

MINISTRY OF HEALTH

**CURRICULUM PROGRAMME FOR
SPECIALISATION IN MEDICAL GENETICS FOR ACQUISITION OF THE
BASIC SPECIALTY "MEDICAL GENETICS "**

**SOFIA, BULGARIA
2007**

Introduction

The "medical genetics" specialty is acquired after 3 years of training in the case of doctors trained in related fields and 4 years of training for doctors from other specialties. The basic training required for admission to the specialty is a 'Master's Degree in Medicine'. Medical genetics is a rapidly expanding applied discipline and its achievements have a profound effect on the doctor's daily diagnostic, therapeutic, prognostic and preventive work.

Aim of the training:

The Medical Genetics specialty aims to transmit contemporary knowledge of hereditary pathology, congenital anomalies and diseases with a genetic predisposition, to ensure the acquisition of practical skills for the diagnosis and identification of genetic risk, genetic counselling of patients, and the prevention of genetic diseases. The specialty entitles medical genetics physicians to work as head physicians or interns at molecular genetics units, as well as in cytogenetic, molecular cytogenetic and molecular genetic laboratories.

The medical genetics specialty has been subdivided into:

- **Theoretical part.** Training in the basic problems of different groups of genetic diseases and predispositions - chromosome, monogenic, polygenic diseases and predispositions, congenital anomalies, diseases due to somatic mutations, and hereditary diseases in different clinical specialties, genetic diagnostics, population characteristics, principles of medico-genetic counselling, prevention and gene therapy, and pharmacogenomics.
- **Medical / Clinical Genetics.** Genetic diseases, predispositions and congenital anomalies are addressed in the following logical sequence - genetic disorders of inherited structures and innovations in monogenic and multifactorial pathology, chromosome disorders and congenital anomalies in relation to aetiology, pathogenesis, heredity, classification, clinical and genetic polymorphism, modern approaches to their diagnosis. Also included are genetic problems of inherited cancer, mitochondrial diseases, diseases determined by dynamic mutations and abnormalities in DNA repair. The focus is also on hereditary diseases in the fields of gastroenterology, pulmonology, nephrology, neurology, ophthalmology, endocrinology, dermatology, immunology and other areas.
- **Genetic counselling.** Addresses in detail the principles, organization, tasks, and ethical problems of medico-genetic consultation, prognoses for patients and family members, approaches and indications for prenatal, pre-implantation and preconception diagnosis, organization and nature of mass and selective genetic screening, the preparation of a genetic registry, as well as approaches to the treatment of hereditary diseases and predispositions, both in conventional and gene therapy. Discussion of the legal problems of genetic research enshrined in the Health Act. Detailed examination of Internet sources and databases.
- **Laboratory part.** This includes principles of laboratory techniques for genetic diagnosis, development of practical skills in molecular genetic research, cytogenetic diagnosis, molecular cytogenetic techniques, biochemical genetic tests, prenatal and

postnatal diagnosis, and interpretation of results.

Types of training and supervision:

a) theoretical training in the form of basic and thematic courses, individual training and systematic self-study.

b) practical training involving work in cytogenetics, molecular genetics and molecular cytogenetics laboratories, as well as in medical and genetic counselling units.

Checks of the mastery of the material are carried out periodically by participation in five colloquiums before a committee of three experts for each specialty, presided by the head of the specialty. The specialty is awarded after participation in a state examination before a state commission appointed by the Minister for Health.

CURRICULUM

1. Theoretical preparation

Modules	Periods of study
First year	
General part Human genetics: Chromosomes as the basic cellular structures of heredity. Molecular basis of human heredity. Organization of the human genome. The Human Genome Project and health.	1 month
Molecular and biochemical genetics: monogenic aetiology of diseases. The mutation process. Factors causing mutations. Mutation stages. Types of mutations. Pathogenesis of monogenic diseases.	1 month
Cytogenetics: basic mechanisms and reasons for the occurrence of chromosomal imbalance. Abnormalities in the number and structure of chromosomes as an aetiological factor in the emergence of chromosome disorders.	2 months
Genetic diagnostics: basic methods used to perform genetic diagnoses - biochemical, haemological, clinical-genealogical methods and criteria for determining the type of inheritance of monogenic diseases, criteria for polygenic type of inheritance, cytogenetics, molecular cytogenetics, molecular genetic methods to identify the causative gene of monogenic diseases, methods for detecting known and unknown mutations, methods for conducting genetic screening and genetic monitoring programmes	3 months
Human population genetics: basic genetic patterns, manifested at the level of human population	1 month
Special part Chromosome disorders – nature and mechanisms of occurrence of chromosomal imbalances, clinical features, classification, cytogenetic variants and genetic counselling. Medico-genetic problems of reproduction associated with chromosome disorders;	4 months

