Basic Genetics (SQBS2753)

Variation in Chromosome Structure and Number

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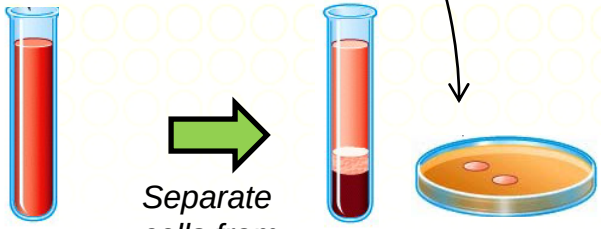
Chapter Outline

- Cytological Techniques
- Polyploidy
- Aneuploidy
- Rearrangements of Chromosome Structure

Cytological Techniques

Geneticists use stains to identify specific chromosomes and to analyze their structures

Cytological Analysis

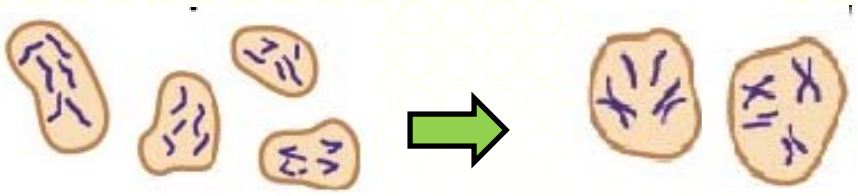


Take blood sample

Separate cells from serum by centrifugation

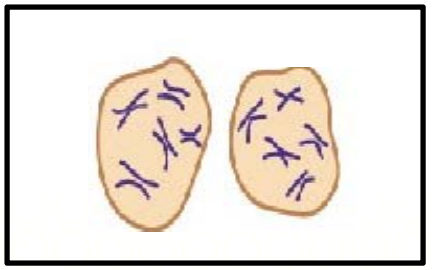
Remove white cells and culture in vitro

Stimulate cells to divide

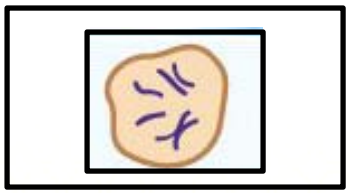


Disable mitotic spindle

Add hypotonic solution to swell cells

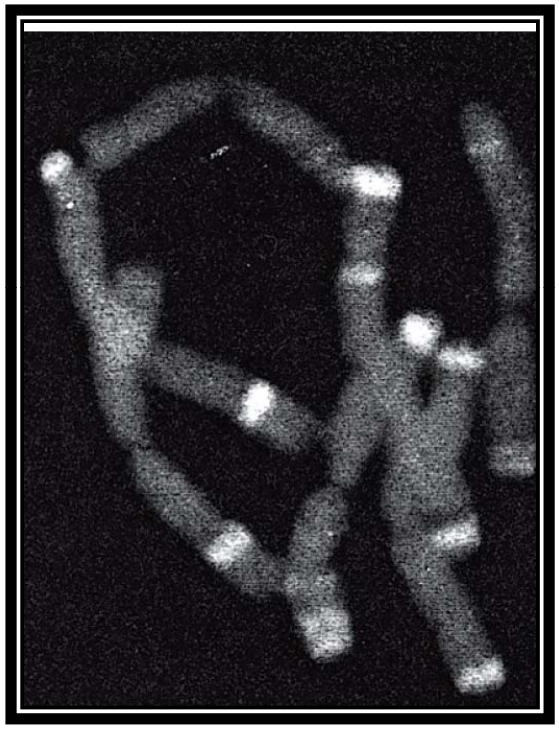


Squash cells on slide, fix, and stain



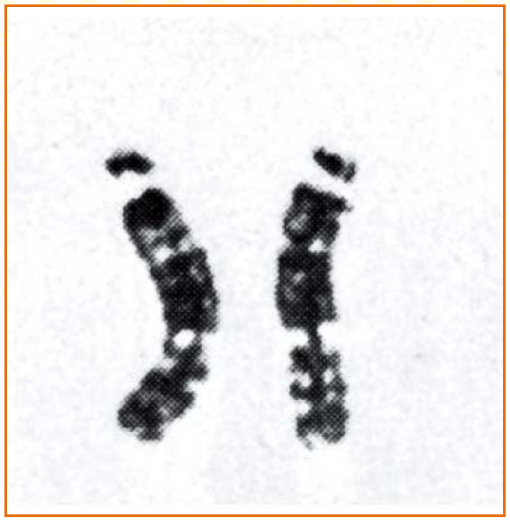
Examine chromosomes

Quinacrine Banding



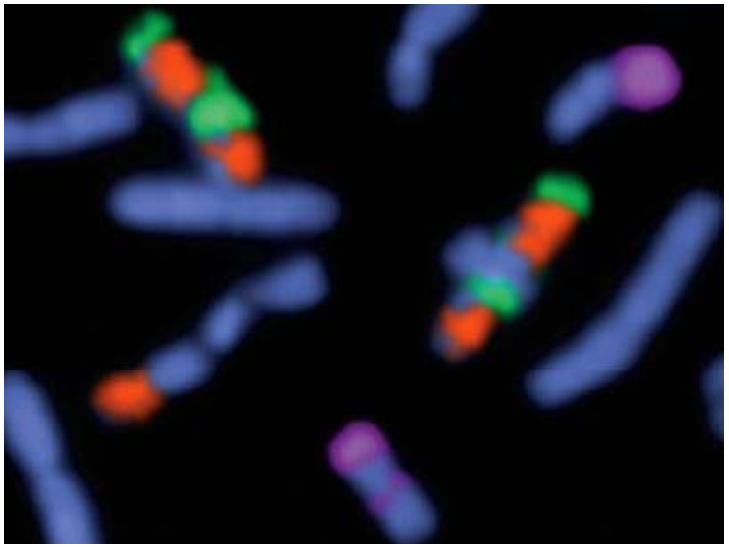
When it is exposed to UV → fluorescent bands

