Chromosomal Variation in Man

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4th Edition

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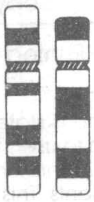

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4th Edition

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List of Chromosomal Syndromes

Preface

In the past, several cytogeneticists have attempted to cope with the bibliographic problem that arose as a result of the rapid developments in this discipline. Some had collected this material and presented it in a concise form. For example, Thompson [1965, 1966] compiled the data on autosomes into a catalog; Hamerton [1971] and Baserga et al [1973] tabulated large amounts of data on abnormal karyotypes in their respective books; Yunis [1977] edited New Chromosomal Syndromes, which includes chapters on recently described conditions; and deGrouchy and Turleau [1977] prepared the Clinical Atlas of Human Chromosomes, and have published a second edition [1982]. Because of advances in techniques for studying chromosomes, however, the literature is inundated with reports of all types of anomalies. Some speciality journals which publish individual case reports with chromosomal anomalies, somewhat reluctantly, have encouraged authors to collate data on similarly affected patients. Thus, a survey was frequently out of date by the time it was published. A more convenient and efficient system for retrieving information on abnormal karyotypes was necessary.

I was fortunate to have had an idea at the right time while in the right place. For some time during the first half of 1974, I was associated with the laboratory of Dr. Frank Ruddle, Department of Biology, Yale University, New Haven, Connecticut. Dr. Chester Partridge and I discussed the use of chromosomally abnormal human cell lines for regional assignment of loci in somatic cell hybridization. Questions about what material was available and how information should be stored arose. A systematic compilation of chromosomally abnormal material was necessary.

The idea to computerize information on abnormal karyotypes in an organized fashion, which could then be retrieved to compile a Catalog, was conceived during the discussions I held with my then colleagues at both Yale and Johns Hopkins [Borgaonkar, Bolling, Partridge, Ruddle, and McKusick, 1975]. Some improvements and changes have been made since then partly because of my discussions with colleagues while I was in Texas (1978-80) and since I have been in Delaware (1980-). I believe the Atma* of the Catalog is in the methodology of organization, its simplicity of use, and the ease and economy with which it can be updated. The speed with which these

*A Sanskrit word meaning, roughly, the immortal soul or spirit of an individual.

revised editions have been prepared provides not only gratifying proof that the Catalog embodies these characteristics but also assures that up-to-date editions could be promptly prepared. In addition, on-line accessibility to data has been achieved through the University of Delaware Computer Center (UDCC) facilities since 1980, with professional input from Robert Shaffer. Since the UDCC is a member of Telenet, Edunet, and DataLink networks, it is possible to retrieve data on any given topic.

The first section of the Catalog, which is necessarily a major component because of the amount and nature of the material available, is concerned with structural chromosomal variations and anomalies such as deletions, inversions, and translocations. Entries in the Catalog are listed according to the chromosome break points. The first two columns of the entry number refer to the chromosome (01 to 22, OX and OY); the third column refers to the chromosome arms (*p* and *q*); and the fourth and fifth column of the entry number refer to the region and band, respectively. Whenever information corresponding to the latter three columns is not available, a *0* is entered in the appropriate column. If and when further information on such an entry becomes available, the revised information can easily be substituted. Following the International System for Human Cytogenetic Nomenclature [ISCN, 1981] recommendations whenever a band was subdivided into units, I have entered the information accordingly in the sixth and seventh columns — eg. 06p2105, implying a break halfway in the band 06p21. Alternatively, if information was available on sub-bands it was entered in the sixth column; if not a *0* was entered. Thus, the first autosome item encoded is 010000 and the last is 22q133. In other words, the minimal information required for a report to be included in this section of the Catalog is that the chromosome involved in the production of the variation or anomaly be known. If an entry is cited under a specific band, generally it is because the authors of the report used at least one of the banding techniques to enable them to designate the break point.

Under each category all the reports are listed alphabetically according to the last name of the first author. The bibliographic citation is followed by chromosome constitution(s) of the individual(s) reported. When available, to avoid possible confusion arising from multiple reporting of the same case, the subjects are identified by their case numbers.

In general, a policy of listing most of the recent reports of structural aberrations has been adopted. References prior to 1970 can be found in the bibliographies of the more recent reports cited in this Catalog. However, certain references prior to 1970 have been included in the Catalog on the basis of their uniqueness, priority, etc.