<p>Microdeletion syndromes - nature, molecular characterization, mechanisms of phenotypic expression of the Prader-Willi Syndrome (PWS), Angelman Syndrome (AS) and other diseases associated with chromosome imprinting;</p> <p>Congenital anomalies of development – dysmorphology and teratogenesis; Congenital malformations, deformations and disruptions, dysplasia, large and small malformations, multiple and isolated forms, Types of combined anomalies, disorders in sexual differentiation, Morris Syndrome, intersexual conditions.</p>	
Second year	
<p>Monogenic diseases - Haemoglobinopathies, thalassemia and other genetically determined diseases of the blood; diseases associated with defects in the metabolism - nature, genetic defects, molecular pathophysiology, clinical characteristics, genetic diagnostics, Medico-genetic counselling, prevention and treatment; hereditary diseases involving disorders in the immune response; hereditary diseases associated with defects in connective tissue, in cytoskeletal proteins, in receptor proteins, in DNA repair systems, etc.</p> <p>Diseases associated with dynamic mutations - Myotonic dystrophy (MD); fragile X chromosome syndrome (Martin–Bell syndrome); Huntington's chorea, Kennedy's disease, Spinocerebellar ataxia 1 (SCA1); Machado-Joseph Disease (MJD) Friedreich's Ataxia;</p> <p>Mitochondrial Diseases – Leber Hereditary optic neuropathy (LHON); Myoclonic Epilepsy with Ragged Red Fibres (MERRF); Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS); Kearns–Sayre syndrome, etc.</p> <p>Genetics of mental deficiency - nature and causes, Genetic heterogeneity and classification, medical diagnostics and genetic counselling.</p> <p>Oncogenetics - Regulation of cell cycle, apoptosis. Mutant genes that inhibit the apoptosis mechanism; Oncogenesis, Tumor-suppressor genes, genomic instability genes, associated with neoangiogenesis and metastatisation.</p> <p>Pharmacogenetic defects.</p>	6 months
<p>Multifactorial inheritance with congenital anomalies; Common diseases with a genetic predisposition in adults.</p> <p>Genetic problems of common diseases of various clinical specialties- reproduction disorders, Hereditary neurological diseases; Hereditary predisposition to mental illness, hereditary disease of the optic analyser, hereditary and acquired deafness, speech disorders; Monogenic diseases and hereditary predisposition to certain internal diseases; Monogenic diseases and hereditary predisposition to certain skin diseases; cancer</p>	6 months
Third year	
<p>Genetic counselling, prevention and treatment of genetic diseases: Principles and tasks of medico-genetic counselling; Determination of the genetic risk; Contemporary moral and ethical, legal and social issues;</p>	

Register of congenital and hereditary diseases;

Genetic screening programmes,

Prenatal diagnosis - indications, methods of diagnosing chromosome disorders and monogenic diseases,

Pre-implantation and preconception diagnosis - indications, research material, assisted reproduction techniques, methods of pre-implantation and preconception genetic diagnosis,

Genetic screening programmes - Types, conditions and requirements for testing, selective mass screening for congenital and hereditary diseases among newborns; biochemical screening for some the most common congenital abnormalities of the fetus in pregnant women. Ultrasound screening for congenital abnormalities of the fetus in pregnant women. Ultrasound study of fetal morphology. Genetic counselling for different screening programmes. Moral, ethical and social issues. Importance of screening in the prevention of hereditary pathology;

Genetic monitoring - population and high-risk monitoring; Basic group methods used in genetic monitoring; importance for the protection of gametogenesis and prevention of carcinogenicity; Socio-legal issues related to genetic monitoring.

Therapy of genetic diseases - conventional therapy of genetic diseases, gene therapy of monogenic diseases, antisense therapy of diseases associated with somatic mutations, cancer and viral infections; targeted therapy.

Personalized Medicine

Moral, ethical and legal issues in genetic counselling, genetic screening, gene therapy and the creation of DNA banks.

2. Practical preparation

Modules	Periods of study
First year	
Genetic analysis	1 month
Cytogenetic methods and interpretation of karyotyping results; Analysis of chromosome fragility; sister chromatid exchanges.	4 months
Molecular genetic methods and interpretation of the results - PCR, SSCP, RFLP, DGGE, Heteroduplex Analysis - HA, ASA, ASO	4 months
Molecular cytogenetic methods and interpretation of the results of FISH, mFISH, CGH, microchip technology	2 months
Biochemical methods in the diagnosis of hereditary diseases, genetic screening of newborns and of pregnant women	1 month
Second year	
Prenatal and postnatal cytogenetic diagnosis	6 months
Medical genetic counselling – <ul style="list-style-type: none"> ➤ recording of case history ➤ completion of forms ➤ genealogical analysis ➤ assessment of the methods required for genetic diagnosis ➤ assessment of results of genetic tests ➤ assessment of genetic risk ➤ medical and genetic counselling of patients and genetically affected relatives 	6 months
Third year	
Genetic screening programmes	2 month
Practical work in a medical and genetic counselling unit	10 months

3. Colloquia

Topics	Periods of study
<i>First Colloquium</i> - human genetics, molecular and biochemical genetics, cytogenetics, genetic diagnostics	6th month
<i>Second Colloquium</i> – human population genetics, chromosome disorders, congenital anomalies of development	12th month
<i>Third Colloquium</i> - monogenic diseases, pharmacogenetic defects, genetics of mental deficiency, oncogenesis	18th month
<i>Fourth Colloquium</i> - multifactorial inheritance of common congenital abnormalities and diseases in adults, genetic problems of common diseases in various clinical specialties	24th month
<i>Fifth Colloquium</i> - genetic counselling, prevention and therapy	36th month