Giemsa Banding



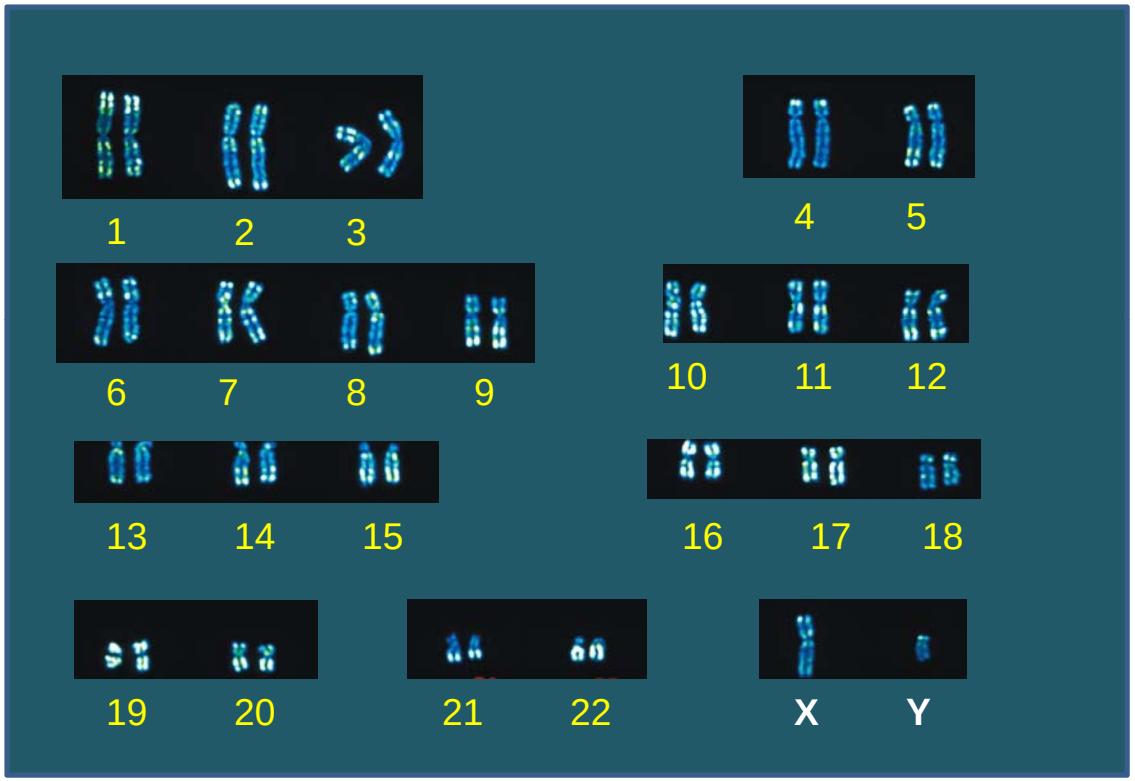
By Gustav Giemsa

Chromosome Painting



Probes (Human DNA) –fluorescent dyes to gibbon's chromosomes

The Human Karyotype



A chart of chromosome cutouts (male)

Cytological Variation: An Overview

- Changes in ploidy
- **Euploid** organisms have complete sets of chromosomes (diploid = 2*n*; triploid = 3*n*; tetraploid = 4*n*)
- **Aneuploid** organisms have particular chromosomes or parts of chromosomes under- or over-represented.
- Aneuploidy implies a genetic imbalance; polyploidy does not.
- **Rearrangements** are changes in chromosome structure.

Key Points

- Cytogenetic analysis usually focuses on chromosomes in dividing cells.
- Dyes such as quinacrine and Giemsa create banding patterns that are useful in identifying individual chromosomes within a cell.
- A karyotype shows the duplicated chromosomes of a cell arranged for cytogenetic analysis.

Allopolyploids vs. Autopolyploids

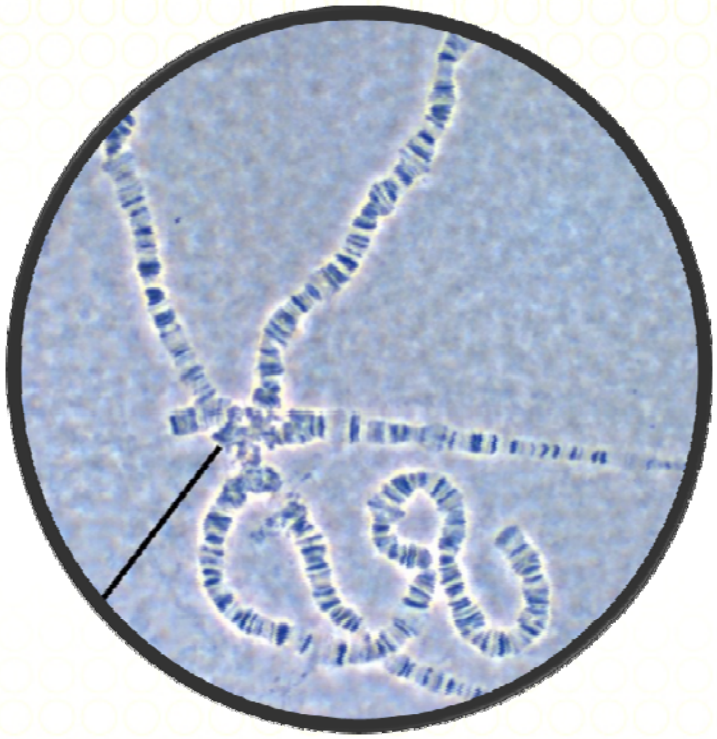
- **Allopolyploids** are created by hybridization between different species.
- **Autopolyploids** are created by chromosome duplication within a species.
- Chromosome doubling is a key event in the formation of polyploids.

