



POSNA

The Core Curriculum

Chromosomal disorders

Objectives

1. Define: diploid (euploid), aneuploid, polyploid, monosomy, trisomy, translocation, duplication, deletion
2. Describe mitosis
3. Discuss the processes responsible for common chromosomal disorders
4. Describe the chromosomal status of children with Down's syndrome
5. Discuss the relationship between translocation and malignancy

Discussion point

1. How is chromosomal analysis performed?

Discussion

Chromosome disorders are common, and account for a large number of spontaneous abortions. The normal human cell is diploid, with 46 chromosomes present in each cell, including 2 sex chromosomes. Polyploidy refers to multiples of the number of chromosomes, and aneuploidy refers to a chromosome number that is not an exact multiple of the haploid set. Cancer cells commonly demonstrate aneuploidy. Monosomy refers to a condition where one member of a chromosome pair is absent, and trisomy to a condition where one chromosome is present in 3 copies. Parts of chromosomes may be displaced from their normal location by translocation, in which a chromosome segment is transferred to another non-homologous chromosome. Duplication implies that part of a chromosome is repeated, and deletion implies part of a chromosome is missing.

Mitosis is the process of cell division. Prophase denotes that chromosomes are being replicated, in prophase, chromosomes become visible microscopically. In metaphase, the chromosomes are aligned at the equator of the cell; and in anaphase, the chromosomes migrate toward opposite poles. Cytokinesis begins during telophase. Chromosomal analysis of cells is most frequently performed during metaphase. A mitosis-inducing agent is added to cells (blood, skin, placental, etc.) and colcemid is then added to stop cells in metaphase. Advances in cytogenetic techniques now allow specific parts of chromosomes to be labeled, and make analysis more accurate. Symbols are used for chromosomal analysis, including "t" for translocation, "dup" for duplication and "del" for deletion. In patients with Ewing's sarcoma, translocation of material from the DNA binding domain of the FL 11 gene (11q24) with material from the transactivation domain of the EWS gene (22q12) occurs. This translocation is designated as t(11;22) [q24;q12].

Chromosomal translocations are the type of rearrangement most often seen with the malignant phenotype. Errors in mitosis or meiosis (division of genetic material of sex chromosomes) can result in trisomy or monosomy. Tetraploidy is lethal, as is trisomy in most instances. Trisomy 21, or Down syndrome, is the most common phenotype compatible with life. Monosomy of the X chromosome is expressed as Turner syndrome; trisomy of the sex chromosomes is expressed either as Klinefelter (XXY) or XYY syndrome. XXX syndrome results in a phenotypically normal female. Deletions of chromosome 15 are associated with Prader-Willi syndrome. Fragile X syndrome is characterized by the lower tip of the X chromosome appearing partially disrupted.

References

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