

Chromosomal Aberrations

Structural & Numerical Changes in Chromosome Organisation

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1. Introduction & Causes

A **chromosomal aberration** (chromosomal mutation) is any change in the normal structure or number of chromosomes of a cell. Aberrations arise **spontaneously**, through errors during DNA replication, recombination, or chromosome segregation, or can be **induced** by mutagenic agents — ionising radiation (X-rays, gamma rays), certain chemicals (alkylating agents, colchicine), and viral infection. They are broadly divided into two classes, based on whether the total chromosome number is affected:

Structural aberrations: the internal arrangement of genes within one or more chromosomes is altered — through breakage and abnormal reunion — while the total chromosome number stays the same.

Numerical aberrations: the total number of chromosomes deviates from the normal complement, either as whole sets (euploidy) or as individual chromosomes (aneuploidy).

2. Structural Aberrations — Overview

Structural aberrations result from one or more chromosome breaks followed by loss, reversal, or faulty reunion of the broken segments. Four basic types are recognised, depending on what happens to the broken piece:

- **Deletion** — a segment is lost.
- **Duplication** — a segment is repeated.
- **Inversion** — a segment is reversed in place.
- **Translocation** — a segment moves to a non-homologous chromosome.

The four types of structural aberration



Fig. 1. Structural aberrations compared against the same normal reference segment (A-G): deletion removes a piece, duplication repeats a piece, inversion reverses a piece in place, and translocation exchanges pieces between non-homologous chromosomes.

3. Deletion (Deficiency)

Loss of a chromosomal segment carrying one or more genes.

- **Terminal deletion** — a single break near the chromosome end; the end piece is lost.
- **Interstitial deletion** — two breaks within a chromosome arm; the intervening segment is lost, and the two flanking pieces

reunite.

In a heterozygote (one normal, one deleted homolog), pairing at pachytene forces the normal chromosome to loop out at the deleted region — a **deletion loop** — which is diagnostic under the microscope. A deletion also unmasks recessive alleles on the intact homolog, since their dominant counterparts are missing — a phenomenon called **pseudodominance**. Large deletions are usually lethal in the homozygous or hemizygous state; only small deletions are compatible with survival.

CLINICAL EXAMPLE

Cri-du-chat syndrome in humans results from deletion of part of the short arm of chromosome 5 (5p–). Affected infants have a characteristic high-pitched, cat-like cry, along with intellectual disability and distinctive facial features.

4. Duplication

A chromosomal segment is present in more than one copy on the same chromosome. Duplications are classified by the position and orientation of the extra copy:

- **Tandem duplication** — the repeated segment lies immediately adjacent, in the same orientation as the original.
- **Reverse tandem duplication** — the repeated segment is adjacent but in inverted orientation.
- **Displaced duplication** — the extra copy lies elsewhere on the same chromosome, or on a different (non-homologous) chromosome.

Like deletions, duplication heterozygotes show a diagnostic **duplication loop** at pachytene.

CLASSIC EXAMPLE

The **Bar-eye** mutation in *Drosophila melanogaster* is a tandem duplication of the 16A region of the X chromosome, which reduces the number of eye facets. Unequal crossing over between the duplicated segments of two Bar chromosomes can generate a further duplicated "Ultra-bar" allele, or revert the chromosome back to normal — direct proof that Bar arose by, and continues to evolve by, unequal crossing over.

Duplication is evolutionarily important: an extra gene copy is free from the constraint of performing the original essential function and can accumulate mutations, sometimes acquiring a new function — a principal route by which gene families arise.

5. Inversion

A chromosome breaks at two points; the segment between the breaks rotates through 180° and rejoins, reversing the gene order within that segment (though no genetic material is gained or lost).

- **Paracentric inversion** — both breakpoints lie in the same arm; the centromere is not included in the inverted segment.
- **Pericentric inversion** — the breakpoints lie in different arms; the centromere is included, and its relative position on the chromosome can change.