Tissue-specific Polyploidy and Polyteny

- **Endomitosis** involves chromosome replication and separation of sister chromatids without cell division. This produces polyploid tissues.

- If sister chromosomes do not separate, the resulting chromosomes are **polytene**.

The Polytene Chromosomes of *Drosophila*



- *Drosophila* polytene chromosomes are produced by 9 rounds of replication.
- Homologous polytene chromosomes pair.
- All of the centromeres congeal into a chromocenter.

Key Points

- Polyploids contain **extra** sets of chromosomes.
- Many polyploids are **sterile** because their multiple sets of chromosomes segregate irregularly in meiosis.
- Polyploids produced by chromosome doubling in interspecific hybrids may be **fertile** if their constituent genomes segregate independently.
- In some **somatic tissues**—for example, the salivary glands of *Drosophila* larvae—successive rounds of chromosome replication occur without intervening cell divisions and produce large polytene chromosomes that are ideal for cytogenetic analysis.

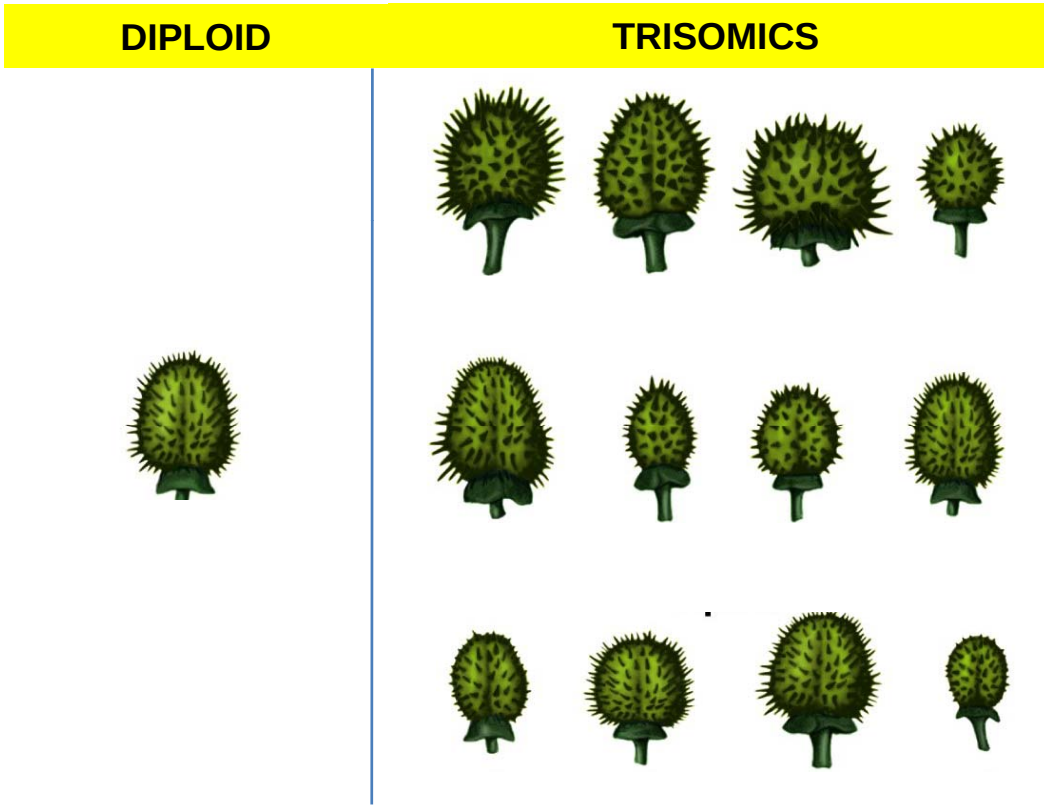
Aneuploidy

The under- or overrepresentation of a chromosome or a chromosome segment can affect a phenotype.

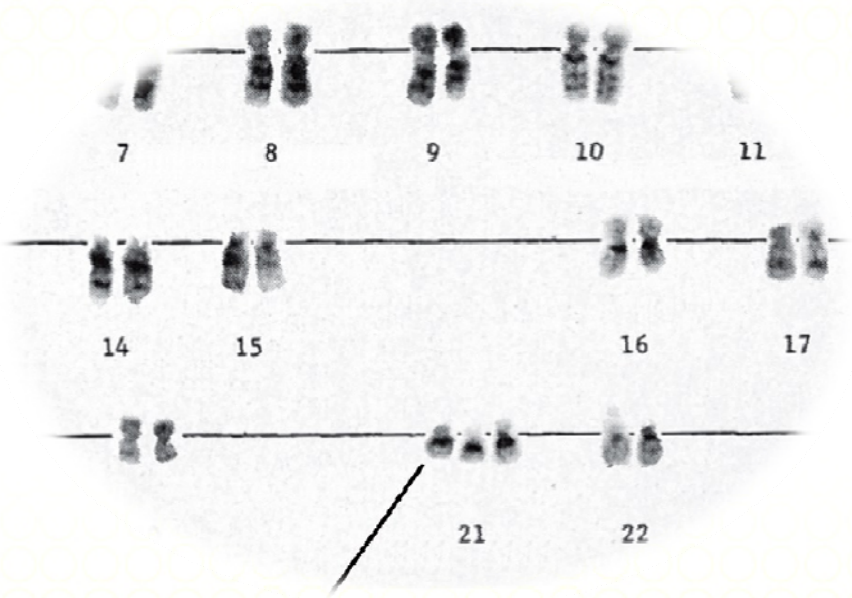
Vocabulary

- **Aneuploidy**—a numerical change in part of the genome
- **Trisomy**—triplication of one chromosome
- **Hypoploid**—an organism in which a chromosome or chromosome segment is underrepresented
- **Hyperploid**—an organism in which a chromosome or chromosome segment is overrepresented
- **Monosomy**—the absence of one chromosome in an otherwise diploid individual

