(2) Mutations can cause several base pairs to be inserted or deleted.
Trinucleotide repeat expansion is a type of mutation where the number of three-nucleotide repeats changes. An example is that of Fragile X Syndrome where affected Individuals have 230-4000 CGG repeats in the long arm of the X chromosome. Normal individuals have 5-54 such repeats.

A notable example of base pair deletion is CCR5 delta 32 gene where 32 base pairs are deleted. This introduces a premature stop codon. the resultant protein is shorter than the normal protein and forms a non-functional coreceptor. This mutation hampers the ability of HIV to infect the cells of the immune system.

Mutations involving **(3) parts of a Chromosome, (4) An Entire Chromosome or (5) Entire set of Chromosome** are called Chromosomal aberrations.

The chromosome set of a species remains relatively stable over long periods of time. However, within populations there can be found abnormalities involving the structure or number of chromosomes. These alterations arise spontaneously from errors in the normal processes of the cell. Their consequences are usually deleterious, giving rise to individuals who are unhealthy or sterile, though in rare cases alterations provide new adaptive opportunities that allow evolutionary change to occur. In fact, the discovery of visible chromosomal differences between species has given rise to the belief that radical restructuring of chromosome architecture has been an important force in evolution.

(3) Parts of Chromosomes: Changes in chromosome structure
Two important principles dictate the properties of a large proportion of structural chromosomal changes. The first principle is that any deviation from the normal ratio of genetic material in the genome results in genetic imbalance and abnormal function. In the normal nuclei of both diploid and haploid cells, the ratio of the individual chromosomes to one another is 1:1. Any deviation from this ratio by addition or subtraction of either whole chromosomes or parts of chromosomes results in genomic imbalance. The second principle is that homologous chromosomes go to great lengths to pair at meiosis. The tightly paired homologous regions are joined by a ladderlike longitudinal structure called the synaptonemal complex. Homologous regions seem to be able to find each other and form a synaptonemal complex whether or not they are part of normal chromosomes. Therefore, when structural changes occur, not only are the resulting pairing formations highly characteristic of that type of structural change but they also dictate the packaging of normal and abnormal chromosomes into the gametes and subsequently into the progeny.

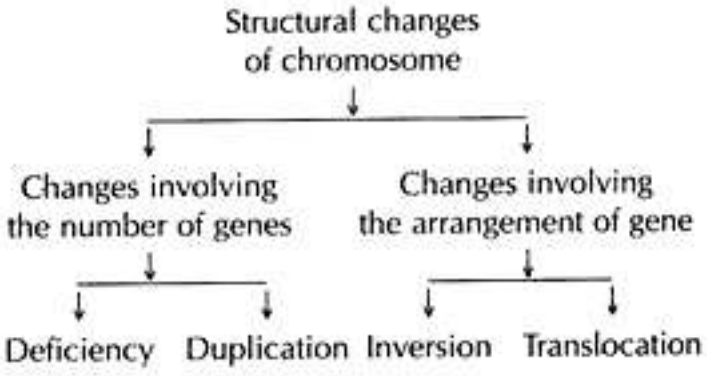


Fig. 12.1: Different types of structural changes of chromosome

Deletions
The simplest, but perhaps most damaging, structural change is a deletion—the complete loss of a part of one chromosome. In a haploid cell this is lethal, because part of the essential genome is lost. However, even in diploid cells deletions are generally lethal or have other serious consequences. In a diploid a heterozygous deletion results in a cell that has one normal chromosome set and another set that contains a truncated chromosome. Such cells show genomic imbalance, which increases in severity with the size of the deletion. Another potential source of damage is that any recessive, deleterious, or lethal alleles that are in the normal counterpart of the deleted region will be expressed in the phenotype. In humans, cri-du-chat syndrome is caused by a heterozygous deletion at the tip of the short arm of chromosome 5. Infants are born with this condition as the result of a deletion arising in parental germinal tissues or even in sex cells. The manifestations of this deletion, in addition to the “cat cry” that gives the syndrome its name, include severe intellectual disability and an abnormally small head.

Duplications
In this, a region of a chromosome is duplicated. A duplication can arise spontaneously or more commonly due to errors during crossing over (during meiosis). If an individual is heterozygous for a duplication (an extra copy of some chromosome region) it results in a genomic imbalance with deleterious consequences. If a duplication becomes homozygous, it can provide the organism with an opportunity to acquire new genetic functions through mutations within the duplicate copy.

