# THE EFFECT OF SOME FACTORS ON METAPHASE CHROMOSOMES IN MAMMALS

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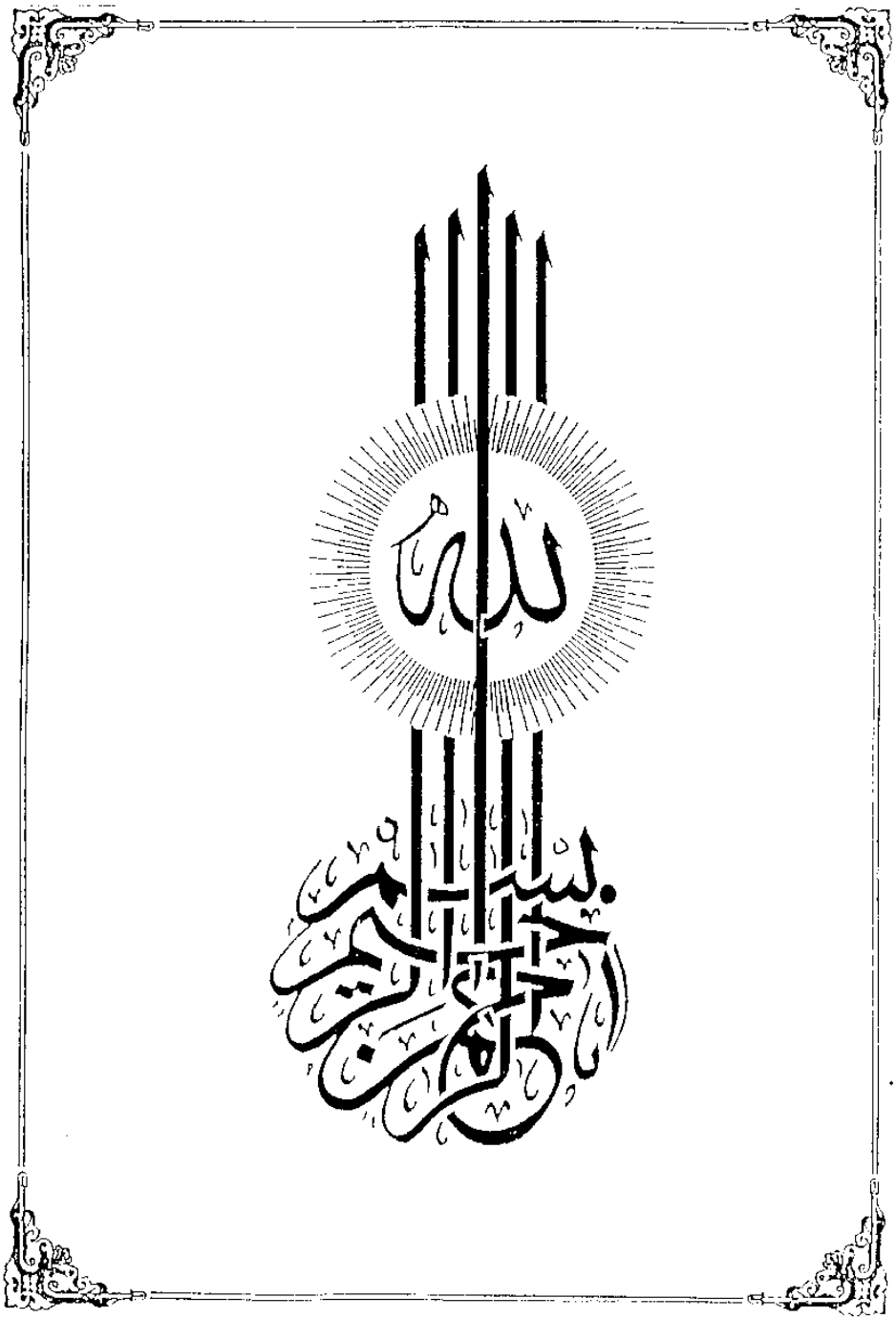

CONTENTS

## INTRODUCTION

The study of human genetics on the cytological level has recently attracted the attention of a large number of investigators. The first approach was carried out on metaphase chromosomes prepared from various tissues of the human body.

