

GENETIC DISORDERS IN RELATION TO SURGERY

Essay

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INTRODUCTION

Nowadays there is an increasing awareness of the importance of genetic factors in the aetiology and pathogenesis of many disorders affecting man. Perhaps of more importance is that this knowledge has also led to possible means of prevention of such disorders through genetic counselling and antenatal diagnosis. It is useful to consider human diseases as forming a spectrum. At one extreme there are those conditions almost entirely genetic in origin such as Down's syndrome, where the environment seems to play no direct part in aetiology.

At the other end of the spectrum are those diseases such as infections and nutritional deficiencies which are entirely environmental in aetiology. Between the two extremes there are many fairly common conditions which are partly genetic and partly environmental in causation such as pyloric stenosis and spina bifida, in which both genetic and environmental factors are involved. (Emery, 1979).

Genetic defects are present in more than one per cent of all neonates, although some of these are not diagnosed in the neonatal period. The best estimate suggests that the aetiology of human malformations may be distributed as follows:-

15 percent are of demonstrable genetic origin, 10 percent result from chromosomal aberrations, 10 percent are of viral or teratogenic origin; and 65 percent are of unknown origin. Most of the unknown origin group probably results from complicated interactions between genetic predisposition and subtle factors in the intrauterine environment. Some will remain attributable to simple mechanical accidents in utero (Fraser, 1959).

BASIC TERMS AND CONCEPTS

The Cell :

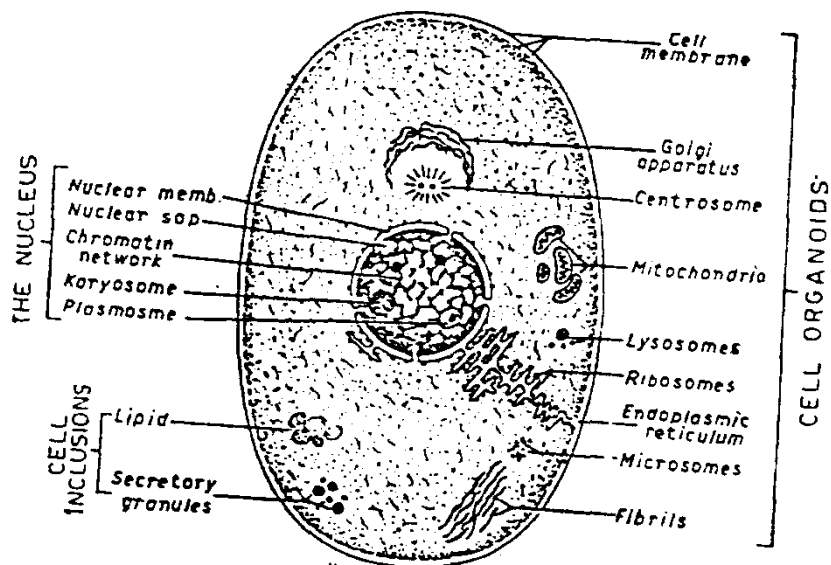
It is a functional unit of all tissues. The cell is composed of two basic parts, cytoplasm and nucleus. In cytoplasm there are two structures, organelles and inclusions. The term organelle means little organ, each organelle performs various functions which are essential to life and metabolism of the cells. The organelles can be classified into membranous and non membranous organelles. The membranous organelles are. The cell membrane or plasma membrane, the mitochondria, the Golgi apparatus, The Lysosomes, and the endoplasmic reticulum. The non membranous cytoplasmic organelles are: Ribosomes, Centrioles (Centrosomes), Cilia, Flagella, microtubules and microfilaments. The cell inclusions are temporary components of certain cells and usually are accumulations of. pigments, carbohydrates and other stored elements. The nucleus consists of four parts : nuclear membrane, nucleolus, nucleoli and chromatin network. Each somatic cell nucleus contains 46 chromosomes which are as follows :-

- 22 Pairs of similar chromosomes known as autosomes.
- One pair of sex chromosomes which differ in the two sexes. (xx chromosomes in female and xy chromosomes in male).

(Brachet, 1961).

