PART - TWO

CHROMOSOMES IN CENTIAL ANALYSIS
Every age has had its explanation of congenital malformations according to its religious or philosophical concepts. Thousands of years ago, the birth of deformed children was considered as a link between the behaviour of the stars and terrestrial events to come. Whenever a society firmly believed in God or multiple deities, deformities of new born children were attributed to the wrath, or a benign warning, of the Super-being that ruled the world. In times of fear of witches and sorcerers, fellow-men or women were suspected of deforming unborn children in the mother’s womb.
Throughout the ages, external events were thought to reach the foetus through the mother's eyes or mind. Concurrent with such 'superstitious' beliefs there existed more 'natural' explanations, i.e. those which were more related to our own beliefs and theories. They attributed, with little proof, unusual teratologic events to male 'semen' or female 'materia'. It is difficult to prove, with our limited knowledge of teratogenicity, that all the ancient theories were nonsensical, i.e. outside the causal nexus. As William (Quoted from Warkany, 1971) put it: "Not a sparrow falls to the ground but some of the remote conditions of his fall are to be found in the milky way, in our federal constitution, or in the early history of Europe". Yet, causes that are so remote that they are useless for prediction or prevention of events should not be included in etiologic explanations aiming at practical solutions. This applies to ancient theories as well as those accepted without substantial proof by modern science. Our present concepts of teratogenicity reflect the general thinking of today and contain many beliefs which are not equally shared by all the scientists and which require substantiation. They reflect the present-day concepts of prenatal development.
whose disturbances are held responsible for prenatal malformations. There are still huge areas of human teratology that remain obscure and there are malformations for which we have reasonable explanations but no practical ways of prevention. In such areas the later modern scientific concepts of causation are beliefs in the modern garb. There are scientists who believe that the bulk of the unexplained congenital malformations are caused by genetic factors or by chromosomal changes that cannot yet be visualized. There are others who attribute them to molecular changes without proof. Some of the scientists believe that diseases of the mother, whether they are viral, metabolic or nutritional, are responsible and some others are convinced that the drugs are the devils that run the normal embryos into the monsters. There is some truth in all of these beliefs, as there was one truth in the beliefs of the ancients. As long as our unproved opinions are treated as hypotheses that stimulate research and experimentation, they are useful and necessary for progress. But if they are mistaken for facts and solutions, and if they are stifling the work of others who have different theories, they may become superstitions even when expressed in the most modern of the scientific terms.
The etiological factors that contribute to the congenital malformations are numerous, but obviously not sufficient to explain all the human teratological facts. Like diseases of the postnatal beginning, disorders of the prenatal life are complex in origin and there often are many etiological factors that contribute to their existence. No explanation of a disease or malformation is entirely satisfactory until it leads to successful preventive measures. There are only a few prenatal diseases and disorders that can be prevented and eradicated like their counterparts of the postnatal origin. But there are hopeful signs that indicate that the modern science is going in the right direction or still better in the right directions. But most of the work in etiological research and preventive teratology still remains to be done.

The child's life begins with fertilization of the ovum and formation of the zygote, in which many of the physical and mental traits of the new organism are predetermined. Development of the first cell, which weighs only 0.005 mg., into the highly differentiated organism in the form of the new born of more than 3,000 gms., requires about 44 successive cell divisions that are directed by the genes contained in the zygote and
influenced by the intrauterine and extrauterine environment. Abnormalities of the nuclear elements of the zygote as well as the prenatal environmental disturbances may result in congenital malformations. The nucleus of the zygote contains 46 chromosomes, the carriers of genes, derived from the sperm and ovum, which contribute 23 chromosomes each. Normal as well as abnormal genes can be passed on along the 'germ track' through many generations, and the origin of numerous congenital malformations date back to events, decades or centuries before conception. Entire chromosomes in the zygote can be abnormal in number or structure and determine malformations in the developing organism. Chromosomal abnormalities are genetic deviations, but they differ from gene mutations in origin and mode of transmission. A healthy zygote can be damaged during its intrauterine development by various agents—inf ectious, actinic or chemical—and become deformed before birth. It is customary at present to divide the causes of congenital malformations into genetic, chromosomal and environmental, although it is often impossible to separate clearly such causative factors, which can interact and bring about the defects encountered or prevent them.
The role of chromosomes in the development of congenital malformation has been visualized clearly only after 1956 when the new and proper techniques were introduced. Actually the new techniques and the successful adaptations of the older ones, augmented by the application of principles, derived from developments in genetics (especially plant and animal cytogenetics) to human investigations, have resulted in rapid advances. On the technical side, these developments were foreshadowed by the methods of Chrustschoff and Berlin (1935) and by the work of Hsu and Pomerat (1953), but really important advances were made with the metaphase blocking and chromosome spreading devices. It, therefore, became possible to apply these practical methods to the study of clinical areas and that lead to the birth of Human Cytogenetics.

Consequently within a short span of 15 years there have catalogued a large bulk of reports describing numerous chromosomal abnormalities pertaining to various congenital diseases, abortions and tumours etc.

Unfortunately whatever data is available, that is from the countries other than India, where this field is still virgin as only a few references are available. A little bit of work is being carried out at Chaudhuri Centre of Human Genetics at Calcutta and some isolated reports
from here and there are also available. But no detailed survey has been carried out. So inspired by this, the present project, to analyze the chromosomal patterns in various congenital anomalies was taken up.

During the last three years starting from January, 1971 more than two hundred patients with congenital anomalies were studied for their cytogenetical analysis. In addition, a good number of normal cases were also analyzed. During the present project, stress was laid on the subjects with congenital anomalies pertaining particularly to cardiovascular and nervous system with regard to their role in congenital chromosomal disorder. In addition, the anomalies pertaining to sex and other systems were also studied.

Finally, it is hoped that the present piece of research will lead to another advancement in the field of medical genetics particularly in India, where no such information is available.