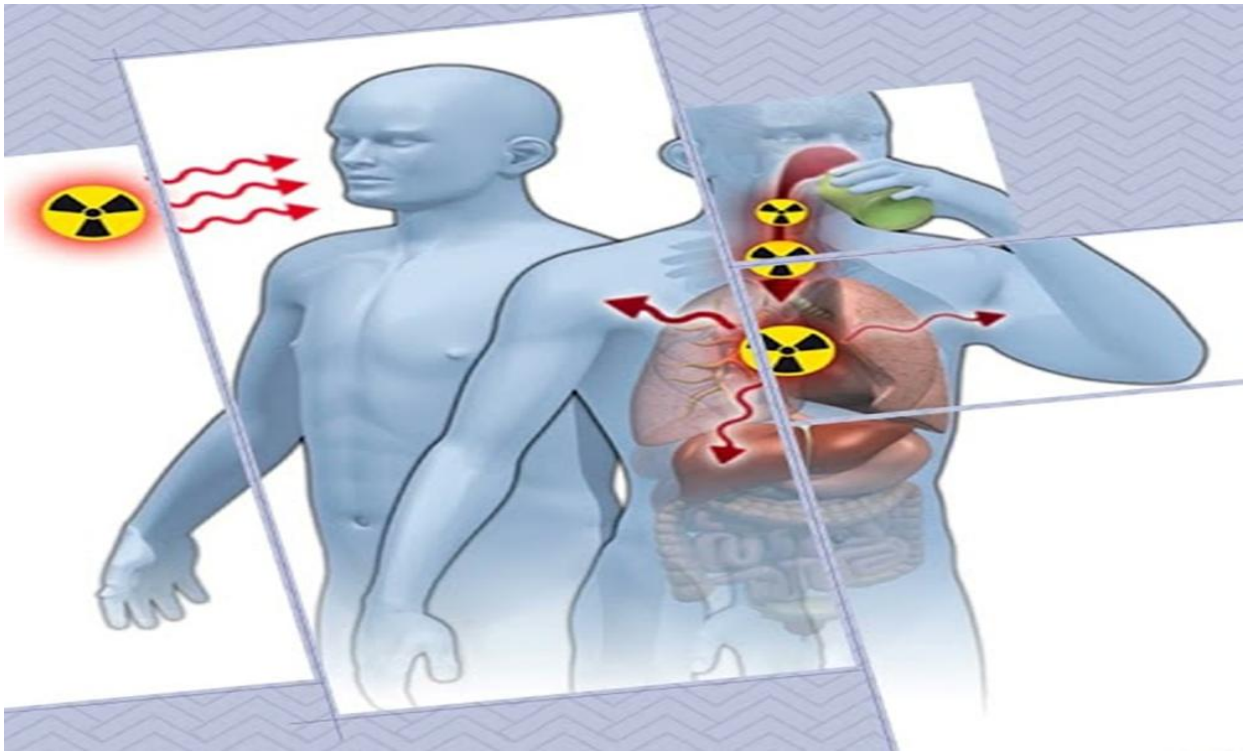
Cytogenetic Effects
6th Lecture



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Teaching of Biological Radiation hazards

