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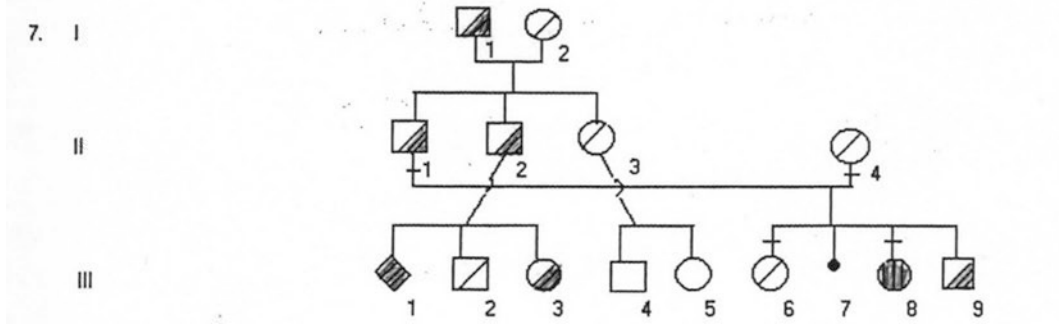
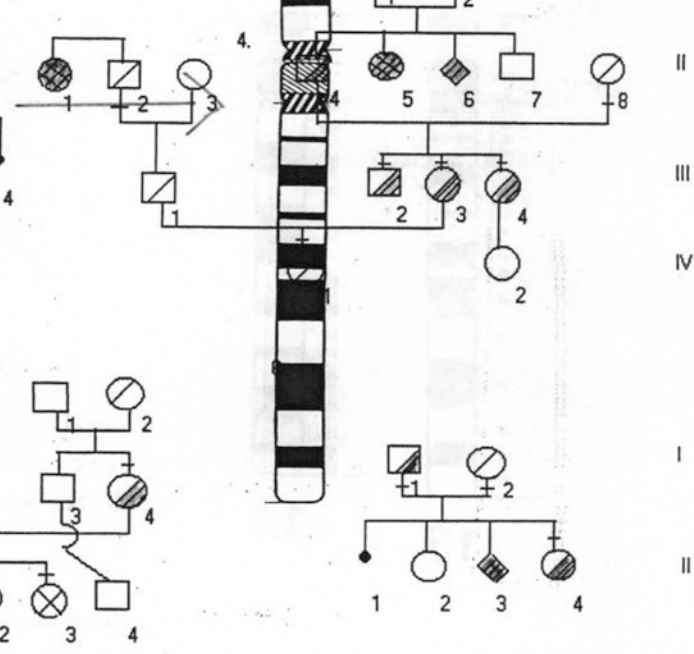
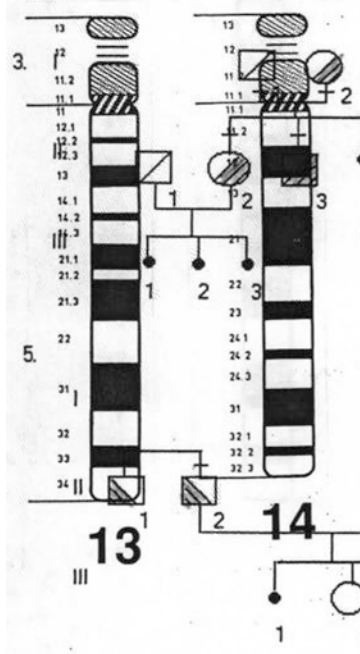
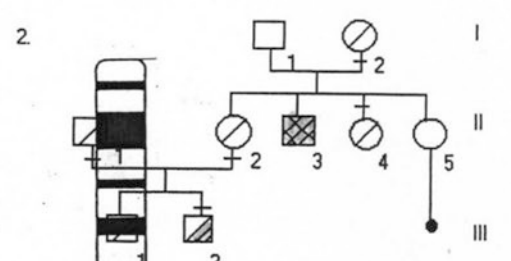
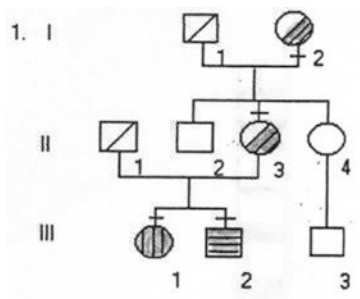
# Human Chromosome Atlas

Introduction to Diagnostics of  
Structural Aberrations

*Second Edition*

 Springer

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Parvin Mehdipour • Heinz Schott  
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Aberrations

