Introduction
Background

The scientific study of variation in man was started by the establishment of human genetics. The practice of human cytogenetics with its clinical applications is somewhat more than 30 years old and extensive progress has been made in the recent years. The year 1956 is often considered as the beginning of modern human cytogenetics. The discovery by Tjio and Levan (1956) that human chromosome number to be 46, instead of 48, was the starting point for subsequent spectacular developments in human chromosome studies. Since then much progress has been made and reviewed frequent

Historically, Hsu (1979) has divided the era of human cytogenetics conveniently into four stages. The dark ages before 1952, the hypotonic period from 1952 to 1958, the trisomy era between 1959 to 1969 and chromosome banding period in 1970. Prior to this, it was postulated that sperm was largely nuclear material and nucleus was responsible for heredity. It was Flemming (1882) who identified chromosomes for the first time within the nucleus. It was then discovered that the behaviour of chromosomes during the production of gametes paralleled the behaviour of Mendel's hereditary
units. It was, therefore, discovered that chromosomes are the carriers of genes.

Methodology

The first satisfactory preparation of mammalian chromosomes was obtained by squashing ascites tumour cells of the mouse by Levan and Hauschka (1953). The importance of hypotonic salt solution for spreading and separating the chromosomes was launched by Hsu (1952). The establishment of this technique has made it possible to find out the right chromosome number in man. Therefore, during this time, the analysis of human karyotype was started.

By the establishment of the new techniques, chromosome analysis of human beings who were congenitally malformed or mentally retarded had begun. Since 1959, it has been accepted that certain chromosomal aberrations are associated with different kind of syndromes having congenital malformations. Various investigations on different congenital abnormalities have been reported till today. Congenital malformations can be caused by any factor which restricts the mobility of the fetus. Etiology of the multiple congenital malformation is almost obscure. Multifactorial inheritance is the commonst
Identifiable cause which can be followed by monogenic and chromosomal disorders, (Connor and Ferguson-Smith, 1987). Various factors have been postulated to affect the genetic material at various levels, such as, carcinogenesis, mutagenesis, chromosomal changes, teratogenesis and very early abortions. According to Piccardi (1977) an individual with a teratogenic malformation, usually is not considered at risk for transmitting the defect itself to offspring, but germinal mutation might be present as an independent effect of the teratogen. The teratogenic potential of various agents like irradiation and certain drugs in long run will change the genetic material itself.

Chromosomes in Disease

The first chromosomal disease in man (trisomy 21, Down's syndrome) was discovered by Lejeune et al., (1959). During the same year, Turner's syndrome with 45, XO chromosome constitution was reported (Ford et al., 1959) and Klinefelter's syndrome by a 47, XXX chromosome complement was discovered (Jacobs and Strong, 1959). The first XXX woman was described by Jacobs et al. (1959), therefore, chromosome karyotype of Turner and Klinefelter's syndrome showed that male sex is determined in individuals by the presence of the Y
chromosome. The effectiveness of Y chromosome for determining male sex, in spite of having combination of four X chromosomes was established.

Later, the autosomal trisomy of chromosome number 13 (Patau et al., 1960) and trisomy 18 (Edward et al., 1960; Patau et al., 1960; Smith et al., 1960) were discovered. With these discoveries, the chromosome studies turned to structural abnormalities and their implication on phenotypic features. The development of chromosomal banding studies by fluorescence microscopy (Casperson et al., 1970) increased the ability to resolve small chromosomal aberrations. Identification of all human chromosomes was possible by careful study of these bands. Yunis (1976) introduced prophase chromosome banding in order to determine chromosomal segments, fragments and breakpoints more accurately.

Chromosomal analysis of multiple congenital malformations in the newborn are assuming tremendous importance. Genetic amniocentesis has become a routine prophylactic examination offered to women with an increased risk of having a child with a chromosome abnormality, neural tube defect or metabolic disease (Simpson, 1981). It has also helped to record
polymorphism in certain population groups (Hsu, 1981). Such findings are important particularly in the studies on incidence of cancer and also population behaviour e.g., conflicting report on the possible link between large Y and an increased link of criminal behaviour include one report suggesting linkage (Nielsen and Friedrich, 1972) and several later studies reporting any association (Schwinger and Wild, 1974; Brogger et al., 1977; Benezech et al., 1978. A visible duplication or deficiency of any of the autosomes is almost invariably associated with mental retardation, postnatal growth deficiency, congenital malformation and dysmorphic features. Many congenital anomalies have been found to be associated with chromosomal aberrations. Various studies on multiple congenital malformation with mental retardations due to chromosomal damage have been reported earlier (Aurias et al., 1978; Buchanan et al., 1978; Fineman et al., 1978; Fryns and Van den Berghe, 1979; Fryns et al., 1980, 1983, 1985, 1986; Parloir et al., 1979; Berg, 1980; Hassold et al., 1980; Pai et al., 1980; Turleau et al., 1980; Meer et al., 1981; Jalenko and Aula, 1982; Zaletajev and Marinchora, 1984; Symon et al., 1984; Young et al., 1984; Warburton et al., 1986, 1987; Kousseff et al., 1987; Neve et al., 1988).
Complex Chromosome Rearrangements (CCRs)