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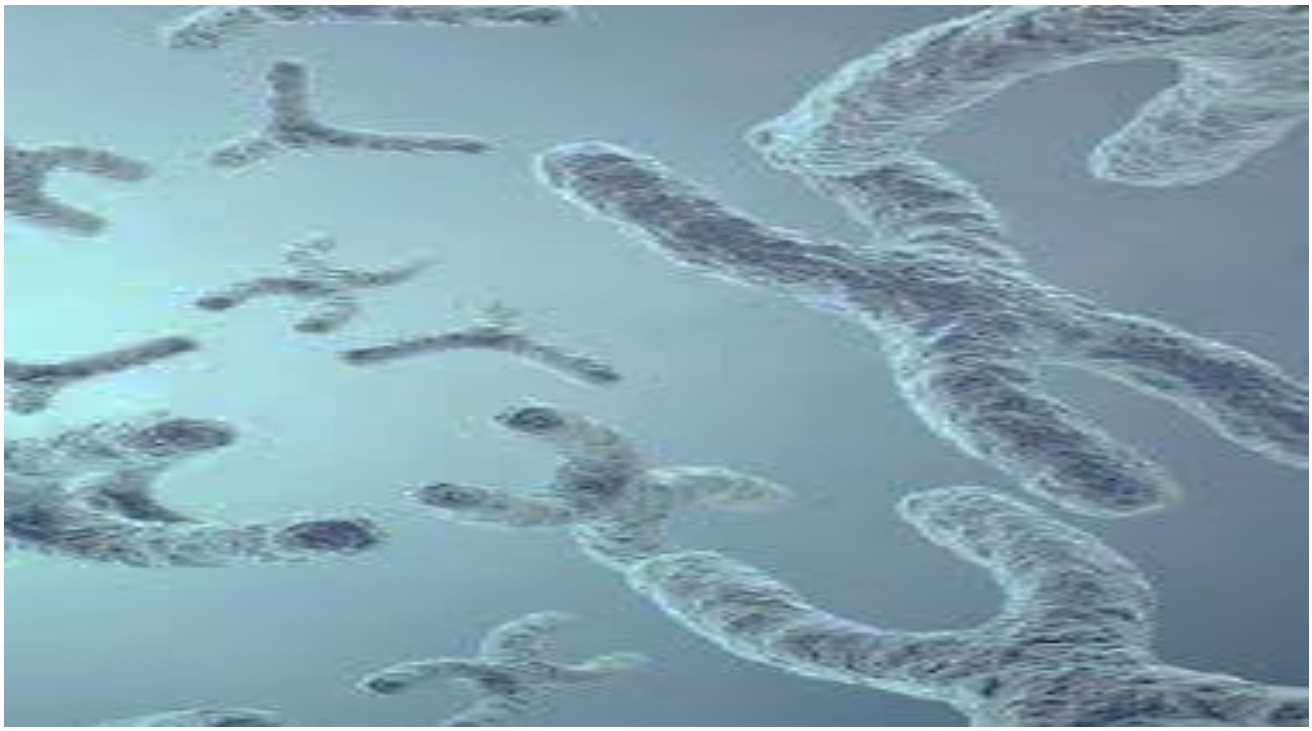
Cytogenetic effects

refer to changes in chromosomes, such as breaks, rearrangements, or extra or missing chromosomes. These effects can be caused by genetic disorders, environmental exposures, or certain chemicals and are often indicators of disease, including some types of cancer. Cytogenetics, the study of these effects, is used to diagnose conditions, plan treatments, and monitor the efficacy of therapies by analyzing samples of tissue, blood, or bone marrow.



- **Chromosomal abnormalities:**

  Cytogenetic effects include any changes to chromosomes, which are structures of DNA that carry genetic information.

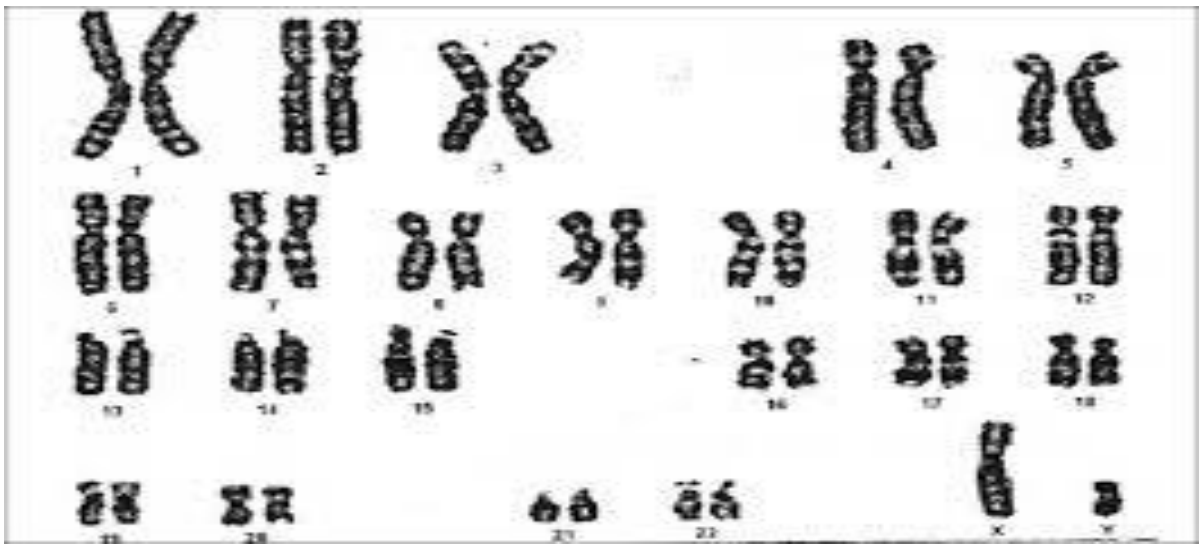
- **Common examples:**

- **Aneuploidy:** Having an extra chromosome (like in Down syndrome, trisomy 21) or a missing chromosome (like in Turner syndrome, monosomy X).