Second Edition

Technical Assistance: Ute Schlütter

 Springer

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ISBN 978-3-031-10587-6

ISBN 978-3-031-10588-3 (eBook)

<https://doi.org/10.1007/978-3-031-10588-3>

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## Preface

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Cytogenetic is a significant subject of research in the field of Genetics, especially in Human Genetics. Over the past 66 years, it has developed explosively, and during this time has been divided into various research and application areas with the most relevant of them being theoretical Cytogenetics as a basic science, followed by Tumour Cytogenetics, investigations on Mutagenesis, Evolution, and Population Cytogenetics. In addition to and in parallel to these fields of research, cytogeneticists established a close cooperation with related areas of research such as Molecular Genetics, Clinical Genetics, Cell Biology, Biology of Reproduction, Oncology, and Pathology.

Progress in the field has always been in conjunction with progression in investigation methods which generally lead to new focus areas of research and to improved capabilities of diagnosis in the investigation of carriers of chromosome aberrations. From the start, cytogenetics excelled in intensive international cooperation, which included joint decisions in questions of chromosome nomenclature (ISCN), specific symposia, workshops, seminars, and events for continuing education on national and international levels. These activities led to close personal contact between scientists and research groups, as well as to counselling of young scientists thus serving as an impetus for many future-oriented projects.

It is desirable that this inspiring atmosphere will accompany cytogenetic scientists in the future as it did in the past.

The Atlas presented here is composed of three major topics:

First, to introduce general social specifics concerning the acceptance of handicapped persons, second, to initiate those ethic principals which have to be taken into account, and third to present the fundamental principles that guarantee the desirable quality in diagnostics and counselling. This is underlined and supported by the results of genetic counselling in cases of chromosome aberrations, specifics in the course of life of carriers of chromosome syndromes, the development of support groups, and the main pathways in the course of diagnostic investigations.

The presentation of 88 single cases of structural chromosome aberrations is divided into intra-, interchromosomal abnormalities and in mutations in polymorphic regions.

The present atlas of structural chromosomal aberrations is intended to be a diagnostic assistance in applied cytogenetics in order to analyse the human karyotype.

It illustrates the spectrum of chromosome abnormalities through a combination of karyotypes and ideograms, it emphasizes the expressiveness of different banding techniques, and it expresses the karyotype formula and morphological features of each case presented. Furthermore, it reveals potential problems

in the detecting of aberrations and lists necessary additional investigations and particularities that have to be taken into account when counselling carriers of a chromosome aberration or their relatives.

It is our intention to present a broad spectrum of chromosome abnormalities. We are not suggesting that we can give a complete collection of all aberration types possible, but we are attempting to give an impression of the spectrum of findings that an institute of applied cytogenetics and clinical genetics can offer.

Most likely, many users of this atlas experienced other additional important cases of aberrations or developed new strategies while investigating problematic cases. We would appreciate them to share their knowledge with us.

To all colleagues working in the field of cytogenetics: Let's aim for a successful future and satisfying research projects. Hopefully, the chromosome atlas presented here will give a helping hand.

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## Acknowledgement

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Work for the second edition of the Chromosome Atlas warranted extensive research due to the added subject topics.

It was supported by two colleagues—Herdit Schueler, Institute of Human Genetics, University Aachen, and Lieselotte Kalz, Institute of Human Genetics Bonn. They were of great assistance with their specialised suggestions in the wording of the new chapters.

We feel obliged to Werner Jung and Ute Schlütter for their assistance of the case presentations.

Tanja Weyandt and Dr. Eliana Acosta—Associate Editors of Biomedicine and Life Sciences, Springer Verlag Heidelberg—were a valued contact persons concerning all the problems that occurred in structuring the second edition of the Atlas, for formal issues and for the desirable progress of the work. Without their help, the process would not have run so smoothly.



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# Social Attitude Towards Disabled People: Historical and Cultural Aspects

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Discrimination and repulsion of disabled people can be observed throughout human history. The tendency to exclude them from "normal" society is a common attitude. Even to kill them may be an option to be realised under certain circumstances. In particular, that has become apparent in Nazi Germany during World War II with its (even then illegal) "euthanasia" programme. It displayed a sophisticated system of murdering ten thousands of patients of mental hospitals in special killing centres on the eve of the holocaust. The motivation for such a criminal atrocity shows characteristic traits of such an extermination strategy. There are three relevant dimensions: (1) The economic argument stresses the financial burdens caused by the disabled seen as unproductive eaters weakening the normal society (this idea became first an ideological argument in the face of the misery of World War I); (2) the biological reluctance assumes that disability caused by hereditary diseases would produce a general degeneration of the "vital race" according to the doctrine of eugenics which was widely accepted in the academic world at the end of the nineteenth century; and (3) for social psychological reasons, the disabled were supposed to be "inferior" and a threat for fellow men because of their typical mind of evil resentment (see below: *Krippelseele*, crippled mind).