In 1956 Ford, et al, selected the active bone marrow for demonstrating human metaphase chromosomes through the use of the squashing technique. They stained the preparations with Feulgen nuclear stain to verify the presence of DNA.

Other authors could induce in vitro mitosis of already differentiated cells. This was accompanied by a special treatment to trap the dividing cells at the metaphase stage.

Nothtle and Simmonvitch (1958) could obtain metaphase chromosomes from kidney cells that were grown in vitro.

Metaphase chromosomes were also prepared by Jerguson (1962) from cells obtained through skin biopsy.

Metaphase chromosome preparations received a very successful push through the [illegible] technique. Moorhead,

et al, in 1960. Leucocytes obtained from peripheral blood were stimulated to undergo mitosis in vitro. The cultured leucocytes were used to obtain metaphase chromosomes. This discovery of Moorhead et al, was followed by a vast number of attempts to obtain metaphase chromosomes that are suitable for cytological study.

That important discovery was followed by a vast number of trials that aim at increasing the number of chromosome metaphases as well as a state of better spreading of the obtained metaphase chromosomes and hence a better chance for their examination.

Hastings, et al, (1961) devised a method for differential separation of leucocytes through the trapping of polymorphonuclear cells prior to cell cultivation.

Other investigators including Fox, et al, (1961) and Schern (1962) as well as many others tried to expose the cultured cells to various physical conditions that were believed to improve the state of spreading of the metaphase chromosomes.

In our country certain difficulties were encountered in the course of chromosome preparation by the standard method. This lead Ibrahim et al (1964) to establish a

method for leucocyte cultures that fits more with the conditions of a moderately equipped laboratory.

Human chromosomes, thus being examinable by the light microscope, they received a further attention. Their accurate number was determined they were classified into groups, each having a special common features among its members; the sex chromosomes were identified. This was first internationally achieved in the historic meeting at Denver in 1960. That meeting resulted in the standard system of Nomenclature of the Human Chromosome Karyotype.

Many authors were interested in Denver system in one way or another.

In 1961 Lennox simplified the method of classification in a manner that is known at beginners in this field of study.

Barr (1961) criticized the Denver system for nomenclature and proposed some additional modifications. Nevertheless, he claimed that the Denver classification was still the most validated for human chromosome karyotyping.

An international conference was held in London (1963) and another one in Chicago (1966) to discuss

the classification of the human metaphase chromosomes. These international meetings still take the Denver system as a standard system, yet they suggested some observations to denote any deviation from normality in a particular chromosome or chromosome group.

This was followed by innumerable attempts to detect the chromosomal karyotypes in cases showing one or another developmental abnormality of the congenital type. Through these studies several abnormal karyotypes were identified in a variety of syndromes.

Recently, the need for a better understanding of the cause of unexpected chromosomal figures was felt. Therefore, the uncommon chromosome morphology which could be spotted in variable pathological and accidental circumstances was reported and defined. This stimulated a classification of the varieties of chromosomal damage and a definition for each variety.

The pathological conditions where chromosomal damage was described include cases with infective diseases, cases with anaemia as well as cases with a family history of malignant tumours.

Aula (1963) reported chromosomal breaks in patients with chickenpox.

Gripenberg (1965) carried out a study on the chromosomes of 20 patients with various virus infections.

Chromosomal aberration in pernicious anemia was reported by Kiossogolou, et al, in 1965.

In 1968, Bloom and Diamond studied the metaphase chromosomes of children with different varieties of hemolytic disorders other than leukemia.

Merz, et al, (1968) discovered chromosome mismatching in individuals with a family history of tumours.

In 1972, Kucherova and Byshovets could spot chromosomal breakage in patients with influenza.

Chromosomal damage through administration of chemicals includes the work of Ramanna and Natarajan, Richmond and Kaufmann, and Sanosh.

Ramanna and Natarajan (1966) lead an experimental study on the effect of the cytotoxic agents alkyl-alkane sulfonates on chromosomes of barely under different conditions of temperature and pH.

Richmond and Kaufmann (1969), discovered the depressing effect of busulfan (myleran) which is used in chronic myeloid leukemia, on bone marrow cells.

Samosh (1974) reported chromosomal damage in women who were accidentally subjected to polychlorocamphene which is an insecticide used in agriculture.

