MEDGEN

Developing Medical Genetics Education Through Curriculum Reforms And Establishment Of Postgraduate Training Programs

# THE CONTENT OF THE CLINICAL RESIDENCY PROGRAM IN CLINICAL GENETICS

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# MODULE 1: BASICS OF CLINICAL GENETICS

## Theme 1.1: Fundamentals of Inheritance and Genetics Theory

**Learning Objective: Define cellular and molecular mechanisms that underpin inheritance in human**

**Knowledge**

• define the chromosomal basis of heredity
• describe the mechanisms of origin of numerical and structural chromosome abnormalities
• describe the outcome of structural chromosome abnormalities at meiosis
• identify the chemical structure of DNA and replication
• describe the mechanisms and main types of DNA mutations
• describe the transcription and translation process, post-transcriptional modifications, (alternative) splicing and non-coding RNA
• describe the human genome and the principles of genetic variation (including recombination).
• explain the mechanism and purpose of X-inactivation

**Skills**

• conduct risk of recurrences in segregation ratios for structural chromosome abnormalities
• evaluate the consequences of nucleotide mutations on the protein encoded by the mutated allele

**Learning Objective: Define patterns of inheritance and undertake risk assessment**

**Knowledge**

• describe modes of inheritance, Mendelian and atypical, including mitochondrial, polygenic, multifactorial inheritance
• explain how empiric risks are derived and used
• conduct risk calculations, including probability and Bayes theorem
• describe the mechanism of imprinting and triplet repeat mutations
• describe the regulation of gene expression
•describe the molecular basis of somatic mutations and the cause and consequences of somatic chromosomal variation
• recognise different inheritance patterns in pedigrees.

**Skills**

• evaluate primary sources of data to assess risk
• conduct empiric risk calculations, occurrence and recurrence risks
• perform calculations including:
    • Bayesian risk calculations
    linkage-based risk calculations
    • simple genetic linkage by logarithm of odds (LOD) score methods
    • gene frequencies
    • Hardy-Weinberg equilibrium
    • chi-square tests
• identify and critically evaluate data to inform diagnoses.

**Learning Objective: Describe the evolution of genetic knowledge**

**Knowledge**

• epigenetics principles
• identify advances in research relating to gene therapy, stem cells and therapeutic cloning
• describe the rapid shifts in understanding of major genetic principles over the past century
• explain the history of use and misinterpretation of genetic information
• identify community attitudes to genetic information and genetic technology.

**Skills**

• evaluate new advances in genetics theory and their application to clinical practice.

## MODULE 2: DIAGNOSTIC METHODS, INVESTIGATIONS AND MANAGEMENT

### Theme 2.1: Clinical Skills

**Learning Objective: Investigate, diagnose and manage genetic conditions**

**Knowledge**

• define natural history and the pathophysiological basis of signs and symptoms of genetic conditions
• discuss the potential impact of investigations, their results and the diagnoses of genetic conditions on individuals and their families
• recognise the terminology related to clinical measurement in genetic diseases
• recognise the characteristic signs and symptoms of genetic diseases
• explain the indications for clinical photography and obtain informed consent for the uses of the photographs
• describe the importance and confidentiality of use and storage of photographs
• recognise appropriate photographic views required for a particular clinical context
• plan appropriate questions to elicit genetic history
• identify information sources, including databases and literature searches
• recognise evolving knowledge about the genetic basis of common and complex disorders
• discuss the importance of obtaining informed consent prior to investigation
• define the indications for investigation
• explain the purpose, the risks and benefits, extent and limitations of investigation results, including financial implications
• describe the causes, frequency and implications of false test results
• define the concepts of variable expressivity, reduced penetrance, somatic or gonadal mosaicism, de novo mutations
• describe the implications of ethnic difference in the incidence of genetic disease
• explain the natural history of genetic diseases
• describe management issues relevant to genetic syndromes
• discuss the significance and importance of family history and consanguinity in rare genetic conditions
• distinguish between common general pediatric presentations and signs that are indicative of genetic conditions.
• recognize the necessity of the diagnostics/testing of relatives

**Skills**

• obtain consent for all interventions, including recording family and medical history
• perform physical examination
• obtain, record and analyse a clinical history
• perform, record, plot and interpret clinical measurements
• take photographs for clinical use
• elicit family history information
• analyse relevant patient and family information to determine genetic risk
• perform an examination to elicit relevant signs of genetic disease, recognising the potential need for involving relatives if indicated
• recognise and refer when additional specialist examination is required
• calculate genetic risk by various means
• use genetic databases and registers for information retrieval
• elicit and record complex pedigrees
• perform investigations and interpret the results
• formulate differential diagnoses for genetic disorders
• overcome difficulties of language and physical and intellectual impairment
• present undiagnosed cases to colleagues
• conduct clinics which require specialist diagnoses, assessment and genetic counselling

• discuss management options and/or surveillance with individuals, families and the professionals involved in their care
• devise management strategies as part of a multidisciplinary team
• provide genetic advice in multidisciplinary clinics, such as child development, vision, hearing, endocrine, skeletal dysplasia, neurological, craniofacial, cancer genetics, and prenatal diagnosis clinics
• explain to patients and families about the concepts of variable expressivity, reduced penetrance, somatic or gonadal mosaicism, de novo mutations
• explain genetic inheritance and risks in a way that is comprehensible to the patient.

**Learning Objective: Use available resources**
**Knowledge Skills**
• identify relevant biomedical journals
• access key medical genetic websites
• retrieve and use data recorded in clinical systems
• understand mechanisms to seek to share and obtain information from colleagues.

**Skills**
• apply the use of available resources, including genetic websites, specialist databases and statistics programs
• undertake literature searches
• explain how to access and use available