On the other hand, there has been always a benevolent attitude towards the disabled, too. There are impressive examples of support and shelter for those people traditionally common in all cultural areas and religions: asylums, charitable orders, auxiliary institutions, sheltered workshops etc. In the second half of the twentieth century, the idea of medical, social, and economical rehabilitation emerged and became an important issue of social medicine and health policy. The reintegration of the disabled is a social political objective under the slogan "inclusion". So, many public and private institutions target this mission (see below "conclusion"). Nevertheless, there remain a lot of problems for disabled people in their everyday life. They originate often from a more or less unconscious rejection of their otherness according to their appearance, behaviour, and insufficient performance. In this respect, it is useful to consider some cultural historical patterns affecting the respective social attitude towards the disabled. This chapter focusses on the treatment of the humans with congenital deformities and physical and/or mental anomalies, for example, people with Down syndrome.

### 1.1 Monstrosities: Consequence of Sin Versus Play of Nature

---

Newborns with congenital deformities were traditionally called "monsters" (from Latin *monstrum* = warning sign). This concept originated from pre-scientific superstition. But it is often inherent today regarding the horror and defence of "normal" people meeting disabled persons. The emergence of monsters

seemed to display future calamities according to the art or science of ancient divination performed by erudite priests and other experts (e.g. augurs in the Roman Empire), along with the interpretation of dreams, astrology, hepatoscopy, or bird flight as methods of prophecy. The clay tablets with cuneiform inscriptions are the earliest written documents showing such a divination belonging to the library of King Assurbanipal (seventh century B.C.) of the Assyrian Empire in Nineveh. There are precise interpretations of malformations of the newborn. For example, "If a woman gives birth to a child who's right ear is small, the house in which it is born will be destroyed". Or: "If the child has no feet, the water streets of the country will be interrupted and the house destroyed".

So, monsters were perceived as signs of impending doom. Even in the renaissance, this attitude flourished again. Although monsters could also refer to lucky circumstances, their meaning as bad omens prevailed among medics in particular. There is a famous example for the interpretation of a monstrosity as a divine sign in a satirical form: "*Der Bapstesel zu Rom*" (The pope donkey of Rome), a flyer edited by Martin Luther and Philipp Melanchthon in 1523.

The idea that the deities punish the humans for committed iniquities with misery and disease originates from antiquity, too. In particular, it should explain the outbreak of an epidemic. Later on, the Christian tradition intensified this theory of sin claiming that the "original sin" would also cause misfits. So, among others, Paracelsus (i.e. Theophrastus Bombast von Hohenheim, 1493/94–1541) interpreted malformations as signs of the evil: "In the same way as hangman marks his children with evil signs, the evil ascendants mark their children with unnatural blasphemous signs, so that one should abstain from such people like from hangmen". Insofar, the physical stigmas also indicated moral deficiencies and were equally signatures of the evil. It was common in early modern medicine to characterise monsters as evidence of punishment for committed fornication, debauchery, and excessiveness. In general, the explanation of diseases as a consequence of sin is essential for medical doctrines of disease throughout modern times. So, mental disorder was deduced from the sinful life of the respective patient still in early nineteenth century by some psychiatrists (shrinks). In a secularised manner, it was (and is) also subversively present in psychosomatics, psychotherapy, and psychoanalysis nowadays in regard to the theory of an "unconscious guilt" producing harmful symptoms. Analogically, also physical medicine provides the theory of bad, i.e. unhealthy behaviour as a sinful one resulting in disorder and disease. In this view, for example, lung cancer appears to be a punishment for chain smoking, a misconduct which is penalised by the abused body. It should be stressed that disease as well as disablement are thought to be causally linked with a previous reprehensible activity.