The entries on chromosomes are arranged in numerical order. Whenever a reference has information on two or more break points (or abnormalities),

an appropriate comment is inserted at the second point of entry. For example, the translocation t(5;14)(p14;q21) will have its complete entry at 05p140, and at 14q210 its secondary entry will have the following notation: "Same entry as in 05p140 (Borgaonkar et al, 1973)." If the break points were not identified precisely — eg, in reports of ring chromosomes and pericentric inversions — then such information has been entered for only the *p* area of the relevant chromosome. There is no secondary entry for such reports on the *q* side of the same chromosome.

The second section of the Catalog lists numerical anomalies including trisomies, monosomies, and polyploids. The first two digits of the entry refer to the chromosome number, and the third column has either a plus (+) or a minus (−) sign indicating trisomy or monsomy, respectively. References on polyploidy are arranged in alphabetical order under triploidy and tetraploidy.

The third section of the Catalog includes comments on conditions that are termed "Chromosomal Breakage Syndromes." Since the aberrations are nonspecific for a single chromosome, they have been entered under a separate category and are listed in alphabetical order.

One of the uses of the Catalog is in chromosome mapping and gene assignment (see Appendix I). Therefore, it was thought desirable to include information on the availability of chromosomally mutant cell lines because of their use in somatic cell hyubridization studies. This was made possible by my fortunate collaboration, in 1974, with Drs. Coriell and Greene of the Institute for Medical Research, Camden, New Jersey. Included in the Catalog are the listing of chromosomally abnormal cell lines of their repository, along with their identifying numbers.

In compiling the Catalog, some arbitrary decisions became necessary. Some of these may have to be reconsidered as additional information becomes available.

1) In part because of the use of the various banding techniques, more and more structural aberrations are being detected. However, if no specific break points were described in the report but could be deciphered easily from the figures or form the content of the paper, then the inferred break points were cataloged. Figure 1 shows that all of the 86 chromosome regions (as defined by ISCN [1981] have now been reported as being involved in interchanges [Kamat and Borgaonkar, 1979]. The importance of position effect phenomenon in individuals with balanced translocations with phenotypic consequences can be evaluated by analyzing data in more detail [Borgaonkar, 1973].

It is important to note that two microscopically similar translocations — identical as per ISCN [1981] — may in fact be genetically different since the break points may be a few loci apart. Obviously, a similar situation holds for other types of structural anomalies. Because one of the uses of the Catalog is in gene mapping, and because more reports of structural anomalies are to be

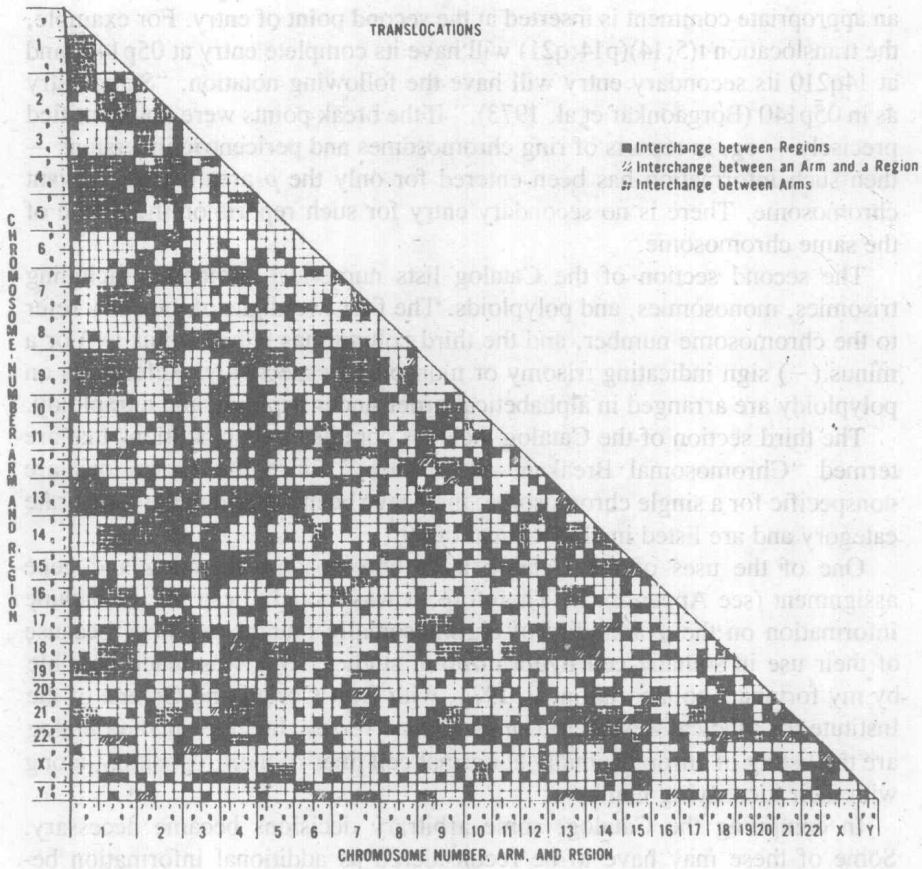

Fig. 1. Chromosomal translocations between chromosome segments as reported in this Catalog. (Figures provided by Dr. Dorene Petrosky, Delaware State College, Dover, Delaware.)

