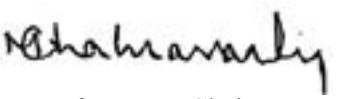
Letter of Appreciation

I am pleased to write about the book "Medical Cytogenetics" written by my student Dr. Sandeep Sharma. Since the tenure of his M.Sc. he is sincere and dedicated on the subject. Later on he has complete Ph.D in Medical Anthropology under my supervision. Dr. Sharma was Research Fellow in DNA Polymorphism program in Anthropological Survey of India at Nagpur and Consultant (population genetics) in NIHFW, New Delhi, Scientist in ICMR New Delhi. He is writing books on subjects with wider ranges and scope of anthropology, human genetics and now a book on Medical Cytogenetics.

Cytogenetics in general and medical cytogenetics particularly is very important and thirst area in the field of bio-medical research and in Human Biology and Bio-anthropology. I appreciate and congratulate Dr. Sharma for this scientific contribution in Bio-medical research.

15/05/2022



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Chairperson

सांस्कृतिक स्रोत एवं प्रशिक्षण केन्द्र
Centre for Cultural Resources and Training
(Ministry of Culture, Govt. of India)

CCRT/Chairperson/31012/022
May 31, 2022

Dear Dr. Sandeep,

I am happy to know that you have written this book titled Medical Cytogenetics. I am sure this book will help readers and students to understand the subject.

I have been informed that you have authored many books on Anthropology, Genetics and Ethnography. I congratulate you for having the discipline to frame and finish your writing projects.

I hope to see more of your work in the future. Best wishes for your future endeavors.

God Bless You

(Dr. Hemlata S. Mohan)
Chairperson, CCRT

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Preface

Medical cytogenetics is a developing discipline as the branch of Medical Genetics. It is gaining importance as key methods in diagnostics in obstetric and Pediatrics, cancer and other non-communicable diseases. In the field of hematology, pathology and in forensic medicine also it is widely using from last three decades.

Principles of human cytogenetics is the core metrics and technologies involved in investigation of medical problems it is called Medical cytogenetics.

The present text book is an attempt to bring basics of human cytogenetics to integrate with medical problems as medical cytogenetics.

Historical review on human and medical cytogenetics have been carried out in the book, traditional laboratory methods with some advanced modern techniques is also taken in account. The book comprises, some fundamental topics to assimilate with certain technical chapters like chromosome preparation, about individual chromosome, sex chromatin, banding techniques, auto-radiography, chromosome polymorphism, Lyon hypothesis, cytogenetics of human pregnancy, Neoplastic disease, chromosome abnormalities and human syndrome, cell cycle, cytogenetic mapping and a chapter on modern molecular cytogenetic techniques is also described.

All chapters are systematized and written in very simple language using appropriate terminology. I am very happy to submit this book to readers, students and researchers from different academic discipline using cytogenetics in their course curriculum. Book may be applied for medical and para-medical students, undergraduate and post graduate students in biology, human biology, zoology, human genetics and anthropology

It is humble request to readers may kindly submit your valuable suggestions, corrections to the author/publisher to improve the quality and to add new chapters to make this book more useful.

Sandeep Sharma
New Delhi
30/12/2021.

Acknowledgement

I am grateful to my beloved father for providing me opportunities and freedom of thought and selection of academic subjects. My parents are constant sources of inspiration. Along with parents I am thankful to my brothers and sisters for their affection, blessings and care towards my life and work. I express my thanks to my beloved wife Sulekha without her management capacity my academic work was not possible. I have taken long period of time in writing and preparation of manuscript. During these period my children Ishita and Kabir deprived from father's care and affection. I am thankful to my children Ishita and Kabir.

I shall always be obliged to Government of India some organizations i.e. ICMR New Delhi, NIHFW New Delhi, ANSI Kolkata, G.G.U. Bilaspur, RSU Raipur where form I had acquired academic credentials. I am extremely thankful to the CCRT (Min. of Culture, Govt. of India) in which I am getting identity, survival and to sustain for the subject and for service to the Nation.

Some important authorities under guidance of whom I had my professional development I express my thanks and gratitude to Prof. Moyra Chakravarty my Ph.D. Guide and mentor. Prof. S.K. Bhargava a renewed Pediatrician, Formar Dean (Pediatrics) Safadarjung Hospital, New Delhi. Dr. Hemlata S. Mohan, Honourable Chairperson, CCRT (Min. of Culture, Govt. of India).

Further I am thankful to my friends Shashikant Sharma, Akhilesh Pandey and Som Kshtriya for their support and unconditional friendship.

I am grateful to Renu publishers for this publication and distribution.

Sandeep Sharma
New Delhi

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CHAPTER

Medical Cytogenetics

All characteristics inherit from parent to children by chromosomes. Chromosomes are thread like structures found intra-nuclear which are responsible for inheritance. Composite study of chromosome is called cytogenetics, when these study carried out on human species is human cytogenetics. Determination of actual number of chromosomes in Homo sapience (Man) is completed by Tjio and Levan (1956). Initiative on numerical and structural studies on human chromosomes conducted by Flemming (1882). Due to lack of knowledge on techniques up to 1956 studies on cytogenetics was also very limited. After 12-year various advancement came in field of research in human genetics. Drosophila and plant genetic research also added new innovative ideas in human and medical cytogenetics and in behavior of chromosomes. Now the medical cytogenetics is advanced with development of biotechnological tools. It has made the cytogenetic explorations easier in desired time. Consequently, scientist become enable to study numerical, structural anomalies in chromosomes and now at molecular level.