EFFECT ON CROSSING OVER

In an inversion heterozygote, the normal and inverted chromosomes must form an **inversion loop** to pair at pachytene. A single crossover within the loop produces abnormal chromatids: in a **paracentric** inversion, it yields an acentric fragment (lost) and a dicentric bridge (breaks at anaphase); in a **pericentric** inversion, it yields chromatids with duplications and deficiencies. Because these recombinant products are usually inviable, viable recombinants are essentially never recovered from the inverted region — an effect called **crossover suppression**, even though crossing over itself is not physically prevented.

Because they suppress recombination, inversions can hold together favourable combinations of alleles and act as a mechanism of reproductive isolation between diverging populations; geneticists also exploit specially constructed multiple-inversion "**balancer chromosomes**" in *Drosophila* to keep whole chromosomes from recombining in stock-keeping crosses.

6. Translocation

A chromosomal segment is transferred to a non-homologous chromosome.

- **Reciprocal translocation** — two non-homologous chromosomes exchange segments with each other.
- **Simple (non-reciprocal) translocation** — a segment moves in one direction only, with no exchange back.
- **Robertsonian translocation** — two acrocentric chromosomes fuse at the centromere with loss of their (small) short arms, reducing the chromosome number by one.

In a reciprocal translocation heterozygote, the four chromosomes involved (two normal + two translocated) associate at pachytene in a characteristic **cross-shaped configuration**, which resolves at metaphase I into a ring or chain of four.

Depending on how this quadrivalent segregates:

- **Alternate segregation** — produces balanced, viable gametes.
- **Adjacent segregation** — produces unbalanced gametes (duplications/deficiencies), which are usually inviable.

Since roughly half the gametes of a translocation heterozygote are inviable, such individuals show **semisterility** (~50% pollen or seed abortion in plants).

CLINICAL EXAMPLE

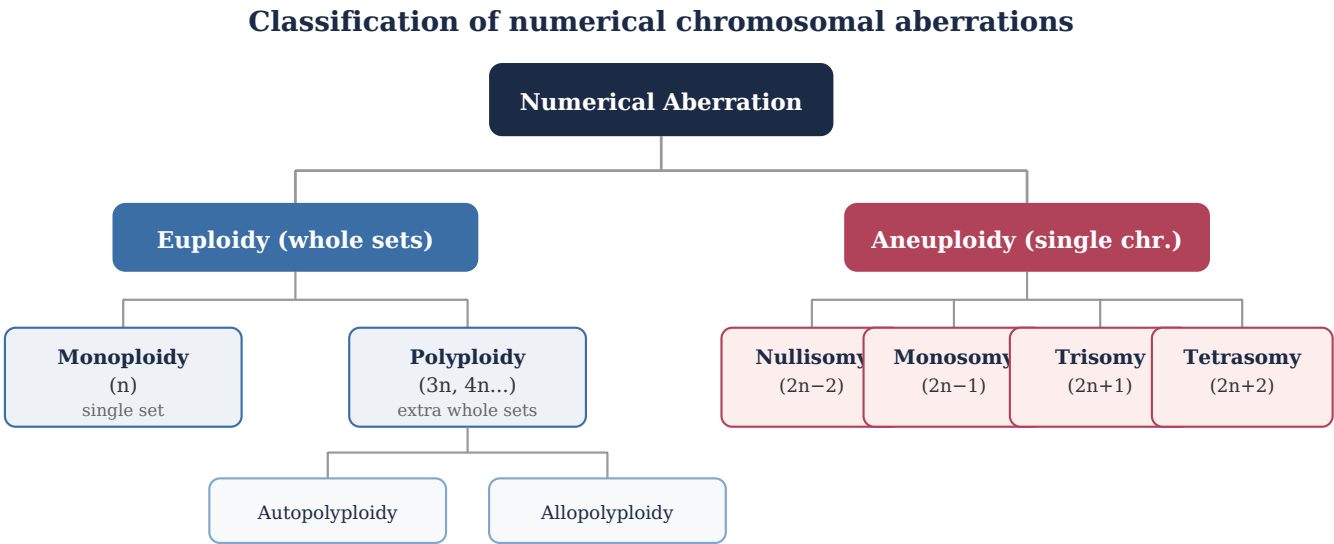
The **Philadelphia chromosome**, a reciprocal translocation between chromosomes 9 and 22 — $t(9;22)$ — fuses the *BCR* and *ABL* genes to create an abnormally active tyrosine kinase. It is the hallmark cytogenetic marker of **chronic myeloid leukaemia (CML)**.