In fact the introduction of banding techniques led to the recognition of a few children with complex chromosome rearrangements (CCRs) (Buchanan et al., 1978) Kleczkowska et al., 1982; Kousseff et al., 1987). The CCRs have been denoted into 2 categories; familial with chromosome aberration present in one or both parents and de novo. In both categories the CCRS can be unbalanced or balanced without detectable loss or acquisition of euchromation. The majority of familial cases have been identified through an offspring with an unbalanced karyotype leading to an aberrant phenotype. According to Kousseff et al., (1987) usually the mother had the balanced rearrangement. Regardless of which parent had the rearrangement, most patients had resultant partial trisomies and/or partial monosomies. In fact these authors have characterized CCRs according to the number of chromosome breaks found; Group I - those with four or fewer breaks; Group II- those with more than four breaks.

Trisomic Syndromes

Trisomies are the most common chromosomal abnormalities among clinically recognizable pregnancies whose incidence is 4% of all such conceptions (Hassold
et al., 1980). These include trisomies of chromosomes 21, 18, 15 and so on.

Autosomal trisomy 21 chromosome Down's syndrome is well established. The clinical features as well as cytogenetic studies of Down's syndrome have been extensively reviewed (Hamerton et al., 1965; Giannelli et al., 1965; Polani et al., 1965 and Penrose and Smith, 1966). It has been accepted that 1 to 2% of all the live born Down's syndrome individuals are mosaics (Taylor, 1968; Richards, 1977).

Various etiological factors have been given for trisomic syndromes especially Down's syndrome. Different factors such as, maternal age, irradiation, viruses and medical treatment during pregnancy may lead to nondisjunction during meiosis I. It was Penrose (1933, 1939, 1954) who conclusively showed the significance of maternal age in the etiology of Down's syndrome. The recent studies in the risk of aneuploid conception are well recognised to increase with advancing maternal age, particularly after 35 years (Ferguson-Smith, 1979; Lamson and Hook, 1981; Hook, 1981, 1983; Schreinemachers et al., 1982; Ferguson-Smith and Yates, 1984; Juberg, 1983; Hook et al., 1984; Hassold et al., 1984; Hassold and Chiv, 1985; Carothers, 1987).

There exist contradictory ideas that the extra
chromosome, trisomy 21, is of paternal origin. Not everyone has accepted the idea of maternal age as sole effect for trisomy 21 (Mantel & Stark, 1966; Stene et al., 1977; Matsunaga et al., 1978; Erickson and Bjerkedal, 1981; Hook et al., 1981).

The recent discovery of paternal age effects as a cause of chromosomal disorders has revived interest in the possibility of paternal age as a risk factor in Down's syndrome independent of maternal age. The existence of a significant association of elevated paternal age and autosomal trisomy 21 has been reported (Hansson and Mikkelsen, 1978; Matsunaga et al., 1978; 1978; Regal et al., 1980; Stene et al., 1977; 1981; 1987; Stene and Stene, 1977; Mantel and Stark, 1966; Hook and Cross, 1982; Erickson, 1979; Stene and Mikkelsen, 1983; Magenis and Chamberlin, 1980).

Therefore, the increased proportion of cases with paternal non-disjunction in Down's syndrome raised considerable interest. Zhi-Hao-Lian et al. (1986) emphasized that it is paternal non-disjunction which leads to autosomal trisomy 21 or Down's syndrome. Identification of the individual 21 chromosome with banding techniques show that non-disjunction for this chromosome occurs in the fathers, possibly one-third of 21-trisomic children have their origin in paternal non-
disjunction (Uchida, 1977; Mattei et al., 1979), and this frequency increases from age 55 onward (Stene et al., 1977). But it is believed that if paternal age affects the occurrence of Down's syndrome, this effect is much smaller than maternal age-effect (Erickson, 1979).

