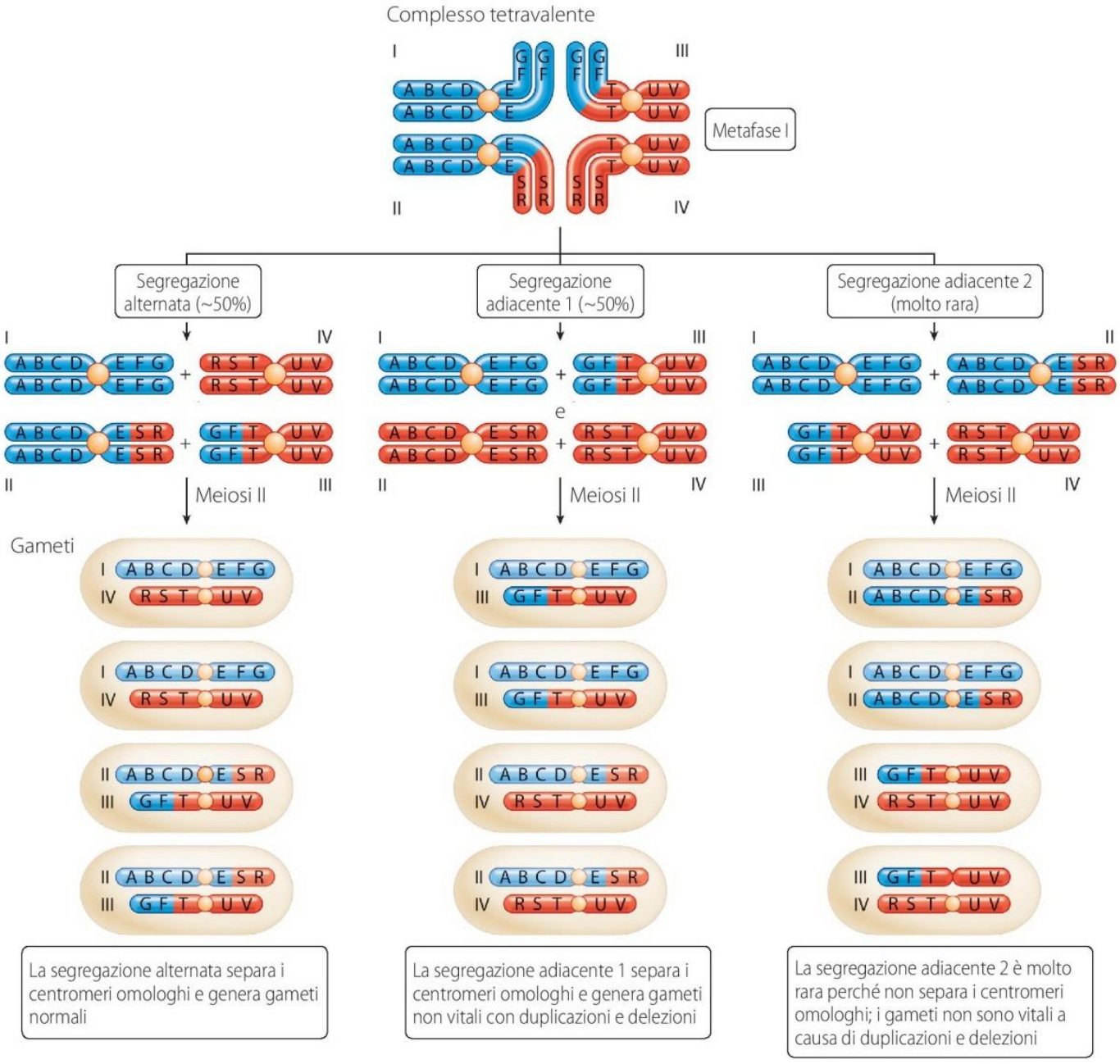


# Translocations



