# Clinical Atlas of Human Chromosomes

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*For Priscilla and Jim Neel*
*with gratitude*

# FOREWORD

The organization Drs. de Grouchy and Turleau have devised for their *Atlas* is innovative and highly useful. As a catalog of chromosomal anomalies, it is comparable to my catalog of Mendelian traits (*Mendelian Inheritance in Man: Catalogs of Autosomal Dominant, Autosomal Recessive and X-linked Phenotypes,* fourth edition, 1975). The de Grouchy–Turleau *Atlas,* however, is much more than a catalog of chromosomal anomalies, since mapping information and comparative cytogenetics are also covered.

A remarkable development of the last seven or eight years—mainly since the advent of "banding methods" for chromosome study—has been the description of many "new" chromosomal syndromes. Chromosomal aberrations that previously could not be precisely defined yielded to analysis by the banding techniques. And when cases thus shown to be chromosomally identical were analyzed phenotypically, a clinical syndrome often emerged. It is these rapid advances that are embraced by the de Grouchy–Turleau *Atlas.* It is useful to have also the information on genes assigned to specific chromosomes and on homologies to primate chromosomes—fields to which the authors have contributed much and fields of phenomenal advance in the last few years.

Among the clinical features of the various chromosomal syndromes it is interesting to note the conspicuousness of those subsumed by the label *craniofacial dysmorphia* (Americans might be more inclined to say *dysmorphism*). Many of these conditions are indeed physiognomonic diagnoses. The succinct listing of the cardinal phenotypic features, together with the marvelously abundant illustrations, should serve to fix the syndrome in mind.

Although the meaning is always clear from the context, it should be mentioned that the *Atlas* contains some terms that have an unfamiliar ring to the American ear. For instance, *evocative* is an adjective often used to mean characteristic or suggestive in relation to the features of a syndrome. The great value of the *Atlas,* however, is not impaired by these occasional Gallicisms.

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# PREFACE

Until the end of the fifties, not so long ago, human chromosomes were mysterious hieroglyphics, kinds of small inverted V's, lined up at the bottom of a page in genetic textbooks, with a haughty caption: "The 48 Chromosomes of Man."

Times have changed. To begin with, two chromosomes have been lost. But most important, chromosomes have become entities, even very important individuals. They are photographed, cut apart, and reassembled on the scientist's whim. They are dressed in bright and gaudy colors, made to fluoresce, and even costumed as harlequins.

Each of the 46 human chromosomes now has a personality, preventing confusion with any other. This personality has several aspects. First and foremost is banding in the different systems (Q-, G-, R-banding, etc.), which is always specific for a given chromosome.

Next is the way in which the chromosome has evolved since the ancestral species common to man and the other hominoid primates, namely our closest cousins, the chimpanzee, the gorilla, and the orangutan. Certain chromosomes have remained extraordinarily stable and can be considered true "paleochromosomes." Chromosome 6 is a good example. Others, such as chromosome 9, have undergone numerous rearrangements and today are different in the four species.

Another aspect of the chromosome's personality derives from the number and nature of genes it carries. At the Congress of Human Genetics held in Paris in 1971 F. Ruddle reviewed the gene map of man. At that time two autosomal localizations were known, those of thymidine kinase on chromosome 17 and of lactico dehydrogenase A on chromosome 11. Today, only five years later, more than one hundred genes are localized. Among these, some are dear to the heart of every geneticist: the Rh factor on chromosome 1, the HLA locus on chromosome 6, and—the latest localization—the ABO blood group on chromosome 9.

Without doubt, a leading element of the personality of a chromosome is the pathology for which it is responsible. In this respect the most notorious chromosome is also the smallest, chromosome 21. Many, such as chromosomes 4, 5, 8, 9, 13 and 18, have a very rich pathology. It includes well-defined syndromes characterized by the craniofacial dysmorphia, by the degree and nature of the encephalopathy, by the presence or absence of growth retardation, by the age at which the patients are first examined, and by many other features. The symptoms of chromosome 8 trisomy resemble neither those of the "cri du chat" syndrome nor those of 9p monosomy syndrome. By contrast, other chromosomes, such as the largest, chromosome 1, have a very scant pathology, even nonexistent. They may have functions of such importance that any unbalance due to monosomy or trisomy is incompatible with survival.

These facets of the personality of chromosomes are the basis of this book, which we envisaged titling: "From 1 to 22, and X and Y"—but this would not have been serious enough.

In brief, a chapter will be devoted to each chromosome, according to its order in the human karyotype. All chapters are designed in the same manner. Each begins with a short résumé of the chromosome's personality. Reference to its evolution in the hominoid primates is based on our own work and that of B. Dutrillaux. Following this is a "physical" description, including the chromosome in its standard staining; the schematic of regions and bands as specified by the nomenclature of Paris, 1971; and several examples of banding obtained by different techniques. When justifiable, this morphological identification is completed by a description of the polymorphism of the chromosome.

This "mark of distinction" of the chromosome is followed by its gene map. The latter is in line with the information bulletin of February 1, 1976, "The Human Gene Map," issued by V. A. McKusick, as well as with the reports of the three conferences dedicated to "Human Gene Mapping"—at New Haven (1973), Rotterdam (1974), and Baltimore (1975). Only more recent papers, not covered in these proceedings, have been listed.

Among gene localizations, certain are solidly established, having been confirmed by several laboratories. Others are less reliable: they have been suggested by a single group of investigators and are not yet confirmed, some having even been contradicted. It is sometimes difficult to draw the dividing line between the two groups. In cases of uncertainty we have exercised prudence in considering the localization as "provisional." Well-established localizations are given on the right-hand side of the chromosomal schematic and the others on the left. In some cases, localizations are given on both sides, indicating that they are definite for the given chromosome, but that the more precise localization has not yet been confirmed.

The names and abbreviations of genetic markers, principally enzymes, are still highly inconsistent; they vary between publications as well as within the same publication. As far as possible, we have tried to retain the names and abbreviations most often employed at the time of writing.

In the majority of the chapters the most important part centers on pathology. The concept of syndrome is difficult to define. The best definition is perhaps "a pattern of symptoms common to a set of individuals." It is evident that the description of a new syndrome necessitates compiling a sufficient number both of clinical features and of observed individuals. Obviously, the description of chromosome 21 trisomy, the "cri du chat" disease, and the like presents no difficulty. By contrast, there are isolated observations whose correlation with a well-defined syndrome is much more open to question. We have endeavored to ascertain a minimum of three observations of patients with clearly comparable phenotypes. The figure on page xvii indicates the syndromes we have retained as valid.

Wherever it was possible to confirm the concept of "type and countertype" defined by J. Lejeune, comparing the syndromes due to trisomy and to monosomy for a given chromosomal segment, we have summarized in a table the main contrasting features.

Regarding the bibliography, we have not attempted to provide all known references, but only the principal ones. For "classical" syndromes we have listed the references, particularly those of recent reviews, that enable the reader to locate the entire bibliography. Where syndromes are based on a small number of observations, all known references are given.

Each syndrome is illustrated by photographs of patients. Figure numbers with letters (e.g., 1a, 1b) indicate photographs of the same patient. The sources of these photographs—publications, the collection of the Institut de Progénèse (Prof. J. Lejeune), and our personal collection—are listed at the end of the book.

The reader may be surprised by the lack of examples of chromosomal rearrangements in the illustrations. We believe that such illustrations would add little to the book's informative value. In complete trisomies, the additional chromosome is not different from the chromosomes of the normal pair. In translocations, resulting in partial trisomies or monosomies, each observation constitutes a special case. When a preferential breakage point seems to exist on a chromosome, we have indicated this.

Considerable importance has been given to the appendixes. They include:

- A description of the current cytological techniques. This is sufficiently complete and detailed to allow their practical application. In each case we have described in detail a proven technique and have mentioned the essential points of several variants.
- A description of the basic concepts necessary for the interpretation of palmar and digital dermatoglyphics.
- The chromosomal nomenclature as defined by the conventions of Denver, London, Chicago, and Paris.
- A list of localized genetic markers and the identification of the corresponding chromosome.
- A "syndrome finder," which classifies the most important symptoms and the syndromes they suggest.

This book was not designed as a treatise of classical cytogenetics. Many such works are indeed available, from the classic *Les chromosomes humains* by R. Turpin and J. Lejeune (1965) to the more recent *Human Cytogenetics* by J. Hamerton (1971). The fundamental principles they expound have evolved very little since then. By contrast, genetic localizations and chromosomal pathology have evolved considerably; they justify the writing of this new book, which has been designed as an atlas.

The reader will no doubt see the resemblance to geographical atlases—the various geographic, political, economic, and historic maps that illustrate the advances and retreats of national boundaries under the influence of the centuries. In the same way, the reader will find a morphological map of each chromosome with its topographical bands, as revealed by the different banding techniques; a map of pathology, indicating the different syndromes for which a given chromosome may be responsible; and a gene map, describing resources—i.e., a given chromosome's wealth in genes.

Everyone consults an atlas at one time or another. The present atlas is intended for a vast audience of biologists, doctors, and above all for pediatricians. By vocation the pediatrician is an amateur of rare diseases. Today, he is invited to recognize the abundance of new cytogenetic syndromes, challenging his perspicacity.

Destined for the pediatrician's consulting room, this atlas is also intended for the cytogeneticist, as much for his office as for his laboratory bench, where it can provide the necessary formulas for obtaining chromosomal preparations of good quality.

It is also intended to provide the physician and cytogeneticist with the means of a common language, comprehensible to both. The doctor must know when to ask for a karyotypic examination and also how to interpret the results provided by the cytogeneticist. This is the aim of the nomenclature presented in detail in the appendix.

Other important specialists should also be concerned—for example, the biochemist, the hematologist, or the immunologist, of whom the pediatrician or cytogeneticist will solicit an assay of a given enzymatic activity, which may be increased or decreased. They may also be asked to determine a given blood group, whose locus is situated on the chromosome or chromosomal segment present singly or in triplicate, or again to assay a given gammaglobulin. Such is the aim of the gene map of each chromosome, indicating which abnormal biological activity should be most profoundly studied.

We hope that the reader will approve our ambitions and at the same time perhaps be further impressed by the remarkable organization of man's hereditary material—an organization that certainly remains full of surprises.

Jean de Grouchy
Catherine Turleau

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Jean de Grouchy
Catherine Turleau

# Definitions of Symbols Used in the Figures

***Methods for Mapping Genes***

F. Study of traits of families

S. "Segregation" of cellular markers and chromosomes in clones from somatic cell hybrids

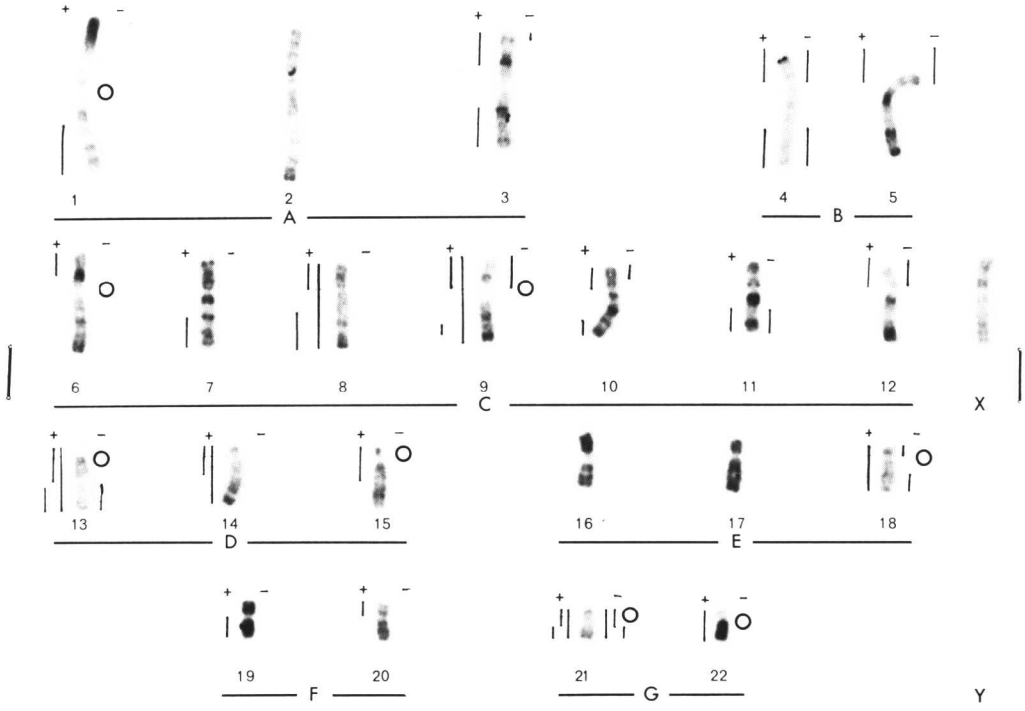
A. *In situ* DNA-RNA annealing ("hybridization")

D. Deletion mapping, trisomy mapping, and gene dosage effects

***Banding Techniques (see also the appendix)***

| | |
|---|---|
| QFQ | Q-bands by fluorescence using quinacrine |
| GTG | G-bands by trypsin using Giemsa |
| RHG | R-bands by heating using Giemsa |
| RBA | R-bands by BrdU using acridine orange |
| THA | T-bands by heating with acridine orange |
| C | C-bands |

# Map of Chromosomal Diseases



# CONTENTS