- **Structural abnormalities:** Broken, rearranged, or deleted chromosomes.

- **Detection:**

Scientists can detect these changes by examining chromosomes in a laboratory setting using techniques like banding.



Causes of cytogenetic effects

- **Genetic diseases:** Some genetic conditions are directly caused by chromosomal abnormalities.

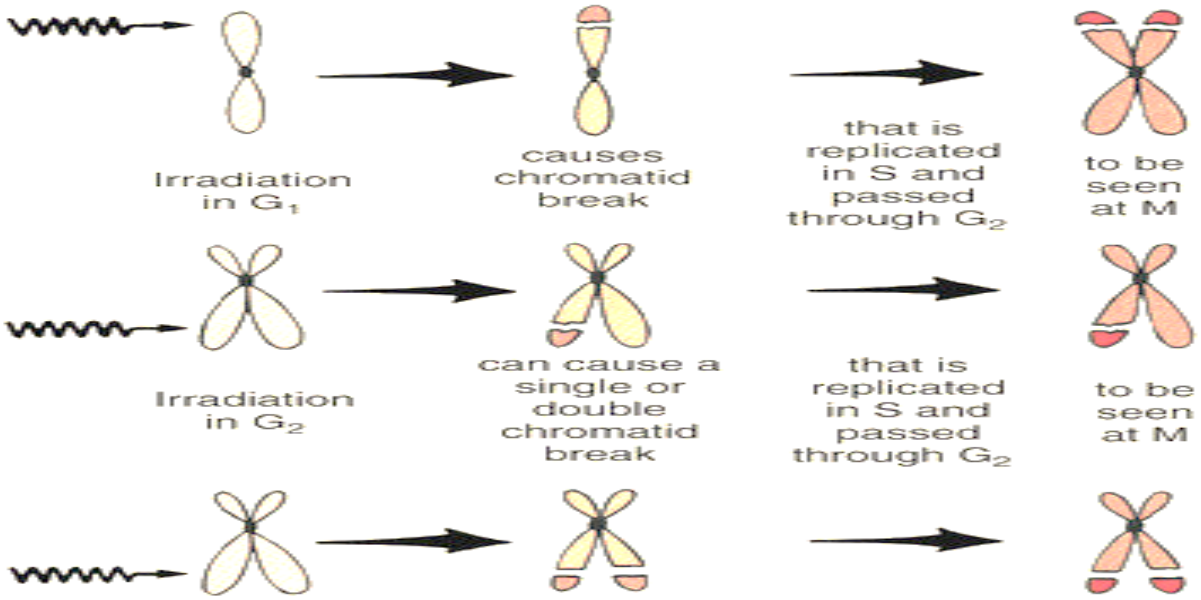
- **Environmental and chemical exposure:** Exposure to certain substances can cause cytogenetic changes. Examples include:

- **Radiation:** Exposure to ionizing radiation can cause chromosomal damage.

- **Chemicals:** Some pesticides and formaldehyde have been shown to cause cytogenetic changes in studies, such as increasing micronuclei frequency in cells.
- **Nanoparticles:** Some nanoparticles can generate reactive oxygen species and may cause negative effects on cells and chromosomes.