In the renaissance—within the context of natural magic, astrology, and the belief in witchcraft—the assumption spread that misfits and "cretins" would directly descend from the devil. For Paracelsus and his contemporaries, it was obvious that misfits would be procreated by the conjunction of devils and witches. In the sixteenth century, it was seriously discussed, whether it was allowed or forbidden to kill the monsters. Paracelsus denied killing them. They should remain as creatures of God: "So, I just let them alive like animals". In contrast, "The Hammer of Witches" (*Hexenhammer*), the most important textbook of the inquisition of the Roman Catholic church, approved the extinction of the monsters. In the course of the witch-hunt, even small children were tortured and killed.

A special product of devil's work was the so-called changeling. It was assumed that shortly after the birth the devil or other evil demons would exchange the newborn with a devil child. Such "changelings" (*Wechselbälge*) would show all signs of the evil: extremely voracious, lazy, and misshapen. The most cruel mistreatment of the changeling should enforce the return of the original child. And even its killing was allowed according to Luther, who said in one of his table talks in 1541 that such changelings would only be a piece of flesh (*massa carnis*) because there would be no soul in it which could be done by the devil. So, even young children were treated brutally like presumptive witches and possessed by the devil. Only in the eighteenth century, they were finally seen as medical objects and a challenge for scientific research, for example, changelings were identified sometimes as children suffering from rickets. Now, disability was no longer interpreted as a punishment for sins or negligence of the parents but as a natural disorder or consequence of the "play of nature" (*ludibrium naturae*).

After the French Revolution, for the first time, there was a systematic practical approach to treat the disabled medically. So, lunatics, blind people, or deaf-mutes in particular were cared in special institutions. They were taken seriously as severely disabled who had to be supported according to human dignity. From today's perspective, that guiding principle was contrasted by a brutal reality, for example, in lunatic asylums in the nineteenth and twentieth centuries.

Nevertheless, one can state a general shift from repulsion and exclusion of the disabled to an attempt to adapt them to normal life by physical and psychological treatments.

## 1.2 "Cripples": The Power of Imagination, Crippled Mind, and Show Business

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Besides the religious or demonological explanation of congenital malformations, there was also a sort of psychosomatic theory. The "accidental look" (German: *Vorsehen*) of a pregnant



woman could produce an introjection of an object of the environment having an immediate impact on the foetus inside her body. This seemed to be due to the power of "imagination" (Latin: *imaginatio*), a central concept of early modern medical anthropology. Paracelsus among others used this concept to explain congenital malformations. It has a long tradition in popular culture. The terms "*Hasenscharte*" (unilateral cleft lip and palate) and "*Wolfsrachen*" (bilateral cleft lip and palate) point at this tradition. A woman catching sight of a hare or frightened by a wolf could involuntarily coin her unborn child by respective introjected images. Therefore, it seemed to be dangerous for a pregnant woman to look at cripples or otherwise disabled persons (e.g. lepers) which was supposed to cause eventually monstrosities. In a way, the stigma of the evil seemed to produce itself another stigma of the evil. It seemed to be contagious. So, for centuries, pregnant women were recommended to avoid encountering disabled persons. For example, in 1708 the city council of Nuremberg banned deformed and mutilated people to stay at the marketplaces in order to avoid the disastrous consequences when pregnant woman looked at them. The prevention to be infected by the evil was just to ban the respective figures from the public sphere. At the same time, the imagination doctrine provided an apologetic explanation. Not a sinful behaviour would generate deformation of the child, but the evil influence emanating from crippled beggars, mutilated troopers, or certain animals. So, the doctrine of imagination (bad look of a pregnant woman in particular) did not replace the theory of the disablement as a consequence of sin, but rather implied it. It projected it into an evil impact from outside analogously the "evil eye" producing harm and disorders in somebody else.

Monstrosities like changelings were supposed to exist without a soul, being just a "piece of flesh". But if a soul was attributed to them, what was likely to be the case in milder forms of malformation or disability, the soul of the respective individuals seemed to have also a malformed or disabled soul. One supposed that a physical deformity would hint at a mental one due to the traditional signature theory founding also the popular doctrine of physiognomics: Physical signs of natural things would indicate their hidden inner qualities. So, the hunchback seemed to have a wicked "hunchback soul" (*Buckelseele*). Even in the early twentieth century, this theory was officially discussed in sociomedical literature. The influential German pioneer of the special education of disabled young people (the so-called *Krüppelpädagogik*) Hans Würtz (1875–1958) propagated a theory based on the "individual psychology" of Alfred Adler. In this perspective, the hunchback or other disabled individuals would suffer from an "inferiority complex" and therefore strive to overcome it by a maximum performance or "over-compensation". So, crippled persons seemed to be particularly sophisticated, calculated, and devious, but also witty

and sensitive. Of course, such an inferiority theory is refused by modern medical psychology. One does not accept that the disabled should have generally an abnormal mental attitude.