Datura stramonium Trisomics



Down Syndrome: A Human Trisomy



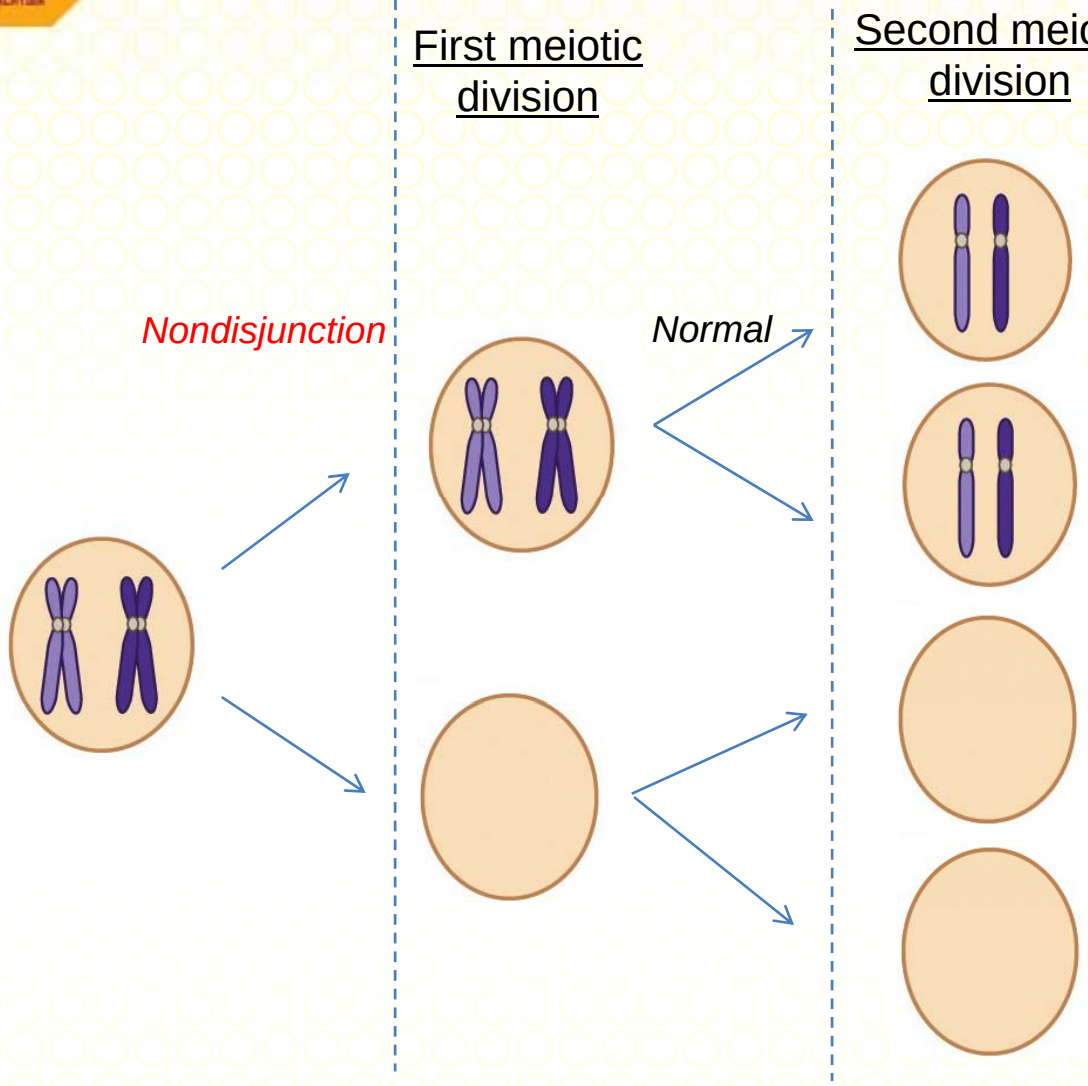
Trisomy

NONDISJUNCTION OF X CHROMOSOME

- **Nondisjunction** occurs when chromosomes fail to separate properly to opposite poles during cell division resulting in cells with incorrect number of chromosomes.

