SOME GENETIC ASPECTS IN MALE INFERTILITY

THESIS

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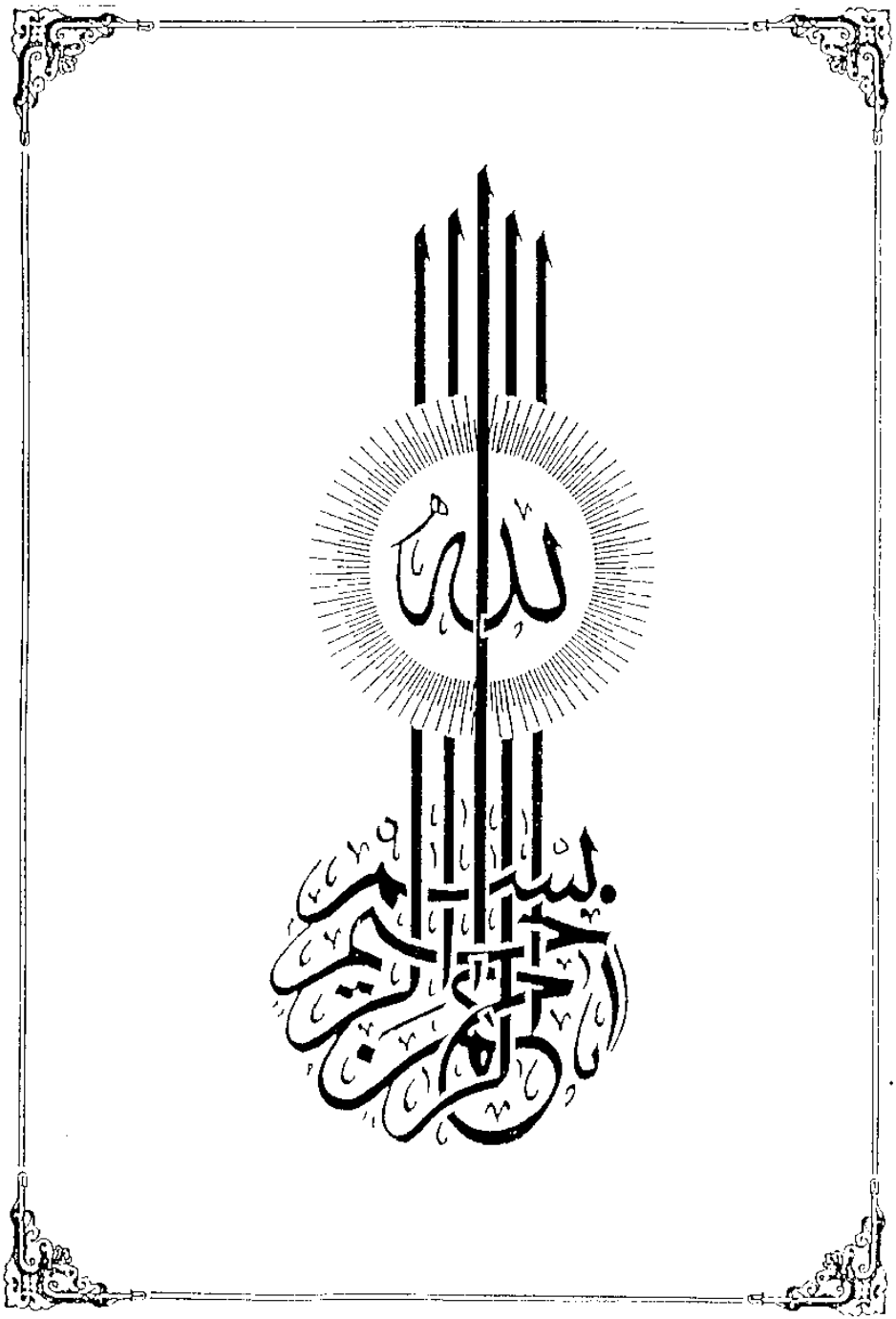
A C K N O W L E D G E M E N T



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Aziza Erian

Content

INTRODUCTION

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Infertility constitutes a problem to about one in every ten marriages and in one third of the cases it is due to the male partner "Departmental committee on human artificial insemination, (1960)".