Inversions
An inversion occurs when a chromosome breaks in two places and the region between the break rotates 180° before rejoining with the two end fragments. If the inverted segment contains the centromere (i.e., the point where the two chromatids are joined), the inversion is said to be pericentric; if not, it is called paracentric. Inversions do not result in a gain or loss of genetic material, and they have deleterious effects only if one of the chromosomal breaks occurs within an essential gene or if the function of a gene is altered by its relocation to a new chromosomal neighbourhood (called the position effect). However, individuals who are heterozygous for inversions produce aberrant meiotic products along with normal products. The only way uninverted and inverted segments can pair is by forming an inversion loop. If no crossovers occur in the loop, half of the gametes will be normal and the other half will contain an inverted chromosome. If a crossover does occur within the loop of a paracentric inversion, a chromosome bridge and an acentric chromosome (i.e., a chromosome without a centromere) will be formed, and this will give rise to abnormal meiotic products carrying deletions, which are inviable. In a pericentric inversion, a crossover within the loop does not result in a bridge or an acentric chromosome, but inviable products are produced carrying a duplication and a deletion.

Since recombination within the inversion loop leads to aberrant meiotic products that are not viable, inversions are called crossover suppressors. Therefore, genes within the inversion loop are more likely to be inherited together as a block (ie without being recombined).

Translocations
In this, a region from a chromosome is moved to a different spot on a non-homologous chromosome. A cell bearing a heterozygous translocation has a full set of genes and will be viable unless one of the breaks causes damage within a gene or if there is a position effect on gene function. However, once again the pairing properties of the chromosomes at meiosis result in aberrant meiotic products. Specifically, half of the products are deleted for one of the chromosome regions that changed positions and half of the products are duplicated for the other. These duplications and deletions usually result in inviability, so translocation heterozygotes are generally semisterile (“half-sterile”).