Structural chromosome rearrangements in the parents of a Down's syndrome child, such as translocation and inversions may be responsible of meiotic non-disjunction (Uchida and Freeman, 1986). Translocation involving chromosome 21 and other chromosomes in the parents is another mechanism for the identification of Down's syndrome children (Mckusick, 1978; Hook, 1984). The probability of a D/D translocation carrier producing a 21 trisomic child may be higher, the estimate being 2% other chromosomal anomalies such as, XO, XXY associated with D/D translocation have been reported. But whether causal relationship of a chance are involved is unknown (Harris et al., 1979). Robertsonian translocations are the most common structurally abnormal chromosomes in which the whole arm transfers between human acrocentric chromosomes. Robertsonian translocation do not seem to affect the phenotype of a balanced carrier, apart from occasional male sterility (Therman, 1980). In a family study (Therman, 1980) three
children had Down's syndrome, the father was mosaic and the affected children had 46, t(21q; 21q). Translocation between Dq ; Gq chromosomes are reported. One family with a t(13 q; 21 q) (Perez-Castillo and Abrisqueta, 1987) and two families with 13 q 22 q and Y translocation. (Abe et al., 1975; Daniel and Lam-Po-tang, 1976) have been detected.

Robertsonian translocations have been reported in individual with total sterility and habitual abortions (Fried et al., 1974; Farah et al., 1976; Zizka et al 1977; Mameli et al., 1978). Many hypothesis have been put forward to explain the relatively high incidence of Robertsonian translocation and highly non-random participation of the different acrocentrics in them (Hecht and Kimberling, 1971; Mikkelsen, 1973).

One of the assumption is the centric heterochromatin and the satellite stalks are especially prone to breakage. Another hypothesis is the participation of satellite association among acrocentric chromosomes which may play an important role in bringing their centric region together.

In an induced Robertsonian fusions Hsu et al., (1978) mitomycin-C preferentially cause these Robert-
sonian translocations. Therefore, most of the differences between Robertsonian translocations and other translocations lies on the fact that the former, as a rule, are the result of an exchange in meiosis and not of breakage and rejoining.

The highly significant increase in the satellite association for chromosome 21 in parents were found by Hansson and Mikkelsen (1978). They reported that the number of 21-21 association was significantly increased in parents with non-described by Ferguson-Smith and Handmaker (1961) and later the phenomenon of satellite association was given to this acrocentric association (Schneiderman and Smith, 1962). The acrocentric chromosomes were connected by a thin fibers which can be occasionally visible in light microscopy. By means in situ hybridization of $^{3}H$-labelled, RNA to human chromosomes, Handerson et al. (1973) have demonstrated the presence of DNA connectives between satellite regions of acrocentric chromosomes.

The results indicate that satellite association may play a role in the etiology of Down's syndrome. In a study of fluorescence and other chromosomal variants in 26 families (Hansson and Mikkelsen, 1978). Maternal non-disjunction was found in 19 and paternal one in 7
cases. This study showed a highly significant increase in the satellite association for chromosome 21 in the parents where non-disjunction event had taken place.

Therefore, the correlation between satellite association and meiotic failure indicates that there is a high tendency of satellite association which increases the risk of non-disjunction and satellite association can be considered as a criteria for the etiology of Down's syndrome children.

Maternal age effect may cause autosomal trisomy or aneuploidy in the offspring. Various data from spontaneous abortions and live births with autosomal trisomies XXY and XXX were examined (Ayme and Lippman-Hund, 1982) in order to determine the nature of aneuploidy and its relation to maternal age. (Carothers et al., 1978; Hook, 1985). The effect of elevated maternal age was seen in autosomal trisomy 13 and trisomy 18 (Magenis et al., 1968; Taylor, 1968) and in 47,XXX and 47,XXY sex chromosome abnormalities. Hecht et al. (1963) have reported trisomy 17-18 with multiple congenital anomalies in case with elevated maternal age. Therefore, aneuploidy is the main reason which usually arises from failure of chromosomes to disjoin in
anaphase. Alternatively delayed movement of a chromosome at anaphase may lead to aneuploidy. In spite of many efforts to correlate the parental age, still very less information is available regarding the cause of meiotic non-disjunction.