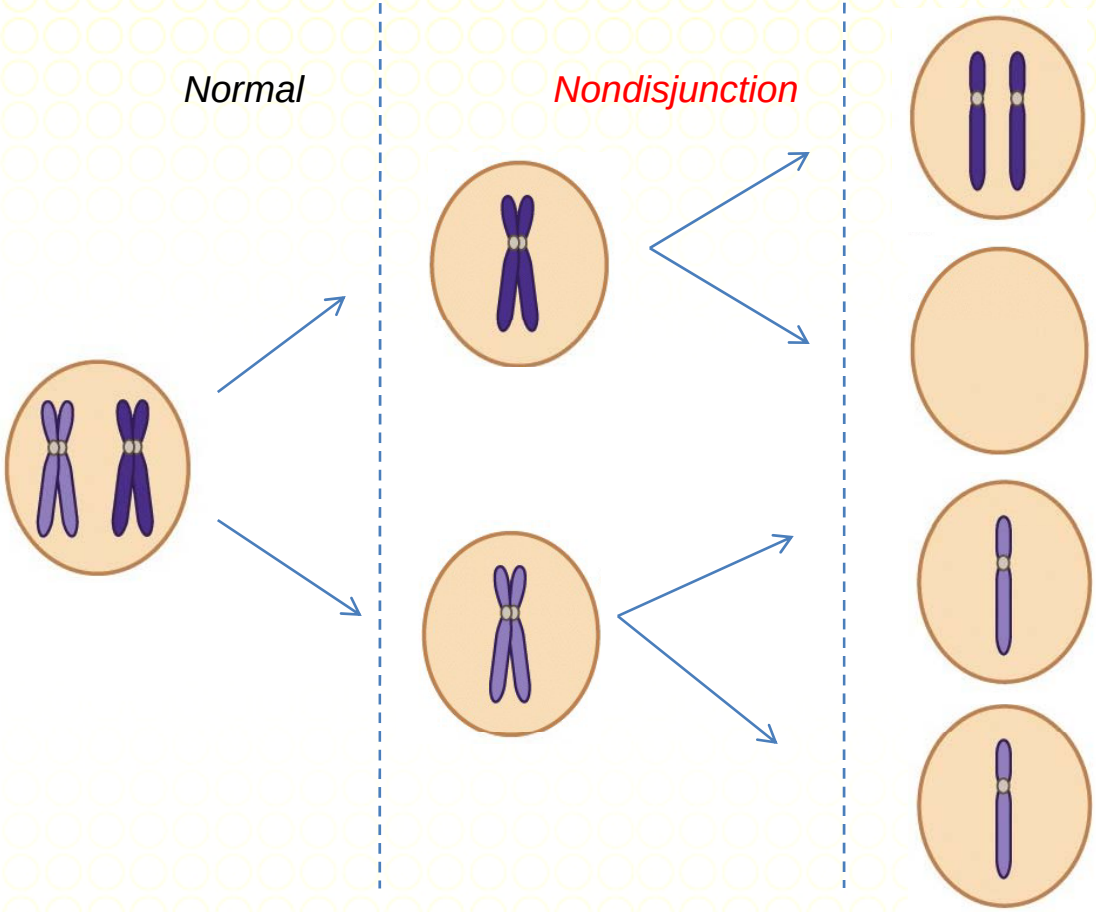
- Can occur in meiosis (I & II) or mitosis.

(A)



Meiotic nondisjunction of chromosome 21 and the origin of Down syndrome

(B)



Meiotic nondisjunction of chromosome 21 and the origin of Down syndrome

Aneuploidy resulting from nondisjunction in human beings

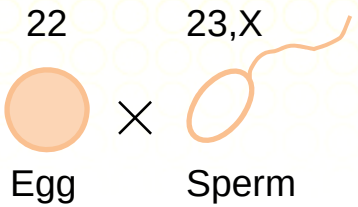
Karyotype	Chromosome Formula	Clinical Syndrome	Estimated Frequency at Birth	Phenotype
45, X	2*n* - 1	Turner	1/2500 female births	Female with retarded sexual development, usually sterile, short stature, hearing impairment
47, +13	2*n* +1	Patau	1/20,000	Mental deficiency and deafness
47, +18	2*n* + 1	Edward	1/8000	Congenital malformation of many organs, mental deficiency
47, +21	2*n* + 1	Down	1/700	Short, broad hands with palmar crease, short stature, broad head with round face, mental retardation
47, XXY 48, XXXY 48, XXYY 49, XXXXY 50, XXXXXY	2*n* + 1 2*n* + 2 2*n* + 2 2*n* + 3 2*n* + 4	Klinefelter	1/500 male births	Male, subfertile with small testes, developed breasts, feminine-pitched voice, knock-knees, long limbs
47, XXX	2*n* + 1	Triplo-X	1/700	Female with usually normal genitalia and limited fertility, slight mental retardation

Monosomy

- Diploid organisms missing one chromosome with the genetic formula of **2n-1**.
- Genetic diseases involved affect chromosome 21 (21-monosomy) & 18 (18-monosomy).
- single X chromosome; female; ovaries are rudimentary (undeveloped or immature)
- somatic mosaic – two type cells: 45,X and 46, XX.
- No bar bodies

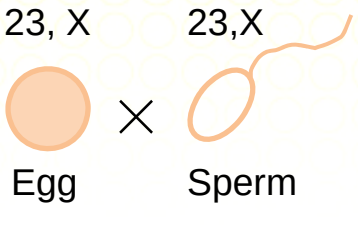
Turner Syndrome (XO)

Origin of monosomy at fertilization



Turner Syndrome
(45, X)

Origin of monosomy in the cleavage division following fertilization



Somatic mosaic
(45, X/46,XX)

Chromosome Mosaics

- Turner Syndrome Somatic Mosaics
  (45, X and 46, XX cells)

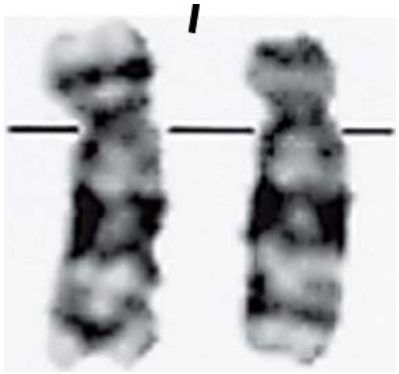
- *Drosophila* gynandromorphs
  (XX/XO mosaics

Deletions and Duplications of Chromosome Segments

- A deletion or deficiency is a missing chromosome segment.

- A duplication is an extra chromosome segment.