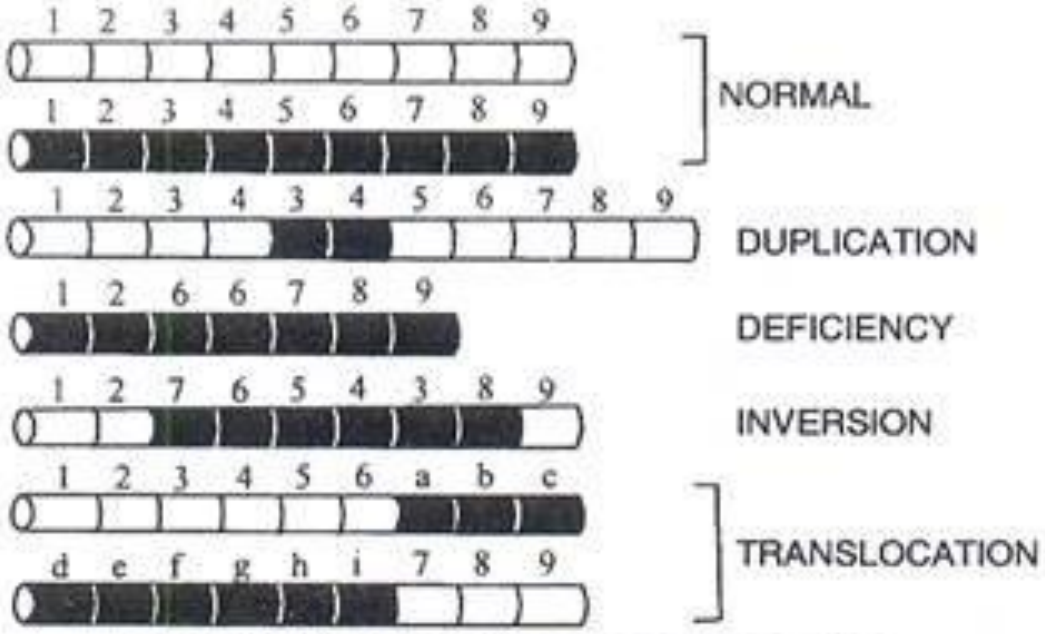
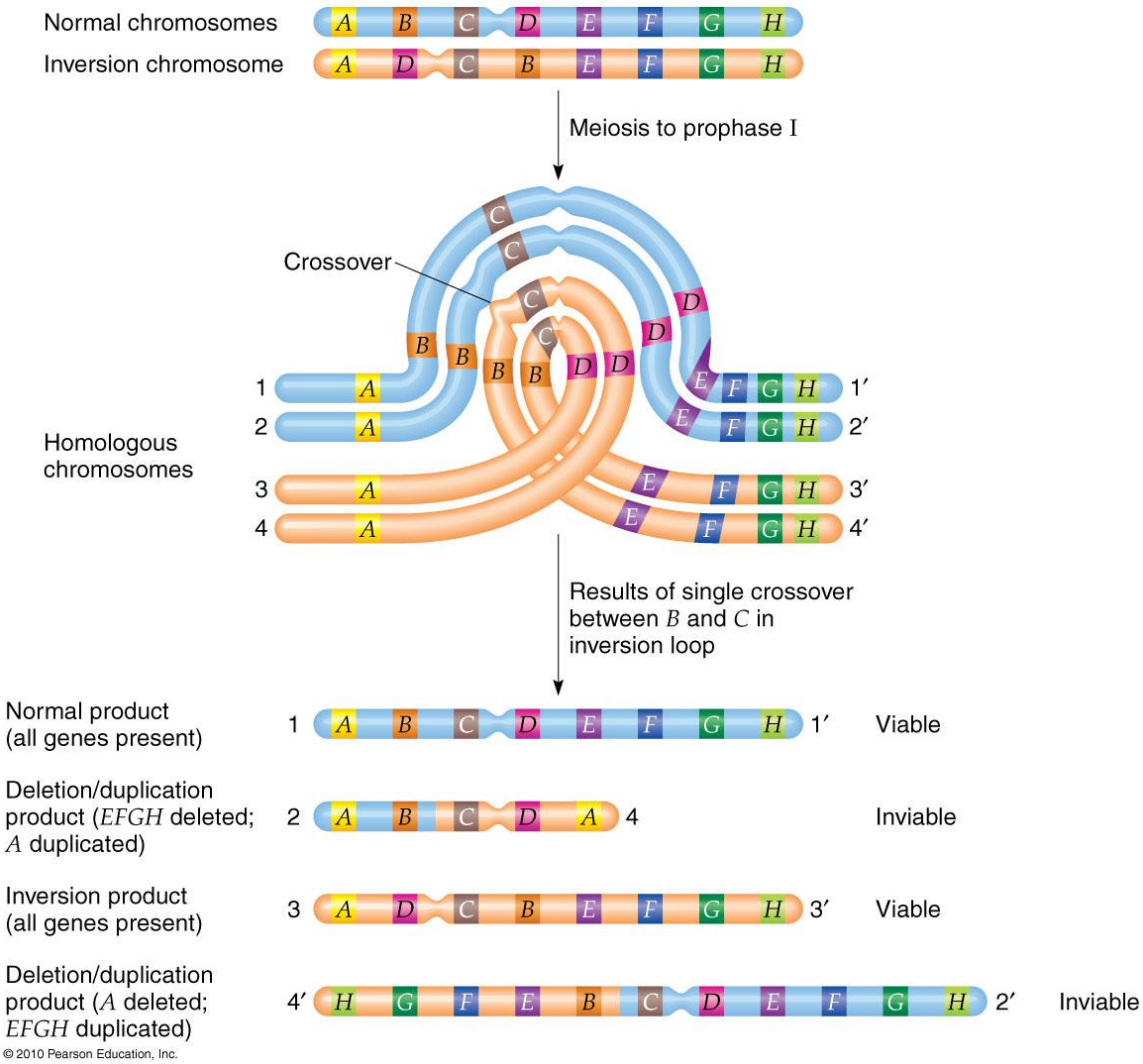