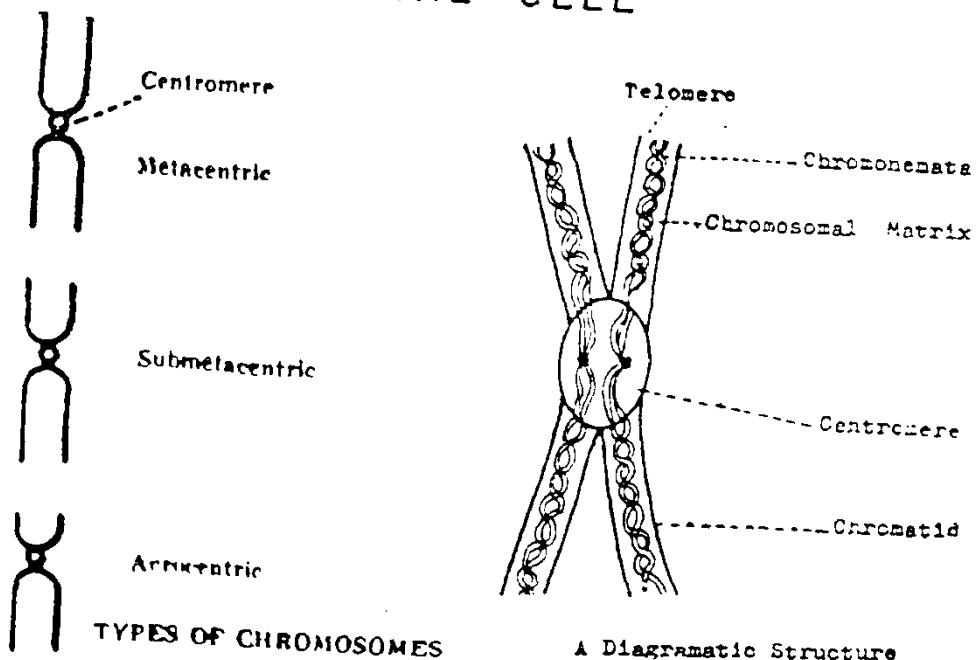
Cell Division :

The process of cell division involves both division of



(Fig. 1)

THE CELL



A Diagrammatic Structure
Of One Chromosome

(Fig. 2)

SPOTLIGHTS ON MEDICAL GENETICS, Fourth Edition, 1952.

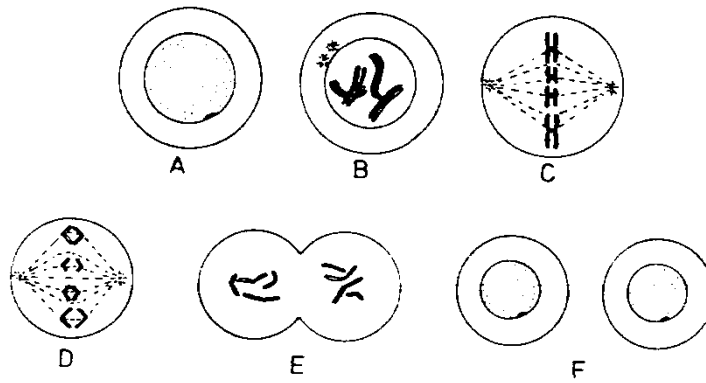
Cell division :

The process of cell division involves both division of the cytoplasm (cytokinesis) and division of the nucleus (Karyokinesis). Cytokinesis and karyokinesis usually occur together, but karyokinesis can occur without cytokinesis resulting in the formation of a cell which is binucleate (or multinucleate after several karyokinesis), e.g., some liver cells and megakaryocytes. There are two modes for division of the nucleus. (Lesson, 1975).

1) Mitosis :

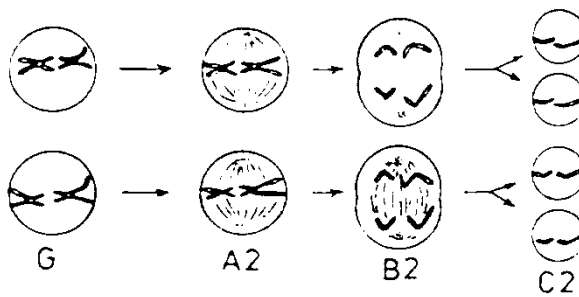
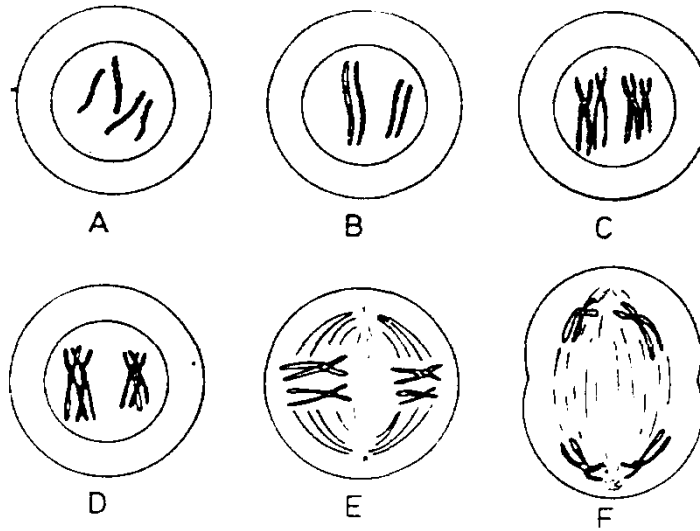
It occurs in the somatic cells, each new cell will contain a full number of chromosomes i.e. the same amount of genetic material. Mitosis can be divided into stages. These stages are known as interphase, prophase, metaphase, anaphase and telophase.