found and there is now more interest in partial monsomic and partial trisomic clinical syndromes, the structural anomaly section of the Catalog is much more detailed than other sections. However, not all reports are cited in the Catalog by any means (for example, reports on ring chromosome 18). As elsewhere in the Catalog, it has been the goal to provide key references on all kinds of chromosomal variants and anomalies, and through these, readers should be able to locate the literature on any given condition or topic.

2) Of numerous reports on relatively common conditions such as the trisomies of chromosomes 13, 18, and 21, partial monosomies of 5p, 18p, and the 45,X and 47,XXY chromosomal abnormalities, only a few reports have been cataloged on the basis of priority, uniqueness, or general coverage.

3) Reports on chromosome changes in tumors, cancers, and leukemic cell

lines have been almost entirely excluded.

4) Data on experimentally produced chromosomal break points have also been excluded.

Regarding the use of nomenclature, I have attempted to adhere to the guidelines put forward by the ISCN [1981] and its predecessors. Several departures or modifications seem appropriate, however.

1)In the aneuploidy section the first two digits in the entry for the chromosome number have been maintained. These are followed by the designations (+) for a trisomy and (−) for a monosomy. Double aneuploidy is entered in the same manner. In this section all entries are in numerical order, followed by X and Y. For multiple sex chromosomal anomalies, those of the X chromosome are listed first.

2) In translocations where only changes in length were known, single parentheses are used — eg, 46,XX,t(5p+;13q−). No assumption is made with regard to the reciprocal nature of a translocation unless this was so stated in the report. A statement of balanced translocation in a report was not interpreted as necessarily implying a reciprocal translocation!

3) Whenever an existing band is subdivided, the ISCN [1981] recommendations called for a decimal point placed after the original band designation, followed by the number assigned to the sub-band. The decimal point has not been used in the entry numbers.

To facilitate the collection of data regarding preferential involvement of certain chromosomal regions in aberrations, the entry number has been included with the banding pattern for the band or sub-band — ie, Negative, Positive, or Variable as per the Q and G banding techniques (see Table I). As we begin to understand the biochemical basis of the banding techniques and its relationship to chromosome breakage, this information may be helpful in understanding the mechanics of aberration. Admittedly, these figures reflect only those break points that are reported in the literature and entered in the Catalog, and considerable bias goes into what the investigator considers a significant finding and what is fit for publication! The difference between

TABLE I. Number of Entries in the Catalog by Type of Band and Break Points

Band region	1st edition 1975 n (%)	2nd edition 1977 n (%)	3rd edition 1980 n (%)	4th edition 1983 n (%)	Proportion in the genome
Negative	450 (64.4)	907 (65.5)	1,554 (67.63)	2,343 (67.04)	54.2
Positive	101 (14.4)	264 (19.1)	487 (21.29)	765 (21.89)	38.2
Variable	148 (21.2)	214 (15.4)	257 (11.18)	387 (11.07)	7.6
Total	699	1,385	2,298	3,495	100

the expected involvement of the three band regions (Negative, Positive, and Variable), based on their proportionate occurrence in the genome and that actually observed in the break points has been demonstrated to be statistically significant [Yu et al, 1978].

In addition to the reasons stated in Borgaonkar and Bolling [1976], there were other significant reasons for undertaking a computerized chromosomal Catalog.

1) The geneticist may pool linkage data obtained by the pedigree approach using marker chromosomes (Table VI). The Catalog could be used in the selection of cell lines for regional assignment of loci by the somatic cell hybridization approach.

2) In the description of new clinical material with chromosomal abnormalities, it is becoming increasingly difficult to ascertain from the literature what, if anything, has been published on the same type of chromosomal abnormality. The information that is available in abstracting journals is not easily culled. For example, the phenomenon of centric fission has been reported five times in human populations but twice for chromosome 7. It is hoped that the Catalog will satisfy such needs.

The attempt to collate information on new chromosomal syndromes [Borgaonkar et al. 1976] is continuing. I have included a list of chromosome band numbers (Table II) that are known to be polymorphic by the nature of their quinacrine fluorescence or their staining properties with various other banding techniques, especially constitutive C-banding heterochromatin. Also included in this table are fragile sites that have been elicited by the use of special medium in culture. Availability of such lists has been found to be particularly useful for a variety of reasons, such as, occasions when a variant

TABLE II. Polymorphic (or Variant) and Fragile Site Areas in the Human Genome

Polymorphic:	1q12	Fragile Sites:	2q13
	2q12		6p23
	3p11 and 3q11		7p11
	4p11 and 4q11		8q22
	6p11		9p21
	9q12		9q32
	13p11, 2, and 3 and 13q11		10q23
	14p11, 2, and 3		10q25
	15p11, 2, and 3		11q13
	16q11		11q23
	17p13		12q13
	19p11 and q11		16p12
	21p11, 2, and 3		16q22
	22p11, 2, and 3		20p11
	Xq27 or 8		Xq27
	Yq12		

pattern is found in a case and the investigator becomes aware that family studies may be warranted. Reports assembled in the Catalog are so arranged that monosomic and trisomic reports of chromosomes or of chromosomal regions can be located systematically. Partial chromosomal aneuploidy syndromes are tabulated in Table III, and aneuploidies involving whole chromosomes are listed in Table IV (also see Appendix II). These lists do become

TABLE III. Chromosome Arms Involved in Partical Aneuploidy Syndromes (− Absent) (+ Present)

Chromosome number and arm	Monosomy	Trisomy
1p	+	−
1q	+	+
2p	+	+
2q	+	+
3p	+	+
3q	+	+
4p	+	+
4q	+	+
5p	+	+
5q	−	+
6p	−	+
6q	+	+
7p	+	+
7q	+	+
8p	+	+
8q	+	+
9p	+	+
9q	+	+
10p	+	+
10q	+	+
11p	+	+
11q	+	+
12p	+	+
12q	−	+
13q	+	+
14q	−	+
15q	+	+
16p	−	+
17p	−	+
17q	−	+
18p	+	+
18q	+	+
19q	−	+
20p	−	+
21q	+	+
22q	+	+
Xp	+	+
Xq	+	+
Yp	+	+
Yq	+	+

TABLE IV. Chromosomes Involved in Full Aneuploidies

Chromosome number	Monosomy	Trisomy
1		
2		+
3		+
4		+
5		+
6		+
7		+
8		+
9		+
10		+
11		
12		+
13		+
14		+
15		+
16	+	+
17		+
18	+	+
19		+
20	+	+
21	+	+
22	+	+
X	+	+
Y	+	+

outdated, and we will be talking and writing about specific segments of chromosomes as being responsible for specific syndromes. In fact, a beginning has already been made; the Down syndrome is now known to be due to trisomic state of sub-band 21q221. In addition, we have established at the Thomas Jefferson University a computerized data base entitled "Chromosomal Syndrome Counseling System" [Reed, Jackson, Shaffer, Eleuterio, and Borgaonkar, 1982] wherein considerable detailed information is avialable on all syndromes and/or aneuploid states. Collation of reports on chromosomal variants, anomalies, and aneuploidies has been found to be of considerable value and usefulness in genetic counseling to patients and families with chromosomal problems; knowledge about the phenotype of carriers of seemingly similar balanced translocation or inversion carriers has been an important factor in parent's decisions to continue a pregnancy.

It appears that man as a biological species is able to "tolerate" extra chromosmal material better than the lack of it. Thus, fewer monosomies than trisomies have been documented so far in chromosome studies on abortuses,

stillborns, and liveborns. Furthermore, certain chromosomes, such as 16, are rarely involved in anomalies of the liveborn.

3) In structural aberrations it will be possible to relate the involvement of the type of band (i.e. Negative, Positive, or Variable) to the occurrence of a certain type of aberration in the human karyotype; in other words, there will be an extension of earlier studies [Yu, et. al., 1978].

4) The chromosomal variations and anomalies were categorized into 27 groups which were then coded for computerization and retrieval purposes (Table V). The nomenclature of the categorization mostly follows that of the ISCN [1981] report. Into which group an aberration falls is determined by examining the chromosome constitution of the individuals reported. This

TABLE V. Aberration Code*

1.	IC	Isochromosome	14.	CT	Complex translocation
2.	TD	Terminal deletion	15.	ST	Simple translocation, trans-location
3.	ID	Interstitial deletion			
4.	IP	Inversion paracentric	16.	DU	Duplication
5.	PI	Pericentric inversion	17.	TX	Tandem translocation
6.	RI	Ring chromosome	18.	RE	Recombinant chromosome
7.	DI	Dicentric chromosome	19.	MA	Marker chromosome
8.	RT	Reciprocal translocation	20.	WT	Whole arm translocation
9.	TR	Robertsonian translocation	21.	TA	Terminal rearrangements
10.	IN	Direct insertions within a chromosome	22.	DD	Direct duplication
			23.	CF	Centromeric fission
11.	II	Inverted insertion	24.	FS	Fragile site
12.	IX	Direct insertions between two chromosomes	25.	DT	Double translocation
			26.	UT	Unstable translocation
13.	XI	Inverted insertions between two chromosomes	27.	DA	Double aberration

*Explanations of the above terms are as follows. For details the reader is to consult standard textbooks on cytogenetics, and ISCN (1978).

IC–Isochromosome: The two arms of the chromosome are identical to each other.

TD–Terminal deletion: A terminal segment of a chromosome is deleted.

ID–Interstitial deletion: An intermediary segment, i.e., excluding a centromere and terminal ends (telomeres), of a chromosome is deleted.

IP–Inversion paracentric: An inversion of a chromosome segment that includes the centromere.

PI–Pericentric inversion: An inversion of a chromosome segment that includes the centromere.

RI–Ring chromosome: Two broken ends of a chromosome have joined to form a ring-like structure.

DI–Dicentric chromosome: A chromosome with two centromeres.

RT–Reciprocal translocation: In a translocation the segments of chromosomes have been exchanged.

TR–Robertsonian translocation: Translocations involving acrocentric chromosomes, e.g., 13 and 21, and resulting essentially in a single chromosome with long arms of both chromosomes.

IN–Direct insertions within a chromosome: A segment has been inserted into the same chromosome at another point.

(continued)

TABLE V. Aberration Code (continued)

II–Inverted insertions within a chromosome: The segment that has been inserted into the same chromosome at another point is inverted in relation to the centromere.
IX–Direct insertions between two chromosomes: A segment from one chromosome that has been inserted at a point into another chromosome.
XI–Inverted insertions between two chromosomes: The segment from one chromosome that has been inserted at a point into another chromosome has been inverted in its relationship to the centromere.
CT–Complex translocation: A translocation involving three or more chromosomes (refer to ISCN (1978) p. 39 for further details).
ST–Simple translocation, translocation: A transfer of a segment of one chromosome to another.
DU–Duplication: A chromosome in which a segment is present in duplicate.
TX–Tandem translocation: A transfer of a segment of one chromosome to the end of an arm of another chromosome.
RE–Recombinant chromosome: A structurally rearranged chromosome with a new segmental composition resulting from meiotic crossing-over between a displaced segment and its normally located counterpart in certain types of structural anomalies.
MA–Marker chromosomes: This term has been rather loosely used here to include any chromosome with a polymorphic or variant feature.
WT–Whole arm translocation: Whole arm exchanges that involve nonacrocentric chromosomes.
TA–Terminal rearrangement: Two chromosome are joined end to end.
DD–Direct duplication: A duplicated segment is found on the same chromosome.
CF–Centromeric fission: Splitting of the centromere to provide two functional centromeres.
FS–Fragile site: A fragile site, elicited by any of the techniques, of a chromosome in the genome.
DT–Double translocation: Two independent translocations in the same person involving four chromosomes altogether.
UT–Unstable translocation: When translocations are found which are not uniformly present and are constantly in a changing milieu.
DA–Double aberration: When more than one kind of anomaly is present, e.g. a translocation and a ring chromosome in one person.

information has been retrieved from our computer bank and tabulated. Table VI includes, for each chromosome, the number of aberrations listed. This should facilitate a search for, and compilation of, data on the various types of abnormalities that occur in chromosomes; for example, an examination of Table VI demonstrates that ring chromosome has been described only twice for chromosome 16 [Wheeler et al, 1976].

5) The assembling of data on abnormal karyotypes should make it possible to work with problems related to estimation of risk in the transmission of abnormal rearrangements and involvement of factors such as sex and bias of ascertainment. Khaldi, et. al., [1979] have presented some risk estimates for inversion carriers and Petrosky [1983] for some translocation carriers.

6) It was my intention to establish an International Registry of Abnormal Karyotypes according to the method of this Catalog. Accordingly, the Tenth