Neural Tube Defects

The incidence of neural tube defects at birth is known to be highly variable. The highest frequencies occur in Great Britain and Ireland (6.1/1000 total births in Belfast) (Nevin, 1981) and relatively low frequencies occur in the U.S. particularly among blacks (1.6/1000 total births) (Khoury et al., 1982). It has been seen that the incidence of neural tube defects is about 10 times higher in spontaneously aborted pregnancies than in term births (Creasy and Alberman, 1976; Bell and Gosden, 1979; MacHenry et al., 1979; Stein et al., 1982).

Chromosome analysis of multiple congenital malformations with neural system defects has been studied by various investigators. Trisomy 18 is mostly associated with patients with neural tube defects. According to Connor and Ferguson-Smith (1987) trisomy 18 is suspected if other congenital malformations coexist and the combination of encephalocele, polydactyly and
cystic kidneys is characteristic of an autosomal recessive tract. Autosomal trisomy 18 in multiple congenital anomalies such as neural tube defects (Flannery and Kahler, 1986) in meningocele (Passargé et al., 1966; Taylor, 1968; Gullotta et al., 1981) anencephaly (Menashi et al., 1977 Nisani et al., 1981) Hydrocephalus (El-Alfi et al., 1964; Prober et al., 1986), occipital encephalocele (Babini et al., 1963; Passarge et al., 1966) have been reported till today. Anencephaly which is most often the result of polygenic multifactorial inheritance has been associated with X linked or single gene inheritance in some instances & may be an associated phenotype of a chromosomal abnormality (Holmes et al., 1976; Nisani et al., 1981; Khoury et al., 1982; Baraitser and Burn, 1984; Bader et al., 1984). In a survey of spontaneous abortion in New York city, all the 1% tissues with neural tube defects had chromosome abnormality. In addition 9.3% of all karyotypically abortusis had a neural tube defect, demonstrating the high frequency of neural tube defects in non viable fetuses with a chromosome abnormality (Byrne and Warburton, 1986). Different findings on trisomy of an extra metacentric chromosome in a case with microcephaly (Froland et al., 1963; Taft et al., 1965) and trisomy of sex chromosomes with microcephaly
Sexual Disorders

Sexual chromosomal abnormalities were detected with Turner's syndrome (Ford et al., 1957) and Klinefelter's syndrome (Jacobs and Strong, 1959). Afterward, much attention has been focused on individuals suffering from a variety of congenital sexual disorders, such as, hypospadias, male and female pseudohermaphroditism, azoospermia, hypogonadism, klinefelter's syndrome and cryptorchidism or undescended testes. In many cases, sexual maldevelopments are associated with abnormalities of sex chromosomes, both numerical and structural disorders. Spear and Porto (1988) have found 47,XXX chromosome constitution in a fetus with ovarian dysgenesis and genito-urinary malformation. Gonadal dysgenesis cases were reported with chromosomal constitution XXX (Van Benthem et al., 1981) X/XXX and XX/XXX (Kohn et al., 1977 and Vague et al., 1964) onwards. In an investigation on 50 cases with cryptorchidism, one had Klinefelter's syndrome (47, XXX/48, XXXY) and one showed mosaic trisomy 8(46, XX/47, XY+8). In thirty cases of hypospadias and hypogonadism, six cases showed abnormally long Y chromosome.
The XXX/XXY chromosomal aneuploidy, Klinefelter's syndromes are most characterized by azoospermia, gynecomastia and elevated urinary gonadotropin excretion which the male is infertile. The term intersex * is suggested by Polani (1962) for those cases with ambiguous genitalia. According to Hamerton (1971) an intersex with ambiguous but predominantly female external genitalia or a female phenotype with testes is a male pseudohermaphrodite (testicular intersex), while an individual with ovaries but masculinized external genitalia is a female pseudohermaphrodite (ovarian intersex). Several mosaic cases such as those XO/XY, XX/XXX and XX/XY/XXYY were recorded in patients diagnosed as having true hermaphroditism.

It has been seen that most cases with a 45,X karyotype develop as phenotypic females with Turner syndrome. However, very rare 45,X individuals are sterile males with testes (Fraccaro et al., 1966; Locurto et al., 1974; Forabosco et al., 1977, 1978; Tolkdorf et al., 1980; Turleau et al., 1980). How maleness arises in these individuals in unknown similarly individuals with the karyotype 46 XX which
At least 10 families are known in which a 45,XX male was Xg (a-) even though the father was Xg(a+) (de La Chapelle, 1981; de La Chapelle et al., 1984). Such anomalous inheritance of this dominant, X-linked marker led Ferguson-Smith (1966) to propose that maleness in XX men was brought about by an interchange of genetic material between the X and the Y chromosome of paternal meiosis. According to this hypothesis the Xg-bearing portion of the father's X chromosome was replaced by a testes determining portion of the Y chromosome. The blood group and DNA studies of XX males are consistent with this model (De La Chapelle et al., 1984; Guellaen et al., 1984; Page and de la Chappelle, 1984). Indeed certain single copy Y-specific DNA sequences have been detected in 12 of 19 XX males tested (Vergnaud et al., 1986). It is, therefore, possible that XY interchange can account for many cases of XX maleness.