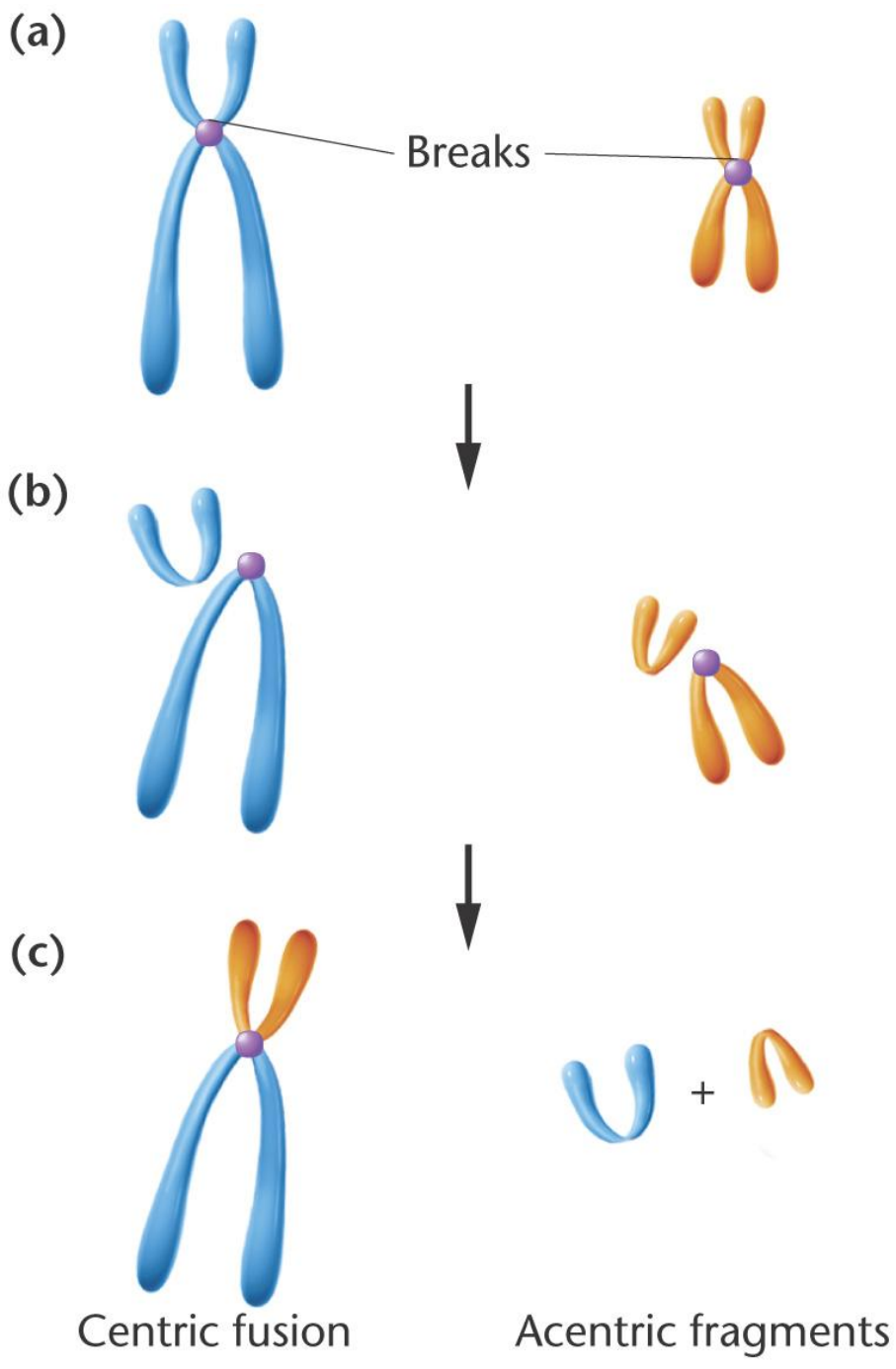
## (b) Synapsis of translocation heterozygote