Interphase is the resting stage between nuclear divisions, by the end of which each chromosome had divided longitudinally into two chromatids, which remain attached to each other at the centromere. The changes which occur during mitosis involve. Changes in the cytoplasm, mitotic spindle is formed by the centrioles. This to bring the chromosomes to the centre at first then to each pole of the cell.



Mitosis

A- interphase B- prophase C- metaphase
D- anaphase E- telophase F- interphase



Meiosis

A - leptotene B - zygotene C - pachytene
D - diplotene E - metaphase I F - anaphase I
C - telophase A₂ metaphase II B₂ anaphase II
C₂ telophase II

(Fig. 3)

SPOTLIGHTS ON MEDICAL RESEARCH, Fourth Edition, 1982.

Changes in the nucleus: the chromatin network forms 46 chromosomes. Each chromosome is formed of two chromatids which separate from each other. Half of these chromatids move towards each end of the dividing cell. Then each chromatid forms a chromosome. Thus at the end of mitosis a cell has divided into two daughter cells each with an identical genetic constitution. (Fig. 3).

2) Meiosis :

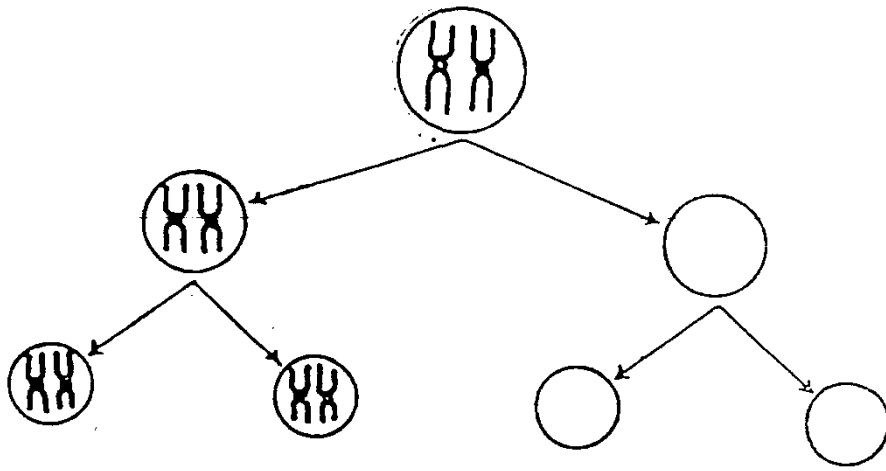
The process by which the chromosome number is halved during gametogenesis is known as meiosis. Although meiosis involves two division stages, the chromosomes divide only once, each gamete normally receiving either of a pair of homologous chromosomes. Each of the two steps in meiosis has a prophase, metaphase, anaphase and telophase stage as in mitosis. During prophase of the first meiotic division the chromosomes become tightly coiled, and homologous chromosomes come together and pair along their length. Following prophase the sequence of events is essentially similar to that occurring in mitosis except that during this first meiotic division the centromere does not divide. Instead the members of each pair of homologous chromosomes migrate to opposite poles of the nucleus so that each daughter nucleus receives only one member of each pair and therefore bears a haploid chromosome complement. In the second stage of meiosis the

centromere divides and the chromatids of each chromosome separate and migrate into different nuclei. Thus each daughter cell from the first meiotic division has in turn divided to form two identical cells. Meiosis therefore results in each gamete having a haploid number of chromosomes and receiving one or the other member of each homologous pair of chromosomes and the genes it bears. (Emery, 1979).

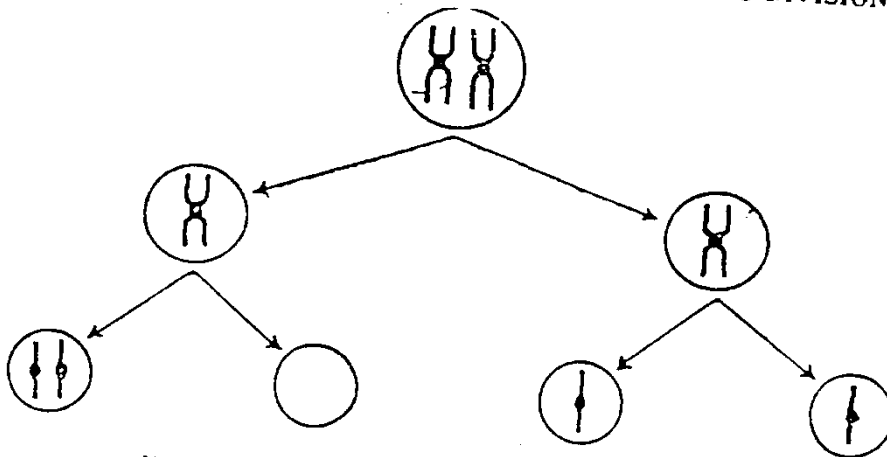
A Abnormalities in cell division :-

1- Non disjunction.