De La Chapelle et al. (1986) pointed out that if 45,X males are also the result of a paternal by interchange, then they should have 45,X males which might be 45,X/45,XY mosaics in whom the XY line is rare or has been eliminated altogether, at least in some
tissues. (de La Chapelle et al., 1986). These authors observed two cases with 45,X in 1986 and indicated that in patient 1, Y chromosome was present in less than 3% of fibroblasts. The DNA hybridization results were consistent with such low-grade mosaicism for a structurally normal Y chromosome. In patient 2, the cytogenetic and DNA studies produced no evidence of Y chromosomal material, even in a minority of cells, but since Hae III fragments are located principally if not exclusively in distal Yq (Bostock et al., 1978; Schmidtke and Schmid, 1980) and, thus, would be of little use in detecting mosaicism involving an abnormal Y chromosome lacking that region. The DNA hybridization studies alone then cannot argue against low grade mosaicism for a structurally abnormal Y chromosome in patient 2. De La Chapelle et al. (1986) however described this hypothesis in the cases of patients studied by them. Both Xg and X-linked RFLP studies indicated that in each of the proband, the single X chromosome was of maternal origin. In their first case the presence of a 46,XY cell line suggested that the zygote was also 46,XY and that the 45,X cell line was the result of mitotic nondisjunction. In case 2, they could not detect certain single-copy Y DNA sequences present in many 46,XX males and therefore, assumed to
be near the male determinated on the Y (sequences detected by probes 47C, 115, 50f2 and 52d) (Vergnaud et al., 1986). They suggested that although the results argue, but does not exclude the presence of a male determining portion of the Y chromosome in the 45,X cells of second case. Thus a paternally derived X that had acquired the male-determining portion of the Y. This is an awkward hypothesis requiring the coincidence of two abnormal events, first, X-Y interchange during or prior to paternal meiosis, and second nondisjunction either during meiosis in the mother or mitosis in the proband.

Alternatively there are hypothesis indicating that some apparently 45,X males carry a small male determining portion of the Y either translocated to an autosome (Turleau et al., 1980; Koo et al., 1976) or segregating independently mitotic chromosome.

Chromosome and Cancer

Chromosomes changes in cells of the patients with cancers have recently been shown to have diagnostic and prognostic significances. It has been well established that there exists a relationship between chromosomal alteration and cancers. Theodore Boveri
(1914) was the first to make a statement in this regard. It is also clear that genetic factors play an important role in the development of human cancers. Today it is believed that the malignant cells of the most neoplasia show chromosomal abnormalities and in many, the defects are consistent (Sandberg, 1980; Yunis, 1981). This has been made possible by the introduction of refined banding techniques especially the high resolution chromosome techniques (HRCT's), the latter are widely recognized as the best tool for the study of subtle cytogenetic abnormalities in malignancies (Bourinbaiar et al., 1986). Now, it is even possible to map the breakpoints by in situ hybridization with the DNA probes.

The chromosome alterations in certain cancers are specific and non random and they involve only a few chromosomes (Mitelman and Levan, 1976). Even among the confusing variety of chromosome aberrations in malignant cells, a few stand out as being specific to certain diseases (Therman, 1980). In fact most of the abnormalities cluster around a few specific chromosomes e.g., abnormalities of chromosome I have been mentioned by several investigators in a number of malignancies (Brito-Babapulle and Atkin, 1981; Douglass et al., 1985; Atkin, 1986; Adhvaryu et al., 1988). The region of
chromosome No. 1 form centromere to I p is the area most frequently involved in breakage leading to malignant growth (Adhvaryu et al., 1988).