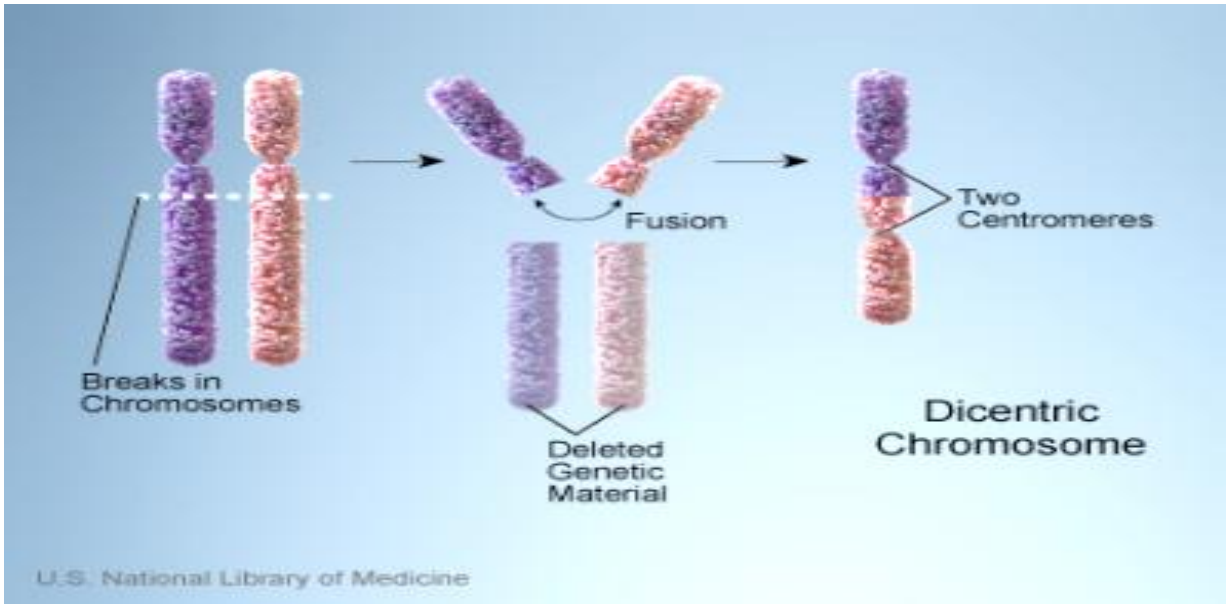
Single-hit chromosome aberrations

Are structural changes caused by a single ionizing event, most common when a cell is in the prophase stage, where a chromosome has two sister chromatids. At this stage, a single hit can break one or both sister chromatids. Examples include a single chromatid break, and the resulting aberrations are often deletions, though two-hit events can occur from a single hit if the broken ends of sister chromatids fuse.



Multi-hit chromosome aberrations

Are structural changes in chromosomes that result from multiple breaks and incorrect rejoining, leading to more complex damage than single-hit aberrations. They are often induced by high-energy, densely ionizing radiation, such as alpha particles, and can involve three or more breaks in two or more chromosomes. Examples include complex exchanges, which can be formed as a product of the repair of this damage.



Kinetics of Chromosome Aberration Formation

The kinetics of chromosome aberration formation describe how fast or slow chromosome changes appear over time after radiation exposure. This process is affected by how well the cell repairs DNA damage.
Simple aberrations usually increase in a straight-line (linear) pattern with dose, while more complex ones follow a curved (non-linear or linear–quadratic) pattern because different repair systems work at the same time.
DNA repair often happens in **first-order reactions**, meaning the repair rate depends on how many DNA breaks exist. The overall speed of formation depends on the **type of aberration**, **radiation dose**, and **cell type**, since some aberrations appear quickly while others last through several cell divisions.

Factors Affecting Aberration Kinetics

1. Repair Kinetics

- The main factor is how double-strand breaks (DSBs) in DNA are repaired, since these breaks cause most aberrations.

- Repair usually follows **first-order kinetics**, where the repair speed depends on how many breaks are present.
- Some repairs happen very quickly, while others (like those involving DNA fragments without telomeres) are slow or incomplete, according to *ScienceDirect* and the *National Institutes of Health (NIH)*.

2. Type of Aberration

- The kind of aberration affects how quickly it forms and disappears.
    - **Fast formation:** Complete exchanges such as *dicentrics* can form quickly and survive cell division without being removed.
    - **Slow formation:** Incomplete aberrations like *terminal translocations* may decrease over time as they get repaired or eliminated.

3. Radiation Dose

- The amount of radiation changes the speed of aberration formation.
    - **Low doses:** Aberrations can appear almost immediately.
    - **High doses:** Some aberrations increase in number more slowly, following a pattern similar to DSB repair over time.

4. Cell Type

- Different cell types repair DNA at different rates.
    - **Resting (quiescent) cells** often repair faster than dividing cells.
    - **Repair-deficient cells**, like those from people with *ataxia-telangiectasia (AT)*, repair more slowly and make more errors.

5. Cell Cycle Progression

- The stage of the cell cycle during exposure and analysis affects the number of aberrations seen.
    - For example, **mitotic delay** (a pause before cell division) can increase the number of abnormal cells seen in mitosis later on.