Cri-du-chat Syndrome Karyotype 46, XY (5p-)

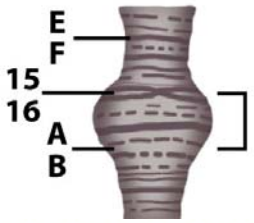


Deletion at *p*-arm chromosome no. 5

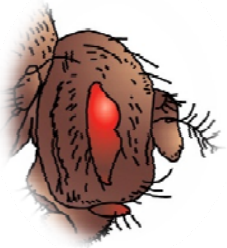
The *Drosophila Bar* Mutation:

Duplication of Region 16A of the X Chromosome

Wild-type



Normal



Bar

Duplication

Double Bar

Triplication

Key Points

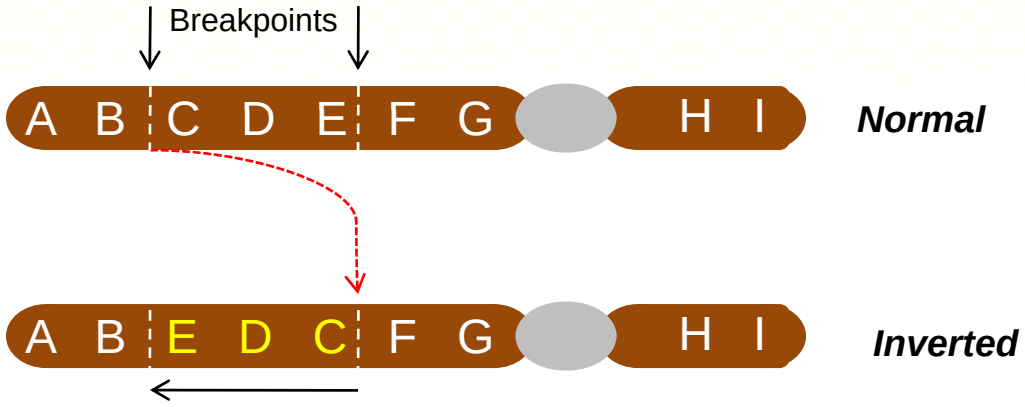
- In a trisomy, such as Down Syndrome in humans, three copies of a chromosome are present; in a monosomy, such as Turner Syndrome in humans, only one copy of a chromosome is present.

- Aneuploidy may involve the deletion of duplication of a chromosome segment.

Rearrangements of Chromosome Structure

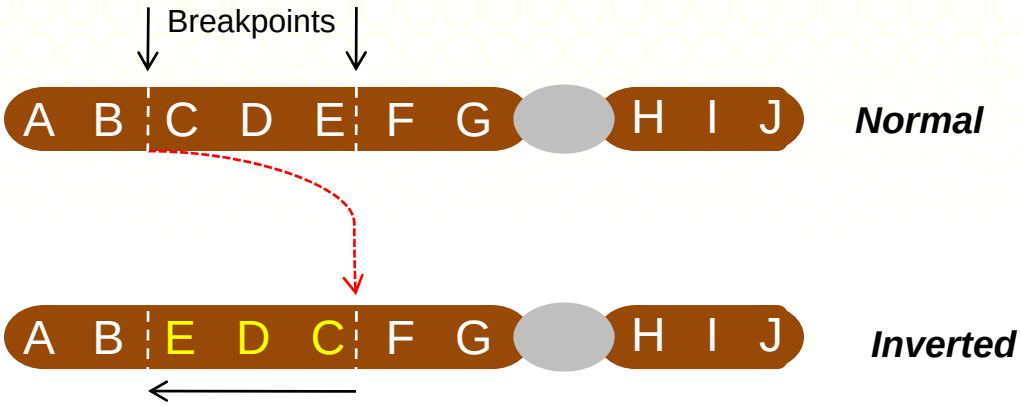
A chromosome may become rearranged internally, or it may become joined to another chromosome.

