Etiology of chromosomal aberrations

Chromosomal aberrations

1. Abnormalities in chromosome number
    1. aneuploidy
        - monosomy
        - trisomy (or tetrasomy, pentasomy...)
    2. polyploidy
        - triploidy
        - tetraploidy,...
2. Abnormalities in chromosome structure
    1. balanced
        - translocation
        - inversion
        - insertion
    2. unbalanced
        - deletion (incl. ring chromosome)
        - duplication
        - isochromosome

Etiology of congenital chromosomal aberrations

- Origin of aneuploidies and polyploidies (see question No. 34 – Abnormalities in chromosome number, their causes and clinical presentations in man)
- Origin of structural aberrations:
    - chromosome breaks and rearrangements during gamete formation (in meiosis) or in pre-gametic mitotic divisions of gonadal cells – resulting in stable products having one centromere and two telomeres
        - one centromere is necessary for regular segregation in mitosis (unstable dicentric chromosomes undergo secondary rearrangements)
        - telomeres maintain the integrity of the ends of linear chromosome structure (in deleted chromosomes new telomeres are added by **telomere synthesis or by mechanism of telomere capture)
    - causes of spontaneous breaks – see below (external effects)

Etiology of acquired chromosomal aberrations

(= chromosome breaks and rearrangements during mitotic divisions of somatic cells)

External effects (physical, chemical, biological)

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    - random environmental factors – spontaneous breaks (UV light, ionizing radiation – cosmic rays, medical radiation (X-rays), drugs, viral infections)
    - professional exposition (mutagens: chemicals – alkylating agents, intercalation substances...; radiation)
    - oncological treatment (chemotherapy, radiotherapy)

Hereditary syndromes of chromosome instability

- congenital defects of repair mechanisms - mostly double-strand DNA breaks repair
- rare genetic disorders with AR inheritance, higher predisposition to cancer development
- higher level of chromosome breaks and rearrangements detected in cytogenetic analysis
    - ataxia teleangiectasia (defect of ATM gene - important for double-strand DNA breaks repair)
    - xeroderma pigmentosum (defect of nucleotide excision repair)
    - Bloom syndrome (extreme genome instability, high level of sister chromatid exchanges - SCEs, high frequency of mutations)
    - Fanconi anemia
    - Nijmegen breakage syndrome

Methods of analysis of acquired chromosomal aberrations (see question No. 31 – Methods of chromosomal examination)