The bad creep, the child-eating monster, the furious giant are well-known figures of popular culture identifying the misshapen body with the respective character. Insofar, the disabled are not only stigmatised, victims of powerful evil influences, but also themselves origins of mental malevolence. Moreover, there is a common assumption that the deformed person in the role of a victim tends to take revenge on normal people. There are novels illustrating this mechanism, for example, "Lady Chatterley's Lover" by D. H. Lawrence (1928). Herein, the paraplegic Sir Clifford is described becoming more and more a wicked cripple. Hunt (1966) called this phenomenon "Chatterley syndrome".

In modern times, cripples played an illustrious role in public. They performed as figures in shows on markets and in circus tents. It is remarkable that just during the Victorian Era, when Darwinism and social Darwinism boomed, the public interest in oddities and abnormalities increased. Some misshaped figures were assumed as a "missing link" between the animal realm and the human world. So, the American entertainer P. T. Barnum (1810–1891) invented the "side show". It was performed in a separate tent. "He included all possible 'missing links': mermaids, lion men, direct descendants of Aztecs, men of a Bornean tribe, etc. Barnum had talent to judge rightly the preference and mental capacity of his auditory. His "missing links" and freaks (snake men, hunger artists, hair and beard men, Siamese twins, giants, and midgets, etc.) attracted then a mass public. (J. Kunze and I. Nippert: *Genetik und Kunst*, Berlin 1986, p. 13) portraits of persons with genetically caused anomalies from different cultural epochs.

But this curiosity at the end of the nineteenth century originated not only from pure pleasure to demonstrate abnormalities. Rather, it reflected also a state of anxiety because of a general doom and gloom in the face of the suspected damages caused by pathogenic factors of civilisation. A new dimension of disease emerged: A sort of inner deformity and mutilation of humans by social vices and psychological abnormalities resulting in neurasthenia, neurosis, hysteria, psychopathy. Nietzsche called this general increasing weakening of vitality—long before Freud's concept of neurosis—the "modern disease". Now, the social normality itself was taken for pathogenic. Nevertheless, the fearful vision of a general decadence, degeneration, and biological downfall of modern society became predominant in the scientific and public discourse. Especially in Germany, the social disturbances after World War I and its disastrous consequences fostered obviously harmful behaviour with bad consequences: alcoholism, sexual excesses, venereal diseases, subversive political activities were assumed to extin-

guish the healthy, fit, reproductive-capable and—worthy members of the nation (*Volksgenossen*). This ideology within the context of race biology became then a ruling guideline in Nazi-Germany. Its practical consequences were fatal as mentioned above.

### 1.3 Changing Social Attitude

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In spite of all efforts to educate the public and to integrate the disabled into normal life, the old "superstitions" are more or less still noticeable. The stigma of a severe disablement stimulates subconsciously the impulse to repel the evil. So, it may be useful to know about some cultural historical sources of such an impulse. Although the critique of poor supply of the disabled is often justified, one has to state that the contemporary society (at least in European countries) cares more about the disabled than societies in former times. According to the general accepted guidelines of the official institutions, the attitude towards disabled people is characterised by the idea of equal human rights and humane dealing with diseased or disabled members of society. It is remarkable that the differentiation between physical and mental disablement regarding the stigmatisation of the respective group of persons has—at least theoretically—disappeared. So, severe chronic psychiatric disorders like schizophrenia or deep depression are judged as medical disorders equal to physical ones entitled to best medical care.

On the other hand, the modern culture of the consumer world, the wellness movement, and the idea of enhancement hide the images of disease and disablement and flee from them. This attitude comes to light in regard to prenatal diagnostics looking for malformations or other disorders of the foetus. In the case of a pathological finding, abortion may be an alternative to childbirth—constituting a tough ethical problem for the mother, respectively, the parents apart from other players. This problem is worsened by the novel method of Non-Invasive Prenatal Diagnosis (NIPD), a genetic test screening for birth defects and hereditary diseases. It can be easily carried out using a simple blood sample of the pregnant mother. So, it is a much more convenient method to diagnose, for example, growing children with Down syndrome than it was before, when invasive and not quite undangerous procedures were necessary. There is a certain tendency to exclude the birth of disabled children. At the same time, there are many initiatives and institutions, public and private, which care for them with highly sophisticated medical and social means. This has to be seen within the context of the emerging concept of medical as well social rehabilitation after World War II. The leading idea was the integration of disabled and handicapped people into ordi-

nary life. They should not be excluded from the working and cultural world and make their own lives as far as possible.