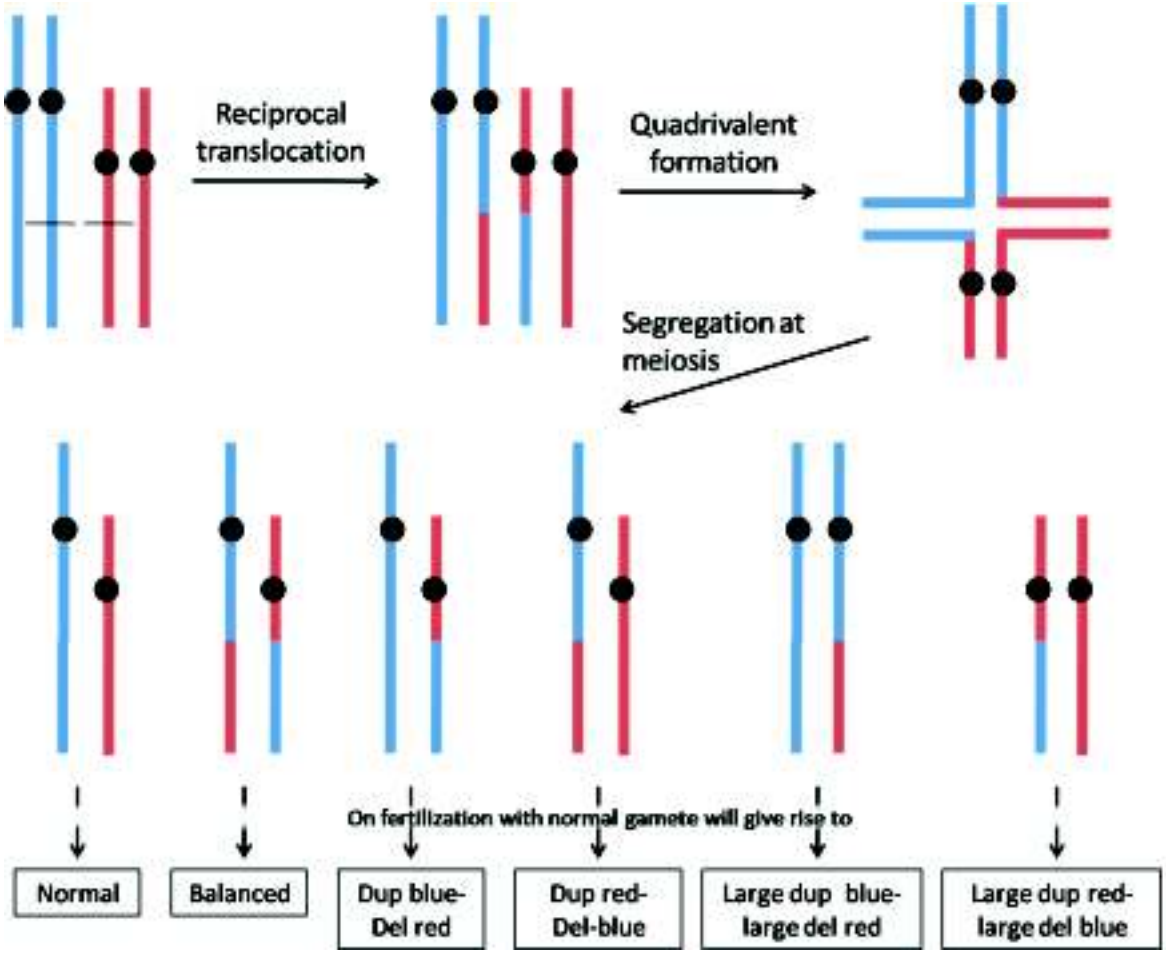