The term infertility in man includes both subfertility and absolute sterility; biologically, it implies that the capacity for producing offspring is diminished (Penrose, 1963). Del Castillo et.al., (1947), Girgis, etal., (1969) found that 55% of azoospermic cases were due to obstruction, while the remaining 45% were due to functional azoospermia, 6% to 15% from the functional azoospermia are due to chromosomal abnormalities (Kjessler, 1972).

The majority of chromosome aberrations causing male infertility are sex chromosome abnormalities. The Klinefelter syndrome or its variants constitutes the largest abnormality, incidence reaching 6% to 7% of patients attending male infertility clinics (Koulischer and schoysman, 1974). Male Turner's syndrome, xyy syndrome and others due to gene defect as testicular feminizing syndrome. (Ferguson - Smith, etal., 1960).

In this study, we try to review all the available litterature about the role of genetic factor in the etiology of these genetically determined syndromes and its relation to male infertility.

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CHAPTER I

BASIC GENETICS

A human being originates from the union of two gametes, an ovum and a spermatozoon, which contain all the inherits from his or her parents. The bearers of these hereditary information are the genes being arranged on a set of long fine filamentous structures present in the nucleus of the cell and are known as the chromosomes.

The human chromosomes are 46 (Tjio and Levan 1956). Each two chromosome are identical and carry the same genes thus can be better considered as 23 pairs, 22 of these pairs are similar in both male and female and are known as the autosomes in contradistinction to the last pair which is different and is referred to as the sex chromosomes (Ford & Hamerton 1956).

In the female the sex chromosomes are identical (homologus) and are given the symbol x, thus the female constitution is (46, xx), while in the male there is one x chromosome; the other is a smaller one called the y chromosome, thus the male chromosome constitution is (46, xy).

During embryogenesis and throughout life, the cells have to divide preserving the original hereditary informations which has been received. To achieve this goal, each chromosome had laid alongside itself an exact copy containing duplicates

of all the genes it bears. Thus a chromosome consist of two complementary structure (chromatids) attached together at one spot (the centromere), when cell division take place each chromatid passes to each daughter cell. Thus, the daughters cells contain the very seme twenty three pairs of chromosomes, bearing up on their length the very same amplement of genes. This type of division is referred to as mitotic division (Swanson, 1957). In order to preserve the kind, an organism has to reproduce. Reproduction is either asexual where the daughter organism receives its genetic constitution from only a single parent or sexual where the daughter cell receives its genetic contribution from more than one parent, therefore differs from either parents though derived from them. Since sexual reproduction is carried by fusion of cells and in order not to duplicate the number of chromosomes which characterizes the species, specific cell undergo a special type of cell division called the reduction division or meiotic division, in which the chromosome pairs separate so that the daughter cell (gametes) contain only the haploid number of chromosome (23). On fertilization the original number 46 (23 pairs) is restored again (Roberts, 1974).

Cell Division

Two distinct events occur in cell division, the division of the nucleus (Karyokinesis) and the Cytoplasm (Cytokinesis)

which are usually coupled. Three types of nuclear division occur. The first is the amitotic or direct division in which the nuclear material is randomly distributed to the resultant cells. In man this type of division is restricted to pathological condition. The other types are more complex and referred to as the indirect division. They comprise, the mitotic and meiotic division. (Gray, 1973).

o Mitosis :

Occurs in most somatic cells and result in the distribution of identical copies of the parent cell as regards its genetic constitution. The nuclear changes which achieve this distribution are divided into four phases.:

I. Prophase :

The strands of chromatin, which are highly extended, begin to shorten and thicken, forming two chromatids joined together by the centromere. Outside the nucleus, the two centrioles begin to separate and each move toward one pole of the cell. Microtubules are synthesized between them to create the central spindle while others radiate out from the centrioles to form the astral rays. Towards the end of the prophase the nuclei