CLASSICAL GENETICS EXAMPLE

Permanent translocation heterozygosity is characteristic of the evening primrose, *Oenothera*, and of *Datura* — in these plants, multiple reciprocal translocations link most chromosomes into a single ring at meiosis, which regularly undergoes alternate segregation to preserve fixed sets of linked genes across generations.

7. Numerical Aberrations — Overview

Numerical aberrations change the total chromosome count of a cell relative to the normal diploid number ($2n$). They fall into two categories depending on whether whole chromosome sets, or individual chromosomes, are affected.



Euploidy changes complete chromosome sets; aneuploidy changes individual chromosomes within a set.

Fig. 2. Numerical aberrations divide into euploidy (whole-set changes) and aneuploidy (single-chromosome changes), each with further subtypes.

8. Euploidy — Monoploidy & Polyploidy

Euploidy refers to variation in the number of complete chromosome sets — every change is an exact multiple of the haploid number (n).

8.1 Monoploidy

Cells or organisms with a single chromosome set (n). Naturally monoploid individuals occur in haplodiploid insects (male bees, ants, and wasps develop from unfertilised eggs). In plant breeding, monoploid/haploid plants (e.g. from anther or microspore culture) are valuable because any recessive mutation is immediately expressed, and chromosome doubling of such plants gives instant, fully homozygous diploid lines.

8.2 Polyploidy

Cells or organisms with more than two complete chromosome sets ($3n, 4n, 5n...$). Polyploids typically have larger cells and organs than their diploid relatives, but often reduced fertility because of irregular multivalent pairing at meiosis.

- **Autopolyploidy** — all chromosome sets come from the *same* species (e.g. AAA, AAAA). It arises from failure of meiotic reduction (unreduced gametes) or from somatic chromosome doubling, e.g. by colchicine treatment.
- **Allopolyploidy** — chromosome sets come from *different*, hybridising species, usually followed by chromosome doubling (amphidiploidy) to restore fertile, regular pairing.

APPLIED EXAMPLE

Bread wheat, *Triticum aestivum*, is a natural **allohexaploid** ($2n = 6x = 42$, genome AABBDD) that arose from successive hybridisations and chromosome doublings among three diploid grass ancestors. **Raphanobrassica**, an artificial amphidiploid combining the genomes of radish (*Raphanus*) and cabbage (*Brassica*), is a classic laboratory demonstration of allopolyploid speciation.

9. Aneuploidy

Aneuploidy is the gain or loss of one or a few individual chromosomes, so the total number is not an exact multiple of n . It usually arises from **nondisjunction** or **anaphase lag** (Section 10).

- **Nullisomy ($2n-2$)** — both members of one homologous pair are missing. Almost always lethal in diploids; tolerated in some polyploids (e.g. hexaploid wheat, where other homoeologous chromosomes can compensate).
- **Monosomy ($2n-1$)** — one chromosome of a pair is missing.
- **Trisomy ($2n+1$)** — one extra chromosome is present, making a triplet instead of a pair.
- **Tetrasomy ($2n+2$)** — two extra copies of one chromosome are present.
- **Double trisomy ($2n+1+1$)** — extra copies of two different chromosomes occur together.

10. Mechanism — Nondisjunction & Anaphase Lag

Nondisjunction is the failure of paired homologous chromosomes (at meiosis I) or sister chromatids (at meiosis II, or in mitosis) to separate properly at anaphase, so both move to the same pole.