Fig. 43.2. Types of Chromosomal aberrations.

Effect of Inversion during crossing over: Inversion loop.



Effect of Translocation on crossing over.



Changes in chromosome number

Two types of changes in chromosome numbers can be distinguished:

(4) Change in the number of a chromosome within a set (Aneuploidy)

(5) Change in the number of whole chromosome set (Euploidy)

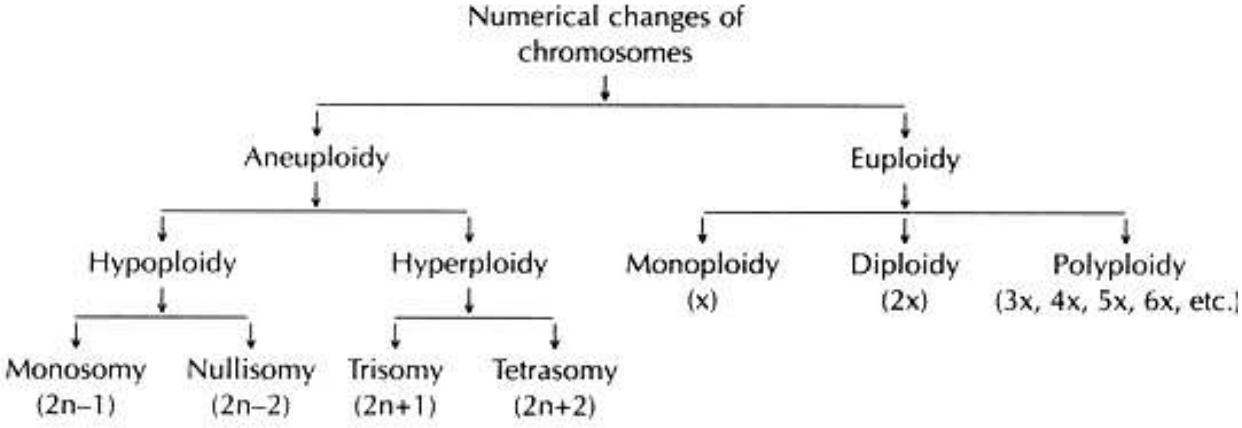
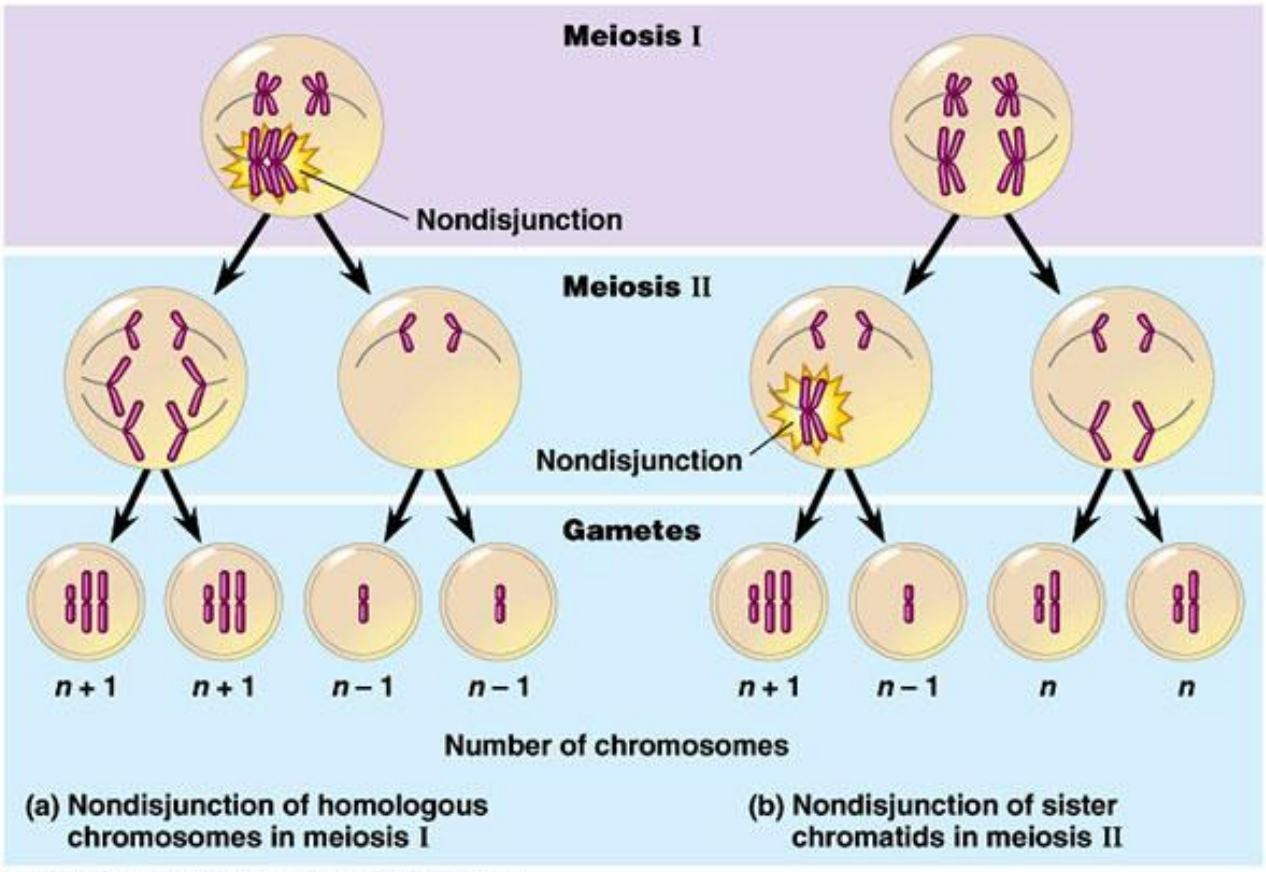