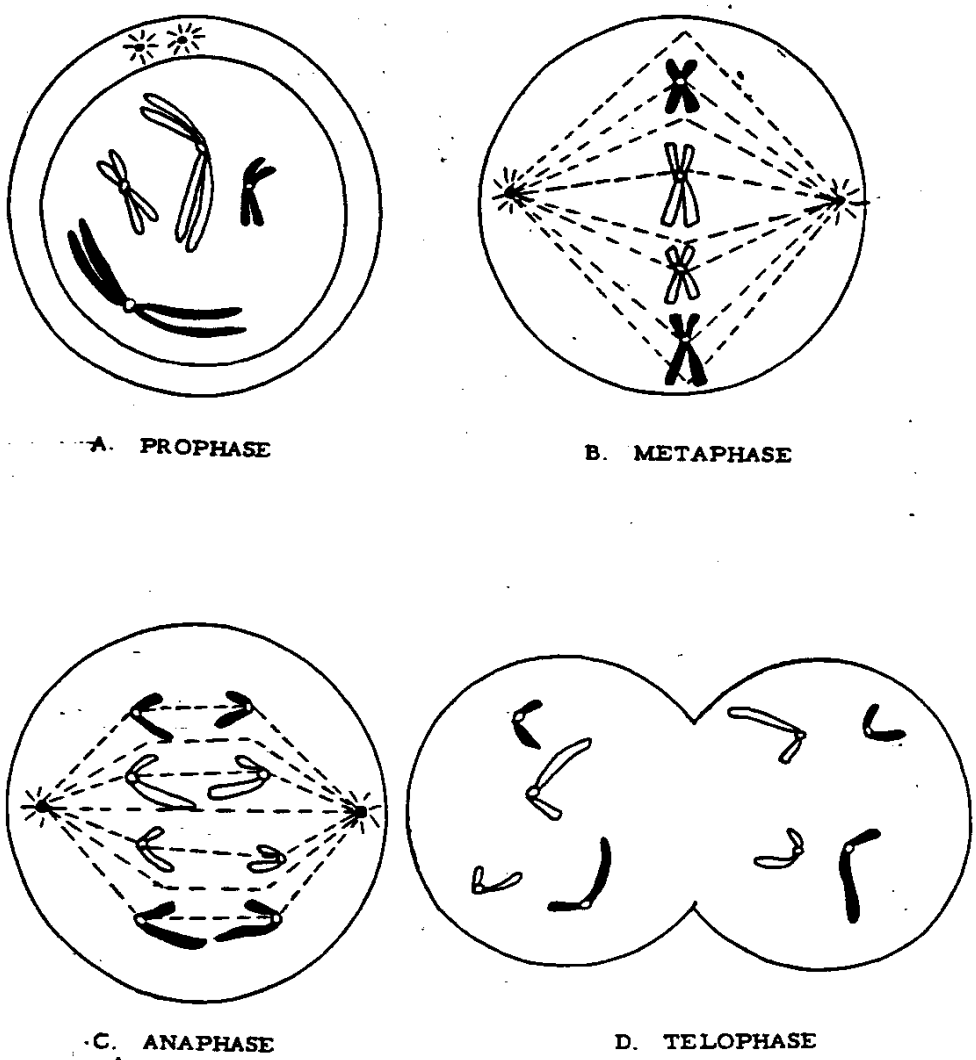

Figure 1 Mitosis. Two of 23 pairs of chromosomes are shown passing through the four stages. Observe that single-stranded chromosomes separate at cell division. See text.

Zellweger, H., and Simpson Jan (1977)

disintegrate and disappear. The termination of this stage is marked by a sudden breakdown of the nuclear envelope, to release the chromosomes.

II. Metaphase :

As the nuclear envelope disappears, the spindle microtubules invade the central region of the nucleus while the chromosomes move towards the equator of the spindle (a period known as Prometaphase) Once arriving to equatorial plate, the chromosome becomes attached with their centromeres to be microtubules and are arranged in a star-like ring when viewed from either pole of the cell.

III. Anaphase :

The centromere is a double structure, it now separates thus each chromosome splits into two chromatids. These move apart towards each pole, the microtubules being an essential guide for this movement to occur.

IV. Telophase :

Chromosome become grouped at either pole of the cell, both groups being diploid in number. The chromosomes now re-extend and a nuclear envelop

reappears. The nucleoli also reappear.