Inversions

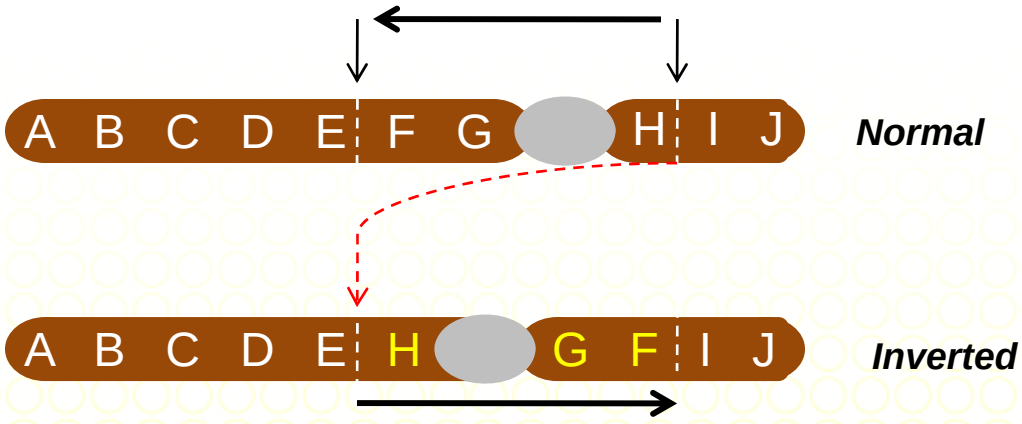


Pericentric vs. Paracentric Inversions

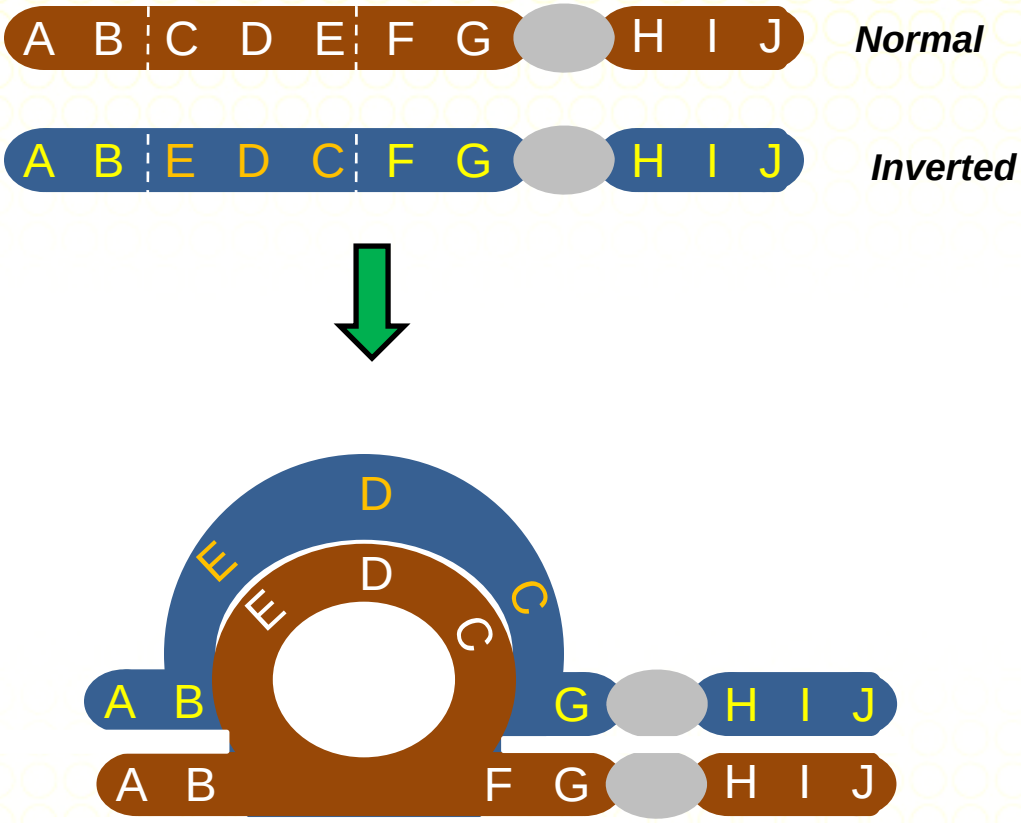
Paracentric inversion – excludes centromere



Pericentric inversion – includes centromere



Pairing Between Normal and Inverted Chromosomes

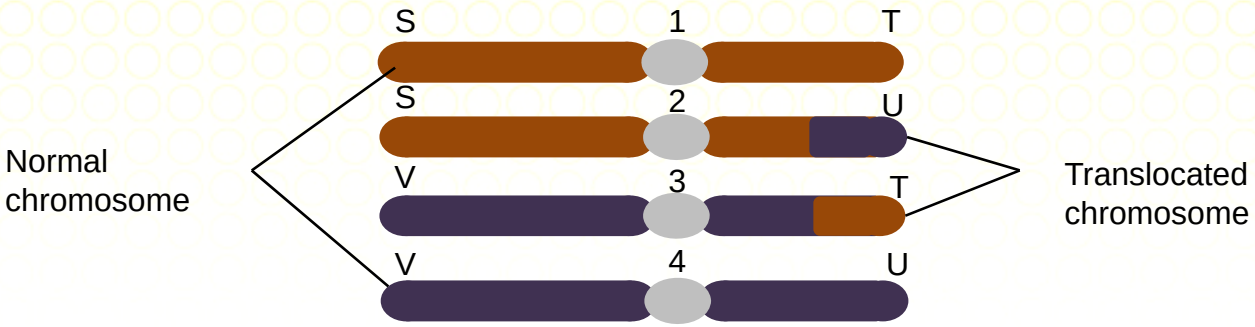


Translocations

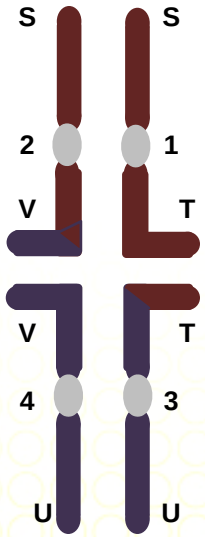
- **Translocations** occur when a segment from one chromosome is detached and reattached to a different (nonhomologous) chromosomes

- In a **reciprocal translocation**, pieces of two nonhomologous chromosomes are exchanged without any net loss of genetic material.

Structure and Pairing of Reciprocal Translocation Chromosomes



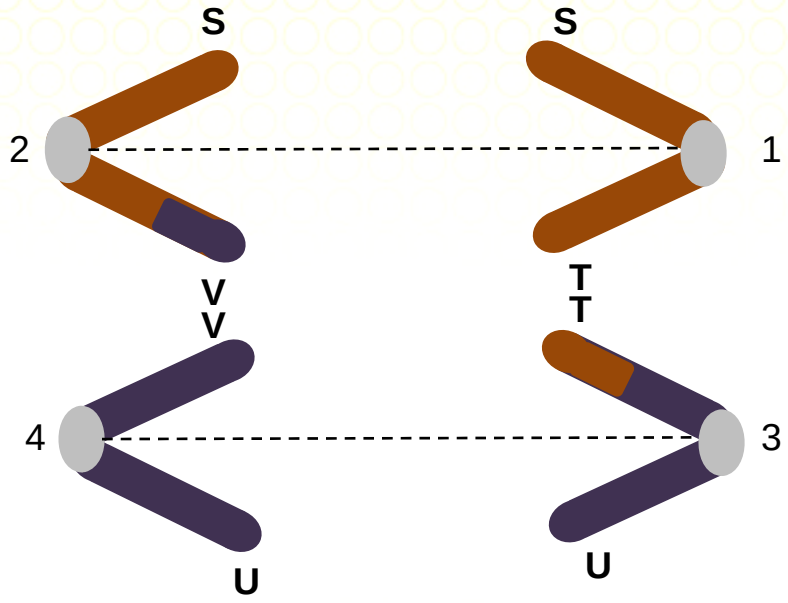
(A) Structure of chromosome in translocation heterozygote