Fig. 11.1: Different kinds of numerical changes of chromosomes (x = basic chromosome number, 2n = somatic chromosome number)

Aneuploidy
When one chromosome in a set is present in a number other than normal (ie one copy, three copy etc), the condition is called Aneuploidy. In general, the number of chromosomes in an Aneuploid individual will be (2n-2), (2n-1), (2n+1), (2n+2) etc.
Most aneuploids arise by nondisjunction, a failure of homologous chromosomes to separate at meiosis. When a gamete of this type is fertilized by a normal gamete, the zygotes formed will have an unequal distribution of chromosomes. Such genomic imbalance results in severe abnormalities or death. Only aneuploids involving small chromosomes tend to survive and even then only with an aberrant phenotype.

The most common form of aneuploidy in humans results in Down syndrome, a suite of specific disorders in individuals possessing an extra chromosome 21 (trisomy 21). Other forms of aneuploidy in humans result from abnormal numbers of sex chromosomes. Turner syndrome is a condition in which females have only one X chromosome. Klinefelter syndrome is a condition in which males have one extra female sex chromosome, resulting in an XXY pattern. (Other, less frequent, chromosomal patterns include XXXY, XXXXY, XXYY, and XXXYY.)



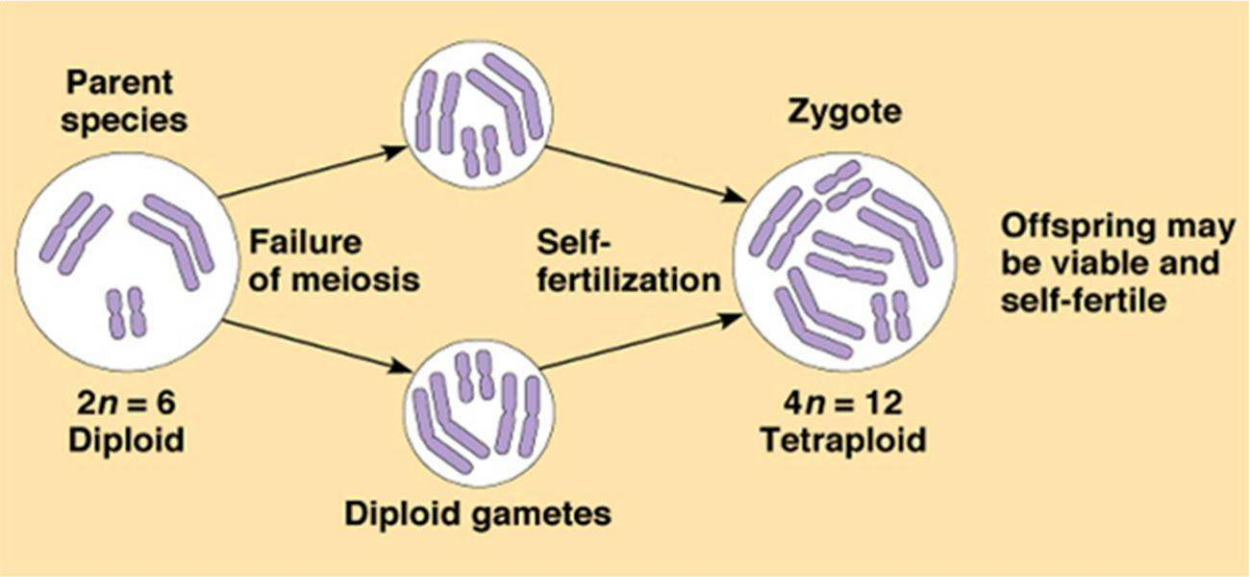
Euploidy:
Individuals that have an entire set of chromosomes missing or have extra sets of chromosomes compared to the normal condition (2n) are called Euploids. Individuals that have only one set of chromosomes are called haploids (n).
An individual with additional chromosome sets is called a polyploid. Individuals with three sets of chromosomes (triploids, 3n) or four sets of chromosomes (tetraploids, 4n) etc. are polyploid derivatives of the basic diploid (2n) constitution.

