Chromosomal mutations - variations from the normal (wild type) condition in chromosome structure and chromosome number and, in humans, they contribute to spontaneous abortions, infertility, and some cancers

Frequency in humans - 50% in spontaneous abortions, 6 out of 1,000 live births
Variations in chromosome number

- **Euploidy** – when an organism has one complete set of chromosomes or an exact multiple of complete sets.

- **Aneuploidy** – variations in the number of individual chromosomes
<table>
<thead>
<tr>
<th>Term</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aneuploidy</td>
<td>$2n \pm x$ chromosomes</td>
</tr>
<tr>
<td>Monosomy</td>
<td>$2n - 1$</td>
</tr>
<tr>
<td>Disomy</td>
<td>$2n$</td>
</tr>
<tr>
<td>Trisomy</td>
<td>$2n + 1$</td>
</tr>
<tr>
<td>Tetrasomy, pentasomy, etc.</td>
<td>$2n + 2$, $2n + 3$, etc.</td>
</tr>
<tr>
<td>Euploidy</td>
<td>Multiples of $n$</td>
</tr>
<tr>
<td>Diploidy</td>
<td>$2n$</td>
</tr>
<tr>
<td>Polyploidy</td>
<td>$3n$, $4n$, $5n$, $\ldots$</td>
</tr>
<tr>
<td>Triploidy</td>
<td>$3n$</td>
</tr>
<tr>
<td>Tetraploidy, pentaploidy, etc.</td>
<td>$4n$, $5n$, etc.</td>
</tr>
<tr>
<td>Autopolyploidy</td>
<td>Multiples of the same genome</td>
</tr>
<tr>
<td>Allopolyplody (Amphidiploidy)</td>
<td>Multiples of closely related genomes</td>
</tr>
</tbody>
</table>
Non-disjunction during meiosis results in changes in the number of chromosomes.
A direct relationship exists between maternal age and the probability of giving birth to an individual with trisomy-21, ranging from 7.7/10,000 around age 25 and increasing to 333/10,000 around age 46.
Trisomy (47,13+)

Patau syndrome

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
### Trisomy (47,18+)

### Edwards syndrome

<table>
<thead>
<tr>
<th>Chromosome 1</th>
<th>Chromosome 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>X</strong></td>
<td><strong>Y</strong></td>
</tr>
</tbody>
</table>

#### Clinical Manifestations

<table>
<thead>
<tr>
<th>Characteristic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth failure</td>
</tr>
<tr>
<td>Mental retardation</td>
</tr>
<tr>
<td>Open skull sutures at birth</td>
</tr>
<tr>
<td>High, arched eyebrows</td>
</tr>
<tr>
<td>Low-set, deformed ears</td>
</tr>
<tr>
<td>Short sternum</td>
</tr>
<tr>
<td>Ventricular septal defect</td>
</tr>
<tr>
<td>Flexion deformities of fingers</td>
</tr>
<tr>
<td>Abnormal kidneys</td>
</tr>
<tr>
<td>Persistent ductus arteriosus</td>
</tr>
<tr>
<td>Deformity of hips</td>
</tr>
<tr>
<td>Prominent external genitalia</td>
</tr>
<tr>
<td>Muscular hypertonus</td>
</tr>
<tr>
<td>Prominent heel</td>
</tr>
<tr>
<td>Dorsal flexion of big toes</td>
</tr>
</tbody>
</table>
Variations in chromosome structure

• All chromosome structure mutations begin with one or more breaks in the chromosome. If break occurs within a gene the function might be lost.

• Broken ands do not have telomeres that prevent degradation but the broken end is “sticky” and can adhere to other broken ends.
Variations in chromosome structure (arrangement)

(a) Deletion of D

(b) Duplication of BC

(c) Inversion of BCD

(d) Nonreciprocal translocation of AB

(e) Reciprocal translocation of AB and HIJ
(a) Origin of terminal deletion

Break
(b) Origin of intercalary deletion

Break A → D → C → Break E → F

Deleted chromosome

(E) Lost
(c) Formation of deficiency loop

Area missing in deleted chromosome

Normal chromosome

Homolog with deleted region C and D

[Diagram showing the formation of a deletion loop through synapsis between a normal chromosome and a homolog with a deleted region.]
Consequences of deletions

- Depend on the gene or genes lost and in a diploid organism on the genes present in the normal homologous chromosome - pseudodominance
Cri du chat – (46,5p-)

Frequency – 1 infant in 50,00 live births
Duplications - Unequal crossing over and its results
Bar-eye phenotype – effects of duplication

(a) Genotypes and phenotypes

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Facet Number</th>
<th>Phenotype</th>
<th>16A segments</th>
</tr>
</thead>
<tbody>
<tr>
<td>$B^+/B^+$</td>
<td>779</td>
<td>![Image of eye]</td>
<td>![Image of segments]</td>
</tr>
<tr>
<td>$B/B^+$</td>
<td>358</td>
<td>![Image of eye]</td>
<td>![Image of segments]</td>
</tr>
<tr>
<td>$B/B$</td>
<td>68</td>
<td>![Image of eye]</td>
<td>![Image of segments]</td>
</tr>
<tr>
<td>$B^D/B^+$</td>
<td>45</td>
<td>![Image of eye]</td>
<td>![Image of segments]</td>
</tr>
</tbody>
</table>
(b) Origin of $B^D$ allele as a result of unequal crossing over

1

2

3

4

$B^D$

$B^+$

$B$

$B/B$
Consequences of duplications

• Evolution of multiple genes with related functions (multigene families)
  – Globin genes
Inversions

• An inversion is a chromosomal mutation that results when a segment of the chromosome is excised and then reintegrates in a different orientation.
  – Paracentric inversion
  – Pericentric inversion
Inversions - One possible origin of a pericentric inversion

- Break
- Gaps created
- Rejoining

Inverted sequence
Paracentric inversion heterozygote

Inversion loop, no crossing over

Resultant gametes

Normal sequence

Inverted sequence
Crossing-over within the inversion

(a) Paracentric inversion heterozygote

Inversion loop, including crossover

Resultant gametes

1 1’ NCO Normal sequence
2 4’ SCO Dicentric; duplication and deletion
3 3’ NCO Inverted sequence
4 2’ SCO Acentric; duplication and deletion
Consequences of inversions

- Position effects

- Evolutionary advantages – keeping together combinations of genes that are advantageous to the species
Translocations

• A translocation is a chromosomal mutation in which there is a change in position of chromosome segments to a different location in the genome. No gain or loss of genetic material is involved in a translocation.
Reciprocal translocations

(a) Possible origin of a reciprocal translocation between two nonhomologous chromosomes

(b) Synapsis of translocation heterozygote

(c) Two possible segregation patterns leading to gamete formation
Familial Down syndrome

Example of translocation in humans
Fragile X chromosome – Martin-Bell syndrome

Frequency of 1/400 males and 1/8000 females (condition not always expressed when heterozygous. FMR-1 gene, a case of anticipation.)