Sasaki and Makino (1963) through their studies on abortive embryos, they discovered a relation between the type of damage and certain chromosomes in particular.

Obe and Lüsers (1972) also tried to find out a relation between the frequencies of aberrations and the relative length of the chromosomes.

The studies were then directed towards the search for any of the reported chromosomal damage that may arise through administration of a drug of common use. The factors that were suspected to induce chromosomal damage include analgestics sedatives, tranquilizers, hormones, antibiotics.

Habbit-forming drugs that are occasionally administrated by delinquents as well as toxins that accidentally come in contact with some patients, also received a special attention.

Antibiotics have bifar attracted the attention of many investigators, most probably because of their widespread use in the treatment of a wide range of infections.

Neu, et al, (1965) investigated the response of cultured human leucocytes to a number of antibiotics on the chromosomal level. The studied antibiotics include penicillin G potassium, streptomycin sulphate, chloramphenicol and tetracycline.

Chloramphenicol, however, seemed to be of a special interest to several authors. In 1968, Castoldi, et al, studied the metaphase chromosomes of patients with septicemia and treated with high doses of chloramphenicol.

In the same year, its effect on phytohaemagglutinin stimulated human leucocytes was tested by Nasjleti and Spencer.

In the same year also, Zelkowitz, et al, submitted an explanation for the contribution of chloramphenicol in the synthesis of protein in mammalian cells.

In 1970, Mirus and Bolender reported some pictures of chromosomal damage that occurred as a result of addition of chloramphenicol, penicillin and streptomycin to growing leucocytes in vitro.

Streptomycin was another antibiotic that received a special attention. Its radioprotective effect on human chromosomes was questioned by Berodkin (1972).

The effect of actinomycin and proflavin as chromatid damaging agents was reported by Ostertag and Kersten in 1965.

Miles (1970) verified the damaging effects of actinomycin D on particular human chromosomes during short term cultures.

Acetyl salicylic acid comes next to its attractability to cytogeneticists. Many debates arose about a suspected damaging effect of this drug on metaphase chromosomes.

In 1981, Jarvik and Hare investigated the effect of analgesic aspirin among other drugs on human metaphase chromosomes in vitro.

In 1970, Mauer, et al, reported no, in vitro or in vivo chromosomal damage through the use of acetyl salicylic acid.

In 1971, Loughman et al spoke of chromosome damage yet he had his reasons to agree with Mauer, et al.

In the same year, comments were submitted by Jarvik, et al and Mauer, et al, about the suspicious of acetyl salicylic acid as a damaging agent to chromosomes during mitosis.

The damaging effect of drugs was extended to include even some beverages like coffee, artificial sweeteners, and tranquilizers. The dangerous habbit forming drugs including peyote and lysergic acid were also questioned as chromosomal damaging agents. Such compounds are used by a lot of people who are unaware of their probably unpleasant effect.

Stoltz, et al, (1970) discovered some pictures of chromosomal damage in human blood cultures to which sodium cyclamate, and cyclohexylamine sulphate were added. The study extended to include N-hydroxycyclohexylamine which is metabolite of cyclohexylamine and dicyclohexylamine sulphate which is an occasional contaminent of sodium cyclamate.

A test for the effect of caffeine on human chromosomes in vitro and in vivo was carried out by Weinstein, et al, in 1972.

In 1973, Weinstein and others made a further investigation of the effect of caffeine on human chromosomes in vitro.

Peyote, which is commonly used by Indians due to its hallucinogenic properties was also questioned as an effective cytogenetic factor.

Among the tranquilizers diazepam was tested by Stenchever in 1970. It proved to act as a chromosome destructive agent in patients using it as a tranquilizer and those using it for its muscle relaxing properties.

Cohen, et al, (1967) observed some signs of chromosomal damage in in-vitro human leucocytes that were left under the effect of lysergic acid. In the same year, he published another paper with another group of co workers about the in vivo and in vitro chromosomal damage induced by LSD-25.

In the same year also, Irwin and Egeton made a comparative chromosomal study between LSD users and control subjects who never used this drug.

In 1968, Ehrenreich and Irwin confirmed the assumption that LSD has a damaging effect on chromosomes.