(B) Pairing of chromosomes in translocation heterozygote

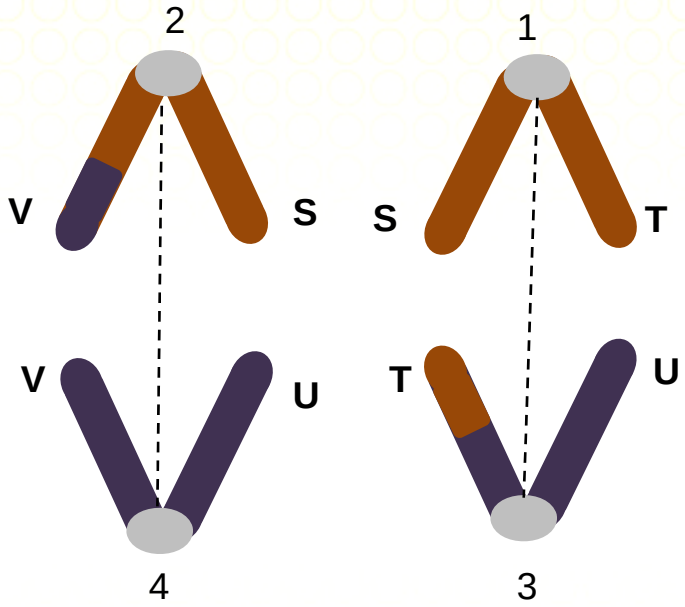
Disjunction in a Translocation Heterozygote

Adjacent disjunction I



Centromeres 1 and 3 go to one pole and centromeres 2 and 4 go to the other pole, producing aneuploid gamates

Adjacent disjunction II



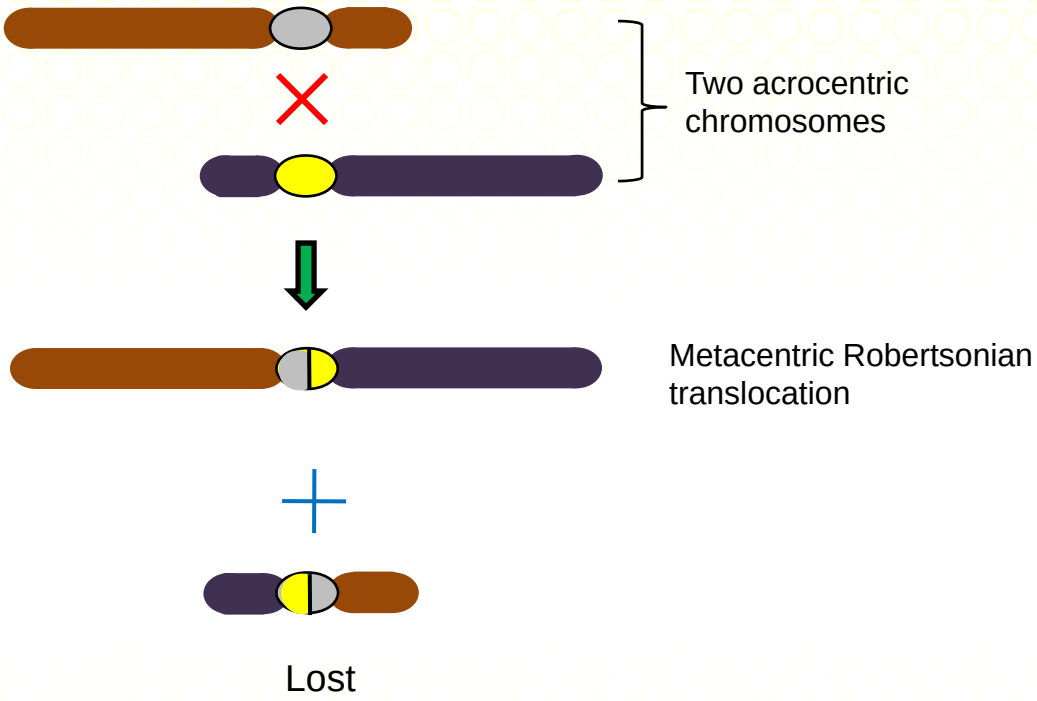
Centromeres 1 and 2 go to one pole and centromeres 3 and 4 go to the other pole, producing aneuploid gamates

<u>Alternate disjunction</u>: Centromeres 2 and 3 go to one pole and centromeres 1 and 4 go to the other pole, producing aneuploid gamates

Compound Chromosomes

- **Compound chromosomes** are formed by the fusion of homologous chromosomes, sister chromatids, or homologous chromosome segments.

Robertsonian Translocations



Robertsonian translocations are formed by the fusion of two nonhomologous chromosomes at their centromeres.

Key Points

- An **inversion** reverses the order of genes in a segment of a chromosome.
- A **translocation** interchanges segments between two nonhomologous chromosomes.
- **Compound chromosomes** result from the fusion of homologous chromosomes, or from the fusion of the arms of homologous chromosomes.
- **Robsertsonian translocations** result from the fusion of nonhomologous chromosomes.

References

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- Hartwell LH, Hood L, Goldberg ML,Reynolds AE, Silver LM (2011) Genetics: From Genes to Genomes. 4th Ed. McGraw-Hill Companies, Inc.,NY