DEFINITION

(i) "Cytogenetics is the study which deals with analyzing, interpretating the number, structure and chemical composition of chromosomes.

(ii) The branch of genetics which study the chromosomal inheritance and variation is called cytogenetics.

(iii) Cytogenetics is the branch of Genetics in which concerned with study of inheritance and variation of chromosomes

Genetic studies are difficult and needs patience because notably length of generation and lack of controlled breeding. It is important to quote the words of Weninger to understand the limitation of human genetics.

"*Man is difficult to study genetically more so then plants and animals children are few, development of the individual is slow and the span ofthe life and generations is long.*"

Principles of human cytogenetics is the core components and technologies involve in investigation of Medical problems it is called medical genetics and cytogenetics involved in medical problems is called medical cytogenetics.

Brief History and Development

Cell division was first described by Virchow (1858) who showed that cells never arose *de novo* but always from other cells. Thus, more than a century ago the principle of genetic continuity of cell by division was discovered and was to form the focal point for all future concept of heredity and development. Arnold (1879) was probably the first to describe human cell division. Fleming (1982) demonstrated cell division in the corneal epithelium of man. However, the first real attempt to determine the chromosome number of man was made by Hansemann (1891) who found three cells and from normal tissue with 18-24 and more than 40 chromosomes. From then until the appearance of Von-Winiwarter classic paper (1912), diploid number ranging from 16-36 were reported the consensus being in favor 24 as the human diploid chromosome number. Von Winiwarter (1912) counted 47 chromosomes in a spermatogonial metaphasic plate and 23 chromosome pair together with one unpaired chromosome in primary spermatocyte. On the basis of these observation he concluded that the human chromosome number was 48 in female and 47 in male and the sex determining mechanism consisted of two x chromosomes in female and only one X and one Y in male. Wieman (1912) made the first study of human somatic chromosome using sectioned fetal tissue and concluded that the chromosome number was probably 34, later (1917) same author reported the presence of Y chromosome in male. Evans (1918) was the first to report a chromosome number of 48 in spermatogonia. The controversy about the presence or absence of a Y chromosome in male could have been finally settled by the work of Painter (1921-23) observed a small Y chromosome in cells on several males. He reported (1921) that in spermatogonial mitosis. “The count range from 45 to 48 apparent chromosomes, although in the clearest equatorial plates so far studied only 46 chromosomes have been found. He suggested that the human diploid number was either 46 or 48”. Two year later in 1923, he concluded that the correct diploid number of man was 48 in both sexes. Chu (1960) has pointed out that this conclusion was based on testicular biopsies taken from three persons with mental disorders. It was possible in light of modern knowledge that these Individuals might have been aneuploid. Painter himself had noted the presence of giant or tetraploid spermatogonial cells and suggested the possibility that an XXY hermaphrodite might Originate in the same way as XXY triploids in Drosophila (Bridges 1922). In 1923 Oguma and Kihara reported a diploid number of 47 and considered that man had an XO-XX sex chromosome constitution, thus agreeing with Von Winiwarter. However, Painter (1924) using fresh human materials and confirmed the presence of both an X and a Y chromosome in males. With

Exceptional work of Von Winiwarter and the Japanese school, most cytologists supported Painter's conclusions (H.M. Evans, Swezy 1929, Kemp, 1930, R.L. King and Beans 1936, Andres and Nawas Chin 1936, Andres and Jiv 1936, Vogel, 1936. However, from Von Winiwarter and his associates Oguma and Kihara (1930-37) adhered to the opinion that three was no Y chromosome in males. The presence of a Y chromosome was finally established by Koller's account of the behavior of the sex chromosome during spermatocyte meiosis (1937). It was also thought that this work together with some later studies (La Cour 1944, Mittwoch, 1952 T.C. Hsu 1952, Darlington and Haque, 1955). Finally proved that the human diploid chromosome number was 48.

All the more reason, therefore the surprise when Tjio and Lévan 1956 reported consistent counts of 46 from *in vitro* fibroblast culture from lungs of human abortuses and referred in the same paper to further counts of 46. Hansen Melander and Kulandan from preparation of liver cells also derived from abortuses. Tjio and Levan were the first to use modern tissue culture techniques for the studies of human chromosome and the high quality of their preparation made an error of counting most unlikely. Another unlikely possibility referred to by these authors was an *in-vitro* loss of two chromosomes. However unlikely this might be it could not be finally discounted untill a further direct examination of human chromosome had been made. C.E. Ford and Hamerton (1956) using an improved squash technique, examined from testicular biopsies from three males. Counts 46 chromosomes were obtained in spermatogonial metaphases and 23 bivalents were found great majority of primary spermatocytes at metaphase. One of these bivalent was clearly unequal and comprised the X and the Y chromosome, which were seen on occasion to be unpaired. These results which confirmed those of Tjio and Levan, reopened the question of the correct diploid number of man. The development of cell culture technique resulted in rapid confirmation that the human diploid chromosome number was 46 as Painter himself first suggested in 1921 and not 48 as he finally concluded in 1923.

Since 1956 only two authors have reported human populations with diploid chromosome number differing from 46. Kodani (1957-58) has suggested variations in human chromosome number with a basic number of 48 chromosomes in a small number of Chinese males. Neither observation has been confirmed and both may it appears be disregarded. Makino and his colleagues (1962-63) Makino and Sasaki (1961) have examined the chromosomes of 218 Japanese fetus and found only a model diploid number of 46 with no evidence of polymorphism. Numerous studies on a variety of groups since 1956 have equally failed to find any evidence