Nondisjunction at meiosis I vs. meiosis II

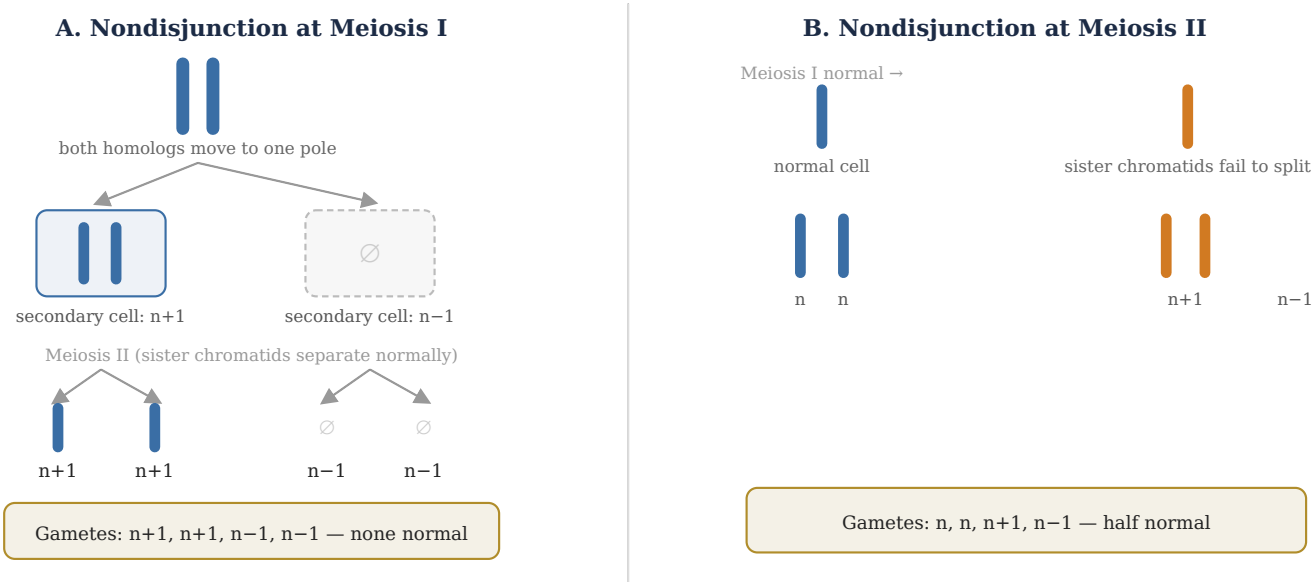


Fig. 3. Nondisjunction at meiosis I sends both homologs to the same pole, so every resulting gamete is abnormal ($n+1$ or $n-1$). Nondisjunction at meiosis II affects only one of the two secondary cells, so half the gametes are normal.

Anaphase lag is a related but distinct mechanism: a chromosome (or chromatid) simply fails to move to either pole in time and is left out of both nuclei, forming a micronucleus that is eventually lost. Unlike nondisjunction, which always yields *both* a trisomic and a monosomic product, anaphase lag produces one normal daughter cell and one monosomic daughter cell only.

11. Clinically Important Human Aneuploidies

Syndrome	Karyotype	Chromosomal basis
Down syndrome	47, +21	Trisomy 21
Edward syndrome	47, +18	Trisomy 18

Patau syndrome	47, +13	Trisomy 13
Klinefelter syndrome	47, XXY	Trisomy of sex chromosomes
Turner syndrome	45, X	Monosomy of sex chromosome
Triple X syndrome	47, XXX	Trisomy of sex chromosomes
Jacob's syndrome	47, XYY	Trisomy of sex chromosomes

12. Significance

- **Human health:** aneuploidy is a leading cause of miscarriage, congenital disorders, and intellectual disability; specific translocations (e.g. the Philadelphia chromosome) are diagnostic and mechanistic drivers of certain cancers.
- **Plant breeding:** autopolyploidy and allopolyploidy have been deliberately exploited to create larger-fruited, more vigorous, or fertile hybrid crop varieties, including many staple crops.
- **Evolution & speciation:** inversions and translocations reduce fertility with the parental type in heterozygotes, contributing to reproductive isolation and the formation of new species (chromosomal speciation); polyploidy is a major route of instant speciation in plants.
- **Genetic mapping & research tools:** deletions, duplications, and balancer (multiple-inversion) chromosomes are routinely used in the laboratory to map genes and to maintain lethal mutations in stock populations.
- **Clinical cytogenetics:** karyotyping and chromosomal microarray analysis, built on these principles, are the basis of prenatal diagnosis and cancer cytogenetics today.