Meanwhile, the cytoplasmic division which start early in anaphase, is now completed leading to equal distribution of the cytoplasmic mass including the cell organelles, to both daughter cells. (Mazia D., 1961), (Swanason, 1957).

o Meiosis :

Meiotic chromosome investigation early done by simple squash preparation made from small pieces of testicular tissue (Ford and Hamerton, 1956; Falek and chiarelle, 1968) This study shows two critical events which occur in meiosis :

1. Pairing of the homologus chromosome.

2. Two successive division of nuclear material so that the resulting cells have only 23 chromosomes rather than (46).

First Meiotic Division :

I Prophase :

The important events in meiotic prophase that do not occur in mitotic prophase are that the chromosomes pair (synapse) and that the strands of the paired chromosomes

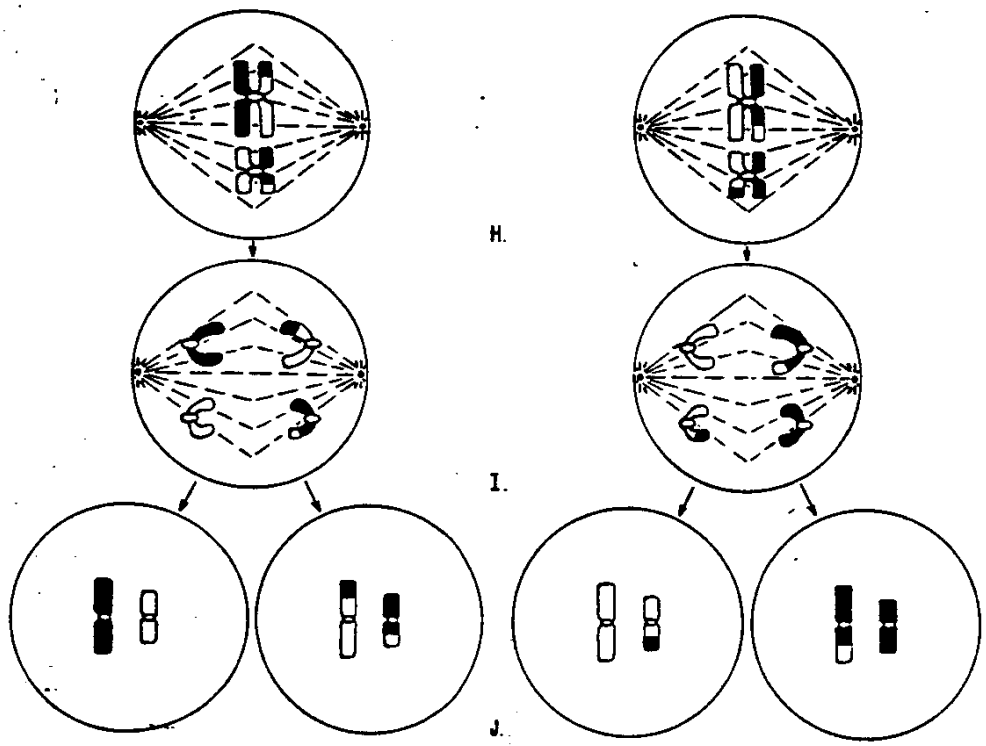

Figure 3. Second meiotic division: H. Metaphase; I. Anaphase; J. Telophase. The 23 double-stranded chromosomes now separate into 23 single-stranded chromosomes.

Zellweger, H., and Simpson Jan (1977)

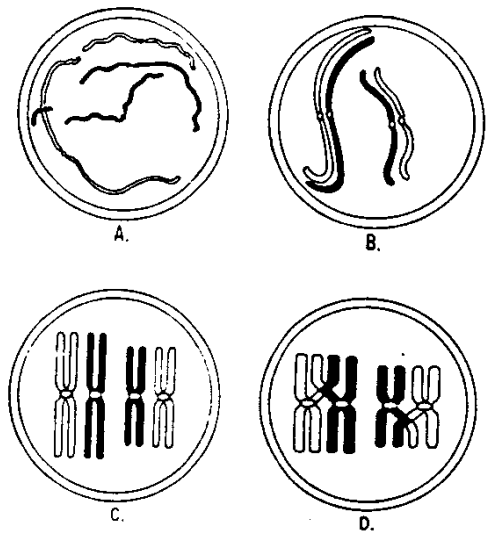

Figure 3. Prophase of the first meiotic division. Two of 23 pairs of chromosomes are shown in the stages of prophase: A. Leptonema; B. Zygonema; C. Pachynema; D. Diplonema. Diakinesis is not illustrated. Note that there is pairing of homologous chromosomes and crossing over. See text.

Zellweger H. and Simpson J. (1977)