Similarly the involvement of chromosome 11 in various types of translocations in cancers has been reported by many investigators (Kolitz et al., 1981; Tsujimoto et al., 1984; Kocova et al., 1985; Huret et al., 1986; Singh et al., 1986; Kubota et al., 1987; Lai et al., 1987; Sato et al., 1987; Wang et al., 1988). Trisomy of chromosome 11 has been found to be the sole abnormality in several patients with leukemic disorders (Yunis et al., 1981; Dang et al., 1985; Gangji et al., 1985; Jacobs et al., 1986; Yamada et al., 1986; Takasaki et al., 1988). According to Takasaki et al. (1988) trisomy 11 and non-lymphocytic leukemia with myelomonocytic features may be a new association in human neoplasia.

Mostly in myeloid leukemia or related disorders rather than lymphoid leukemia, Dang, et al. (1985) described a normal karyotype of a case at diagnosis of agranogenic myeloid metaplasia but trisomy 11 appeared when the disease proceeded to acute myelogenous leukemia. The mechanism in which trisomy 11 acts in leukemogenesis is involved in the abnormal proliferation
of the neoplastic cells through the factors controlled by genes of this chromosome (Takasaki et al., 1988).

In fact the greatest source of hope that tumour specific aberrations may be found, has come from the information that vast majority of cases of chronic myeloid leukemia (CML) are associated with the Philadelphia chromosome (Ph'), first described by Nowell and Hungerford in 1960. The banding techniques (Caspersson et al., 1970) have revealed that it is a deleted chromosome 22 in which a portion of the long arm has been transferred to chromosome 9 (Rowley, 1973).

From the data available so far, it is apparent that the Philadelphia chromosome (Ph') or translocation t (9; 22) (q²4; q¹¹) is present in more than 90% of the patients with chronic myeloid leukemia (CML) (Ohyashiki et al., 1987) and its presence is considered to be specific for the disease (Sandberg, 1986). With the progress of malignancy, additional chromosomal changes may occur in the presence of ph+ in CML. The incidence of these additional changes in the blastic crises may be six times higher than the chronic phase (Rowley, 1985; Sandberg, 1986).

The most common additional karyotypic abnormality
in the blastic phase is the occurrence of second ph (ph+), followed by trisomy of 8(+8), an isochromosome for long arm of chromosome i (17 q); trisomy 19(+19), and -Y (Whang-Peng and Knutsen, 1982; Ishihara et al., 1983; Rowley, 1985).

The occurrence of i(17q) is most commonly associated with blastic transformation in chronic myeloid leukemia (Sandberg, 1980; Rowley and Testa, 1982; Mitelman, 1983). It has been suggested that loss of a part of 17p is a highly non random event related to blastic crisis in chronic myeloid leukemia (Borgstrom et al., 1982). Testa and Cohen (1986) have proposed that i(17q) often involves a break at 17p11 most likely at sub band p11.2. Then the abnormality can be interpreted as a dicentric chromosome dic (17) (p 11.2). Interestingly, the adjacent band 17p12 is known to represent a fragile site (Shabtai et al., 1982) and several investigators have suggested that fragile sites and consistent chromosomal breakpoints in cancer may be related (Yunis and Sorang, 1984; Le beau and Rowley, 1984; Hecht and Satherland, 1984). Two patients with acute blastic transformation of chronic myeloid leukemia associated with strikingly elevated platelet counts showed abnormalities of chromosome 3q in addition to standard t(9 ; 22) (Bernstein et al., 1986).
Besides the normal 22, 9 translocations, a large number of "simple" or "complex" type of translocations involving chronic myelogenous leukemia with Philadelphia chromosomes have been extensively described (Berger and Bernheim, 1978; Sandberg and Sonta, 1978; Rowely, 1980; Carbonell et al., 1980; Adhvaryu et al., 1983; Kubota et al., 1987).

Wang et al. (1988) have recently described a case with a new reciprocal translocation t(11; 21) (q13; q22) in chronic myelogenous leukemia patients having Philadelphia chromosome. The 11q13 involvement in chronic myelogenous leukemia with t(11; 14), t(9, 11) and t(11; 22) have been described (Huret et al., 1986; Singh et al., 1986). Both Philadelphia translocation, t(9; 22) as well as translocations 8 and 11 have been described in a case with chronic myelogenous leukemia (Lai et al., 1987). The complex translocations normally involve three chromosomes i.e. 22, 9 and any third chromosome. Kesseov (1981) has summarized the list of complex translocations found in CML. Barbata et al. (1986) have reported a complex translocation t(3; 9; 22) in blastic crisis of chronic myeloid leukemia. A chronic myelogenous leukemia patients with masked Philadelphia chromosome had t(4; 9; 22) (London et al., 1986). A complex translocation involving chromosome 1, 9 and 22
has been seen by Adhvaryu et al. (1988) in Ph-positive case with chronic myelogenous leukemia. Involvement of chromosome 11 in complex translocation has been very prominently reported e.g. t(11; 14; 22;), t(9; 11; 22;), and t(6;9;11;22;) (Carbonell et al., 1980; Kolitz et al., 1981; Kubota et al., 1987).