Polyploids with odd numbers of sets (e.g., triploids) are sterile, because homologous chromosomes pair only two by two, and the extra chromosome moves randomly to a cell pole, resulting in highly unbalanced, nonfunctional meiotic products. It is for this reason that triploid watermelons are seedless.
Polyploids with even numbers of chromosome sets (e.g. tetraploids, hexaploids etc.) can be fertile if orderly two-by-two chromosome pairing occurs.

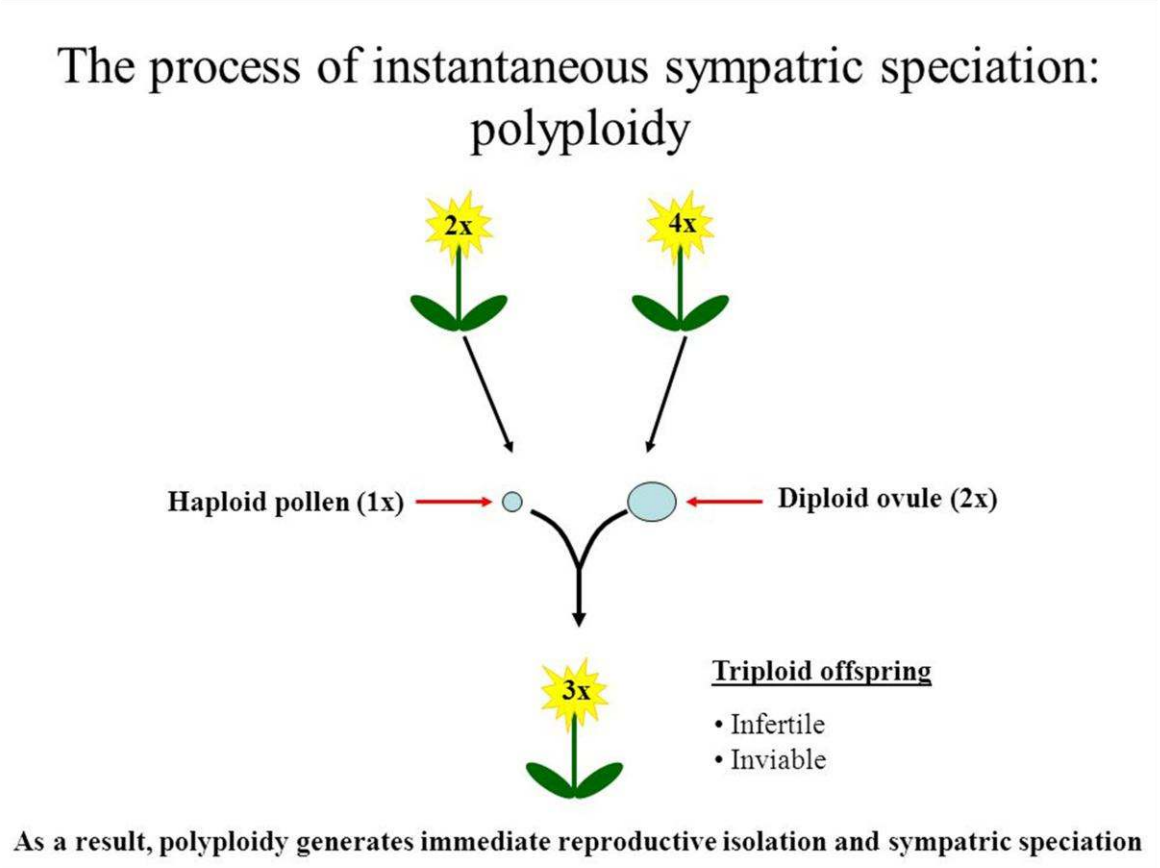
Polyploids formed by the increase in the number of sets of chromosomes from a single species are called autopolyploids.

Sometimes, polyploids are formed by the fusion of gametes from two different species. Though two organisms from closely related species frequently hybridize, the chromosomes of the fusing partners are different enough that the two sets do not pair at meiosis, resulting in sterile offspring. However, if by chance the number of chromosome sets in the hybrid accidentally duplicates, a pairing partner for each chromosome will be produced, and the hybrid will be fertile. These chromosomally doubled hybrids are called allopolyploids. Bread wheat, which is hexaploid (6n) due to several natural spontaneous hybridizations, is an example of an allotetraploid.
Polyploidy does arise spontaneously in humans, but all polyploids either abort in utero or die shortly after birth.