The contemporary concept of inclusion originates from this background of rehabilitation. Today, it is a global goal: The "Convention on the Rights of Persons with Disabilities" (CRPD), an international human rights treaty of the United Nations, became effective in 2008 intending to protect the rights and dignity of persons with disabilities. This created officially quite a new social attitude towards disabled persons. Never before more attention has been drawn to them. But constitution and reality are different things as elsewhere in society. However, the social attitude towards the disabled has become more sensible endeavouring a humane and productive cooperation with them. Progressive approaches should be mentioned like the project "Ohrenkuss ... da rein, da raus" (i.e. ear kiss ... here in, there out), a cultural magazine produced by persons with and without Down syndrome. It is published twice a year in Bonn (Germany) since 1998 by the Downtown-Werkstatt für Kultur und Wissenschaft (i.e. Downtown studio for culture and science). This project shows paradigmatically how deeply the social attitude towards disabled persons can be modified and encourage a creative interaction between disabled and non-disabled people.



# The Role of Ethics Committees

The *German ethics commission* was founded in the year of 2013, in general accordance with the rules of the European commission. It was established by the government in order to monitor methods of genetic investigations in reference to existing laws. It was preceded by the establishment of the Gene-Diagnostics-Commission in the year of 2010, which set up the guidelines for genetic investigations on humans, relying on the current status of approved methods.

Genetic diagnostics, screening, analyses, pre-implantation diagnostics, germ cell selection, heterological egg, and semen donation are examples for current problem areas that have a high significance in patient-oriented diagnostics due to rapidly evolving capabilities.

In recent decades, genetics experienced crucial impulses in basic and applied research with the help of these new techniques.

Subsequently, debates occurred in science and in the public about potential abuse of those investigation methods or the manipulation of findings.

The hereby given challenges led to the establishment of a counsel for bioethics by the department of education and research, including specialists in life sciences, medicine, ethics, law, social studies, theology, and politics.

The new developments in life sciences were documented and their potential application in medicine apprehended, with the understanding that focus areas might change quickly or had to be extended.

In analysing ongoing applications of new discoveries though, it is not always possible to assess potentially adverse side-effects.

Furthermore, the imposed rules can only apply for Germany, since in other European countries as well as globally, moral principles and cultural specifications can make a difference, to some extent.

In addition to the German Ethics Counsel in Berlin, universities founded ethics commissions and academic chairs of their own. Beyond the universities, ethics commissions and similar organisations were established by provincial governments, churches, political parties, and unions. These groups thus launched the objective to expend internationally—primarily in Europe, in order to define and document universal moral principles. Within this framework, joint centres for documentation and communication were established.

Numerous journals with the subject of bioethics were launched and publications such as the dictionary for bioethics were the bases for decisions with areas of application, with reference to specialties such as genetic engineering, neurology, tumour diagnostics and therapy, stem cell research and therapy, and prenatal diagnostics.

An internationally mandatory view to bioethics is represented in the declaration of the Helsinki World Medical Association. Furthermore, the Council of Europe and UNESCO represent the basics for ethnic issues in medicine.

To sum up, at present the topics in deciding bioethic questions of eminent actuality are as follows:

- Genetic investigations of children or adolescents without the ability of consent
- Humans with dementia
- Diagnostics and therapy in disorders of sex development (e.g. intersexuality)
- Fertility preservation with mental retardation
- Carrier testing
- Obligation to inform within a family (see ► Sect. 17.2.1)
- Decisions to immediate consequences of preventive tests
- Evaluative response to the various capabilities of prenatal diagnostics

Ethical principles have always been a relevant issue in medicine and have defined the conduct of those affected. In doing so, the evaluation of the applied techniques as well as their consideration for a treatment approach play a part.

Nowadays, medicine is divided into basic research and patient-oriented domains. Both areas intersect frequently causing the allegations of ethical principles to be complicated and to be debated controversially in many cases.

Legislative power provides the foundation for ethical conduct. Legislation is responsible for the safety of life and the prevention of abuse. It is based on the principles of self-responsibility, on the verified benefits of a therapy for the patient, on the protection of personality, and the preservation of justice.