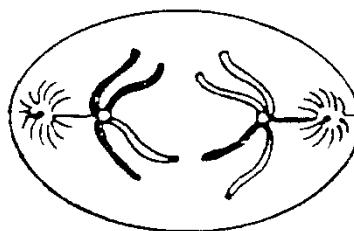
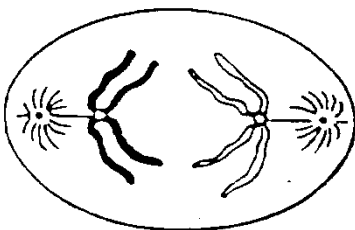
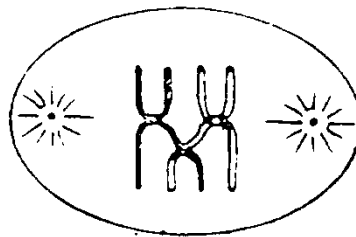
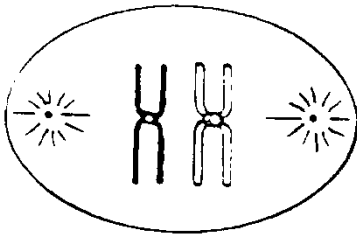
During normal cell division, each daughter cell receives an exact number of chromosomes, (either a copy of each chromosome in mitosis) or one of each pair of the chromosomes in meiosis. If abnormal division of the centromere occurs, non-disjunction of the chromosomes will be the result. This will be followed by failure of migration of one or more chromosomes to the dividing cells. Thus one daughter cell may receive both chromosomes, and the other daughter cell will receive nothing. If during mitosis, a centromere fails to divide and one daughter cell receives both sister chromatids, then the resulting somatic cell will eventually have three copies of that one chromosome and will be trisomic; while the daughter cell would eventually contain only a single copy of that chromosome and thus be monosomic for a single chromosome.



NONDISJUNCTION IN THE FIRST MEIOTIC DIVISION



Nondisjunction In The Second Meiotic Division



Normal Meiotic
Cell Division

Meiotic Division
With Crossing Over

(11.4)

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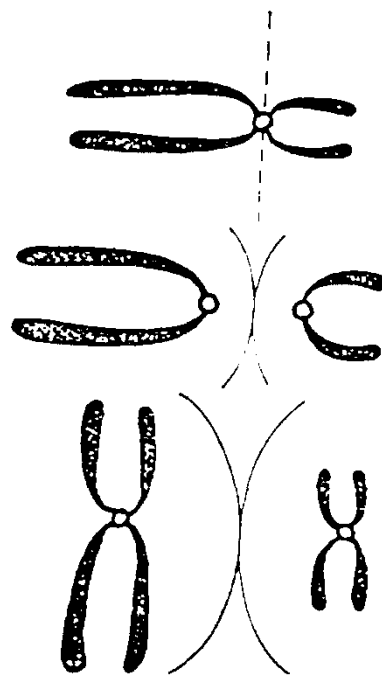
When non-disjunction occurs during meiosis, then the gametes will contain an extrachromatid or one too few chromatids, and if participating in a fertilization, the offspring will be trisomic or monosomic for the involved chromosome.

If non-disjunction occurs at the first meiotic division all the four gametes are abnormal, two having an extra chromosome and two deficient of chromosomes. If non-disjunction occurs at the second meiotic division, only two gametes are abnormal and the other two will have normal haploid number of chromosomes. If non-disjunction occurs late in somatic development of cells, the individual is a "mosaic", some of his cells contain the normal chromosome number, another type of his cells are deficient from chromosomes and third type of his cells being with extrachromosomes. Cells containing abnormal number of chromosomes are said to be aneuploid; cells with the proper number of chromosomes for that species are euploid. (Fig. 4).

2- Misdivision of centromere (Isochromosomes):

Normally the centromere divides longitudinally giving rise to two identical chromatids. Sometimes abnormal transverse division may occur. This misdivision of the centromere will give rise to non similar chromatids. These non identical chromatids change in the daughter cells into isochromosomes

Misdivision of Centromere



Isochromosomes

(Fig. 5)

SPOTLIGHTS ON MEDICAL GENETICS. Fourth Edition, 1982.