Cause of Euploidy



Auto Polyploidy



Species: A group of organisms that can potentially interbreed to produce fertile offspring (Biological Species concept- Ernt Mayr)

4n Seed Parent
diploid egg

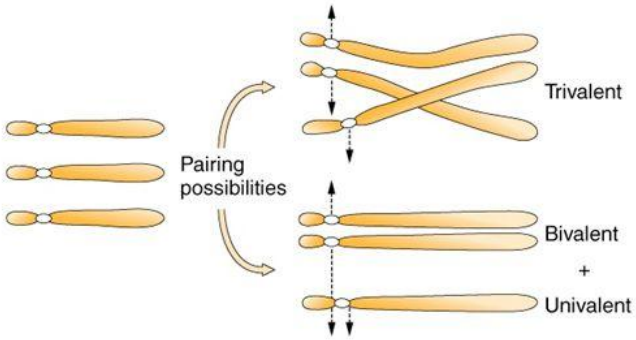
2n

2n Pollen Parent
haploid sperm

n

2n + n = Sterile 3n Plant

FERTILIZATION



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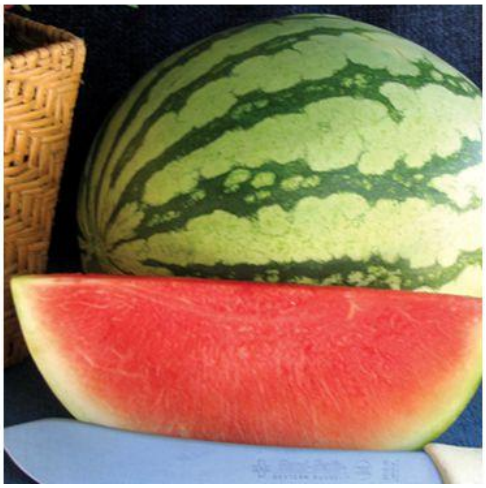
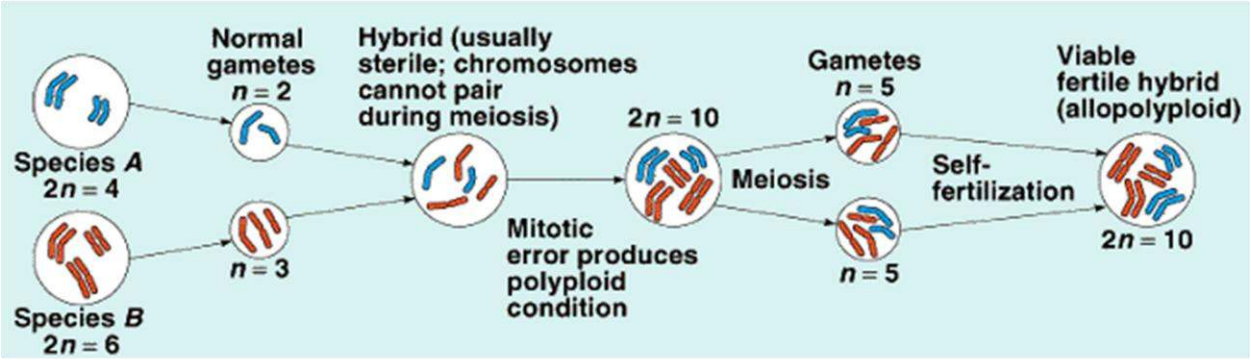


Cause of Euploidy



Allo Polyploidy

Mutation Types based on effects on fitness

1. Deleterious: reduces fitness
2. Beneficial: increases fitness
3. Neutral: has no effect on fitness

Mutation types based on location of mutation

1. Somatic: happens in body cells
2. Germline: happens in reproductive tissue.

Mutation and Fitness

Mutation Accumulation:

"if a given lot of individuals, known to contain no mutant genes at the start, is bred through a series of *n* generations (that is, to "F_n"), and one of the individuals of this last (*n*th) generation is then tested for mutant genes..., this test will reveal all mutant genes that arose in any of the preceding *n* generations." Muller (1928).

References:

Much of this material is from Encyclopaedia Britannica