The rules of bioethics are of trans-cultural importance. Culture-specifically though, they might be interpreted differently.

Leading ethicists like Professor Kueng of the Tuebingen University have played a substantive part in contributing with their publications to the overlapping emergence of principles of ethical conduct in interreligious and intercultural dialogue since 1993.

These statements were of extraordinary importance in the field of ethics in medicine since everyone may be affected by medical-ethic decisions as a proband participating in a research project or as a patient in a potential therapy.

As a consequence, the publications about fundamental ethics in medicine prompted a range of meetings and led to a response of the “Deutscher Ethik Rat”, among others.

The various approaches resulted in the “Declaration Toward a Global Ethic” in the year 1993 in Chicago and 2 years later

in the foundation “Weltethos”, founded by Professor Kueng. This project is aimed at raising awareness of basic joint values in all countries.

Information to ethical principles and their competent supervisory authorities should not be limited to German or even European data. For comparison, the applicable ethical principles of a different cultural sphere are being depicted.

Since two of the authors of the Chromosome Atlas are Iranians, the valid ethical guidelines for the assessment and approval of genetic investigations in humans for this country will be documented.

To some extent, they are based on moral values that are deeply affected by different religious and cultural principles, at variance with the conditions in Germany and Europe.

Academic exchange and social contacts of participating researchers at joint scientific projects lead to regular information about the respective current requirements for the cooperation between both countries.

The *Iran ethics commission* has a long tradition of medical legislation regarding the protection of patients.

It was recorded in writing as early as in pre-Islamic times already, among others in publications of the Sassanids and the Zoroastrians. Following the establishment of the Islam as the official religion, bioethic principles were an important issue in medicine.

Based on this tradition, already in the years 1953 and 1963, respectively, the Tehran university issued publications concerning the significance of ethical standards. Additional publications by the “Ministry of Health and Medical Education” followed in the years 1990 and 1991. In the year 1993, the “Center for Medical Ethic Studies and Research” was established, and the “First International Congress of Medical Ethics” was held in Tehran in that same year. Meetings and workshops followed on a regular basis.

Consequently, the “International Congress of Bioethics” was conducted in collaboration with UNESCO in Tehran. The organisers were the “Ministry of Science Research and Technology” and the “National Research Center of Genetic Engineering and Biotechnology” of Iran.

This congress was used as a forum for interchange of ideas and information between Iranian and international researchers, the second congress followed in the year 2008 already.

Main topics for discussion were:

- Insufficient continuing training of licensed physicians concerning ethical standards in the care of patients
- The lack of specialists for medical ethics
- The need for guidelines to culturally adapt bioethics while training medical students
- The lack of popular scientific publications to inform the population



Subsequently, the Iran established a library for publications in the field of bioethics and published a journal on the subject (Iranian Journal of Medical Ethics and History of Medicine).

Legislation and standards were drawn up to blend Islamic and ethical principles in a society defined by its religion.

In the area of human genetics, the key aspects were as follows:

- Therapeutical abortion
- Egg cell and semen donation for infertile couples
- Assisted reproductive technologies
- Pre-implantation diagnostics
- Cytogenetic diagnostics
- Investigations of gametes and embryos
- Examination of patients unable to consent

Nowadays, the “Medical Ethics Research Center” takes responsibility for nationwide discussions on the university level. In this context, the “National Committee” has to define the Islamic, legal, and ethical principles for biomedical research in order to:

- ensure the protection of test subjects
  - appoint monitors for university and private institutes as well as for industrial projects
- The placement by the “National Committee” integrated the guidelines of the “Declaration of Helsinki”, and the view of the “Head of the National Research Council”.

Today, the standards for each physician include—with due regard to religious regulations and specific cultural principles—an “informed consent”, which is a statement in writing, for the patient or proband. It insures accountability of the project leader for any negative consequences of the study or therapy.

The composition of the ethical committee in the Iran presents a broad range of professionals: physicians, statisticians, lawyers, ethnic specialists, workers’ representatives, and the spiritual leaders.

The forthcoming analysis of the situation of ethical committees was supported by the WHO.

The comparative account of the development of medical ethics in Germany and the Iran emphasises the relevance of international cooperation in this field and, at the same time, may give suggestions for future cooperation.



# Quality Control in the Field of Diagnostics

Human genetics is a special field including basic research as well as patient-related studies that are frequently strongly related, thus stimulating each other. Results in one key aspect may accentuate a new focus in the other. Therefore, quality control of results is crucial.