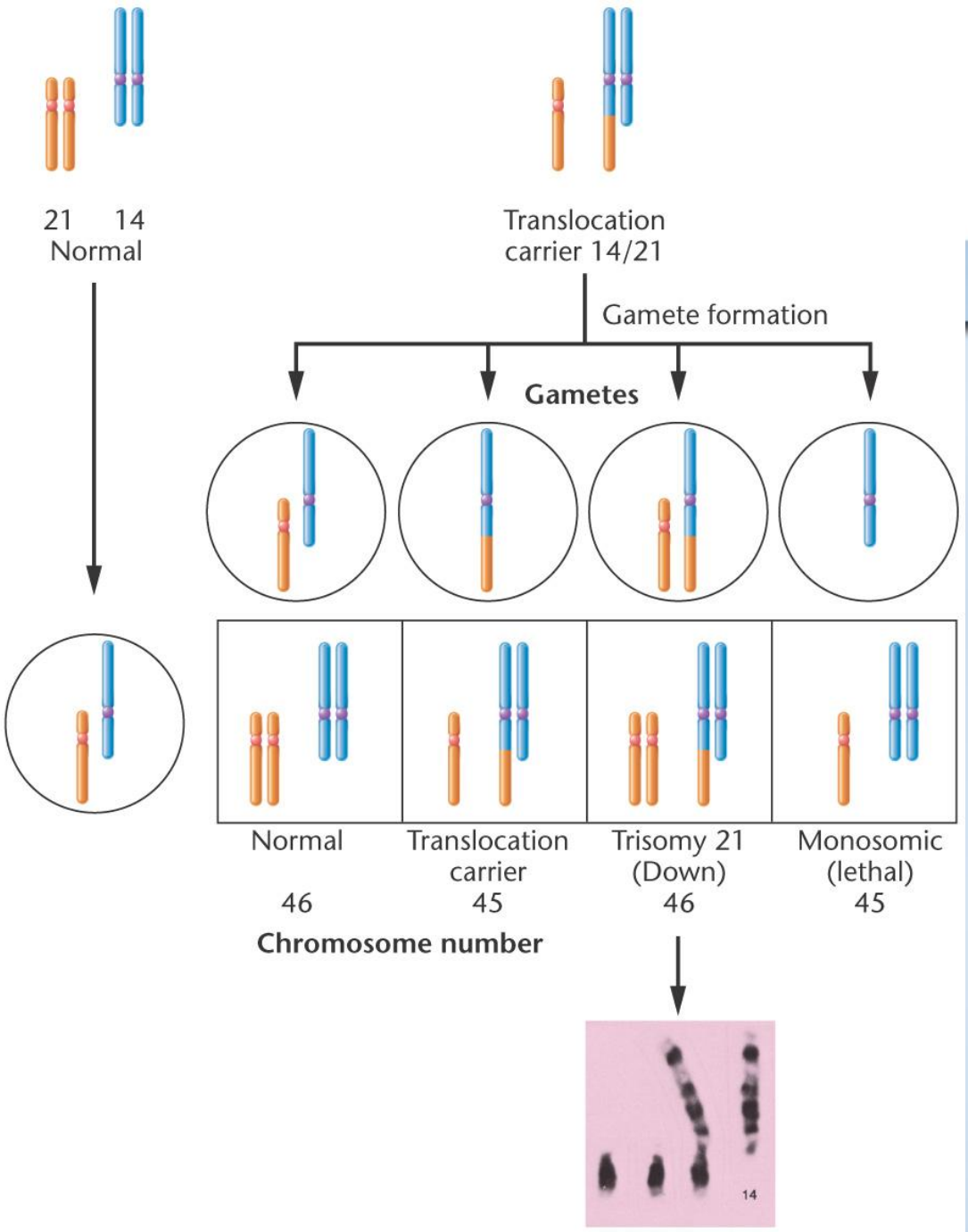

Complesso tetravalente
Metafase I
Segregazione alternata (~50%)
Segregazione adiacente 1 (~50%)
Segregazione adiacente 2 (molto rara)
e
Meiosi II
Meiosi II
Meiosi II
Gameti
La segregazione alternata separa i centromeri omologhi e genera gameti normali
La segregazione adiacente 1 separa i centromeri omologhi e genera gameti non vitali con duplicazioni e delezioni
La segregazione adiacente 2 è molto rara perché non separa i centromeri omologhi; i gameti non sono vitali a causa di duplicazioni e delezioni
Conclusione: solo la segregazione alternata produce gameti e progenie vitali. Questo tipo di segregazione avviene in circa metà delle meiosi ed è responsabile della semisterilità degli eterozigoti per traslocazione

# Translocations in human

- A Robertsonian translocation or centric fusion involves breaks at the extreme ends of the short arms of two nonhomologous acrocentric chromosomes.



- Familial Down syndrome is an example of this.



# Fragile Sites in Humans Are Susceptible to Chromosome Breakage

- Fragile sites are more susceptible to chromosome breakage when cells are cultured in the absence of certain chemicals such as folic acid.

- Fragile X syndrome (Martin–Bell syndrome) is the most common form of inherited mental retardation, affecting about 1 in 4000 males and 1 in 8000 females, and is a dominant trait.

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