Sato et al. (1987) have found a reciprocal translocation in chronic granulocytic leukemia involving the short arm of chromosomes 7 and 11; t(7; 11)(p15; p15). Similar translocation between the short arm of chromosome 7 and 11 have been reported in Japanese patients (Tomiyasu et al., 1982; Ohyashiki, 1984; Kaneko et al., 1983; Ishihara, et al., 1986; Takeda et al., 1986; Ohyashiki et al., 1987).

The frequency of congenital leukemia is relatively less (Liang et al., 1986) and its presence is mostly associated with Down's syndrome (Rosner and Lee, 1972). The children with Down's syndrome are known to be predisposed to leukemoid reactions (Morgan et al., 1985). A new t(1,4,11) has been found in a case with congenital acute non-lymphocytic leukemia (Selypes and Laszlo, 1987) and translocation 4 and 11 t(4,11) have already been described in cases of congenital leukemia (Kocova et al., 1985; Heim and Mitelman, 1986;
According to Sandberg (1986), translocation 4 and 11 frequently occurs in congenital leukemia. It has been explained that the distal part of chromosome 11 (11q23) contains genes of general importance in the neoplastic process and the break in band (4q21) may be specifically associated with lymphoid differentiation (Heim and Mitelman, 1986). The band 4p16 is also a fragile site (Yunis and Soreng, 1984) and fragile sites may act as predisposing factor for certain chromosomal rearrangements in human neoplasia (Yunis, 1983).

The X chromosome is involved in both numerical and structural changes. Barbata et al. (1988) have found a rare translocation between 22 and X chromosomes which was present in 100% of the metaphases of chronic myelogenous leukemic cases. The X translocation with other chromosome were also recently reported. One of the translocation is between X and 18 chromosome in a primary change of cynovial sarcoma (Turc-Carel et al., 1987). Telomeric association of chromosomes was reported in B cells of two patients with leukemia (Fitzgerald and Morris, 1984) which have not been reported previously in human patients with cancer of leukemia (Sandberg, 1980;
Miteelman, 1983). According to Fitzgerald and Morris (1984) the mechanism of the telomeric association may be considered as a potential origin of new stable cytogenetic combination that have a role in oncogenes trasposition and tumour etiology (Yunis, 1983).

The identification of any specific chromosomal rearrangement in solid tumours has lagged behind that of leukemia. Karakousis et al. (1987) have given three important reasons for this lag. These include (1) the often-low mitotic index in tumours (2), the presence of bacteria that can destroy the tumour cells or, thus, not provide an adequate number of cells at metaphase for analysis and (3) frequent multiple and complex chromosomal changes varying in nature from tumour to tumour, that may reflect differences in the responsible causative agents as well as in the secondary process evolving behaviour of the malignant cells.

Therefore, the above reason may render the identification of a specific chromosomal aberration associated with specific solid tumours, such as Wilms's tumour, retinoblastoma in which mostly a single chromosomal change occurs in the process of malignancy.

Recent investigations have revealed specific chromosomal changes in sarcomas (Sandberg and Turc-
Carel, 1987) that can serve as a basis for molecular studies for the primary process of tumourogenesis and can be a criteria for diagnostic and therapeutic approaches.

**Soft Cell Sarcomas**

In a study of the five tumour cases of myxoid liposarcomas, a specific translocation chromosome 12 and 16 t (12 ; 16) (q^13 ; q^11) has been found (Karakousis et al., 1987). They have also found a translocation between the X and 18 t(X ; 18) (p^11.2 ; q^11.2) in six synovial sarcomas. Such Translocation has also been seen in an invesitgation in a primary change of synovial sarcoma (Turc-Carel et al., 1987). The break point 12q^14 with the non random translocations involving segment 12q^13 - 12q^15 has been reported in another type of benign tumour, adenomas of the salivary glands (Mark et al., 1983). According to Karakousis et al. (1987) the proximity of the chromosomal break point 12q^13 and 12q^14 in maxoid liposarcoma and lipoma respectively suggest that the genes for regulation of cell growth are located in the area 12q^13 - q^15. The frequent occurrence of ring chromosome has been observed in nonmyxoid liposarcomas (Karakousis et al., 1987) as well as in lipomas (Heim et al., 1987).
Carcinomas

Carcinomas are quantitatively the most important malignant tumours in humans. Because of technical difficulties less data are available regarding solid tumours especially carcinomas (Mitelman, 1988). In a recent paper, Yue-Sheng et al. (1988) have reported cytogenetic abnormalities with karyotype 46, XY, inv (2) (p22; q24), t(9; 13) (q34; q12) and t(11,18) (q23; q21) in carcinoma of the larynx.

These authors have also examined (Yue-shang Jin et al., 1988b) squamous cell carcinoma of the tongue. No less than 12 pseudodiploid clones were detected. But a chromosomal aberration has been detected in short term cultures of tongue carcinomas (Mitelman, 1988). The rearrangements of chromosome 1, mostly the break points in bands p13, q21 and q32 have also been reported (Hauser-Urfer and Stauffer, 1985) in a malignant tumour of the head and neck region and several deletions of lp and lq have also been found in a patient with squamous cell carcinoma from xeroderma pigmentosum (Aledo et al., 1988). The structural changes of chromosomes 1 have been seen in 10 out of 12 different tumours (Heim and Mitelman, 1987). Jumping translocations with various other chromosomes such as 7, 9, 14 and 22 in which the
breakage has also been observed (Aledo et al., 1988) occur on the short arm of chromosome 14. A large number of apparently unrelated chromosomal abnormalities suggest that the carcinomas have exhibited multi-clonal origin (Yue-Sheng et al., 1988).

The knowledge on chromosomal abnormalities and cellular oncogenes emerged in Burkitt's lymphoma (zech et al., 1976) human meningomas, benign brain tumour, in which a frequent loss of chromosome 22 was seen (Mark, 1974) and Hodgkin's disease (Spriggs et al., 1962; Ricci et al., 1962). These kinds of studies on chromosomal aberrations lead to a hypothesis that non-random chromosomal changes involve a specific site in the genome where a carcinogenic or cancerous gene is located. A reciprocal translocation between 8 and 14 is found repeatedly (Zech et al., 1976).

To sum up it is apparent that there may exist a common factor which induce both cancer as well as chromosome abnormalities. Whether chromosomal changes cause the malignant tumour or whether malignant tumour arise chromosome alterations is yet to be investigated. The translocations or new marker formation in cancer can be considered as a potential origin of new stable cytogenetic combination that have a role in oncogens
transposition and tumour etiology. The oncogene sometimes undergo translocation and the rearrangement of such genes may constitute a key step in many human neoplasm (Heim and Mittelman, 1987), for example in the process of the Philadelpia translocation, the oncogene ABL is transferred to chromosome 22 at 22q.11. (Wang et al., 1988). There are, therefore, some convincing evidence that the majority of malignant tumour have a clonal origin (Nowell, 1976).

AIMS AND OBJECTIVES

Clinical cytogenetics in the west has made tremendous progress with the advent of newer and improved techniques of chromosomes preparations. In India these techniques have not been exploited to the fullest extent. Till recently, the reports from India have been mainly confined to numerical aberrations involving the common types of chromosomal abnormalities such as Down's syndrome and aneuploidies of sex chromosomes.

It is only during the last few years (less than a decade) that sophisticated techniques of differential staining and high resolution banding have been applied for the identification of chromosome structure and its implications in clinical manifestations. Cytogenetic
researches in India have a long way to go. Only a modest beginning has been made. Much more data than have been hitherto collected need to be generated before it can be utilized in providing counselling service to the individuals afflicted with chromosomal disorders.

The present study is an attempt to utilize the conventional staining and C-banding technique as well as sister chromatid exchanges (SCEs) to generate further information on the cytogenetic profile of children afflicted with congenital malformations and of cancer patients. The cases were drawn from a large hospital in Chandigarh. Investigations were carried out with the primary objectives of finding answers to the following questions:

1. Is there any specific marker in the chromosomes of the malformed children and cancer patients? If so, what is the correlation between the disease and specific cytogenetic marker?
2. Is there any association between etiological aspects of the disease and the cytogenetic abnormalities?
3. What is the deviation in the data previously reported in the literature from that of the present study?
In short, a karyotype analysis of the congenitally malformed children and cancer patients was carried out in order to understand the nature of abnormalities, i.e. all kinds of numerical alterations and structural aberrations as well as heterochromatin polymorphism of the chromosomes in diseased human beings.