In the following, because of the topic given, only patient-related areas of human cytogenetics will be referred to.

The society for human genetics and the professional organisation of German human geneticists have established mandatory guidelines in order to guarantee the quality of information in the area of applied human genetics.

Before achieving an occupation in the area of human genetics, an advanced qualification process has to be undergone, lasting 5 years, provided, a patient-related position is being the objective.

In general, the trainees have a degree in medicine or biology. They will then work on gaining the qualification of a specialist in human genetics.

In the course of this education, knowledge in clinical, cytogenetic, biochemical, and molecular genetic diagnostics of genetically related disorders will be conveyed, plus, in addition, the counselling of persons affected and their families.

They will be introduced into the basic principles of genetic processes, the formation, and heredity of mutations, plus the procedures of epidemiological surveys.

Of particular relevance, in the course of the advanced training, is the transfer of fundamental data concerning ethical, psychological, and legal knowledge in diagnostics and counselling.

The emphasis can lie either on molecular genetics or on cytogenetics.

The topics within cytogenetics include the complete study of all methods in the area of pre- and postnatal cell cultures, the required steps for preparation, and the subsequent techniques of cytogenetic, molecular cytogenetic, array-based and sequencing-based nature.

A defined amount of independent investigations, including diagnostic results, is required, covering all the areas above.

Further education includes regular participation in symposia as well as local seminars and workshops.

The continuing education may occur at university or non-university institutions with accreditation. Instrumental for this purpose is a specific catalogue listing the goals.

Alongside this further education in Germany, a European centre for accreditation was installed. Within the context of an exam, the acquired knowledge is being tested, thus establishing a professional standard within all of Europe.

Having completed this continuing training, the human geneticist has several options for an additional qualification:

The German “Akademie Humangenetik” regularly offers seminars with topics like quality management or psychosocial aspects of human genetics, but also to special subjects like “Next Generation Sequencing Diagnostics” or “Variant Interpretation”.

The “Deutsche Gesellschaft für Humangenetik” and the “Berufsverband deutscher Humangenetiker” are representing an association of German human geneticists.

For more than 20 years, the so-called Ringversuche are being performed for the purpose of external quality control, thus supporting the quality of the labs’ results.

In departments with focus on investigations in cytogenetics or molecular genetics, the laboratory head will pursue the accreditation of his institution. For this purpose, documentation has to be submitted to a professional commission in order to prove competence. The panel will then perform an inspection on location and possibly recommend changes in the work implementation. After fulfilment of the necessary requirements, the facility will be accredited. This on-location inspection will be repeated at regular intervals.

This documented evidence of quality as the result of the accreditation normally will be included in their logo.

Following are the official terms and concepts for the various steps of the appropriate quality control in Germany:

- *Weiterbildung (Diploma in Medical Genetics)*.
- *Weiterbildungsordnung der Ärztekammer*.
- *Berufsverband deutscher Humangenetiker* (► [www.bvdh.de](http://www.bvdh.de)).
- *Akademie Humangenetik* (► [www.akademie-humangenetik.de](http://www.akademie-humangenetik.de); [info@akademie-humangenetik.de](mailto:info@akademie-humangenetik.de)).
- *Leitlinien* (► <https://www.awmf.org/leitlinien.html>).
- *Ringversuche: Richtlinie der Bundesärztekammer zur Qualitätssicherung laboratoriumsmedizinischer Untersuchungen (RiLi – BÄK)*.
- *Akkreditierung*: ► <https://www.dakks.de/content/was-ist-akkreditierung>

► Chapter 2 presented a comparative portrayal of the ethical principles that have to be considered regarding genetic diagnostics in humans in *Germany* as well as in *Iran*.

In like manner, the following account will depict education and training for human genetics and quality assurance for cytogenetics in Germany versus Iran.

In Iran as well as in Germany, human genetics is a specialised field that gained very much in importance over the last decades and thus became an integral part of studies in medicine and life science. In each case, there is a lecture covering the basics. In addition, both also offer seminars and workshops. For cytogenetics, these include cell cultures, the microscoping of specimens with a normal or pathological karyotype as well

as the practice of the various staining techniques and hybridisations.

Training for the bachelor, masters, and doctoral degrees are being provided.

Frequently, in Iran the training for a doctoral degree involves a stay abroad in order to study and apply newly established investigation methods. This is usually accomplished in cooperation of the doctoral advisor with a foreign colleague and is being sponsored by a scholarship.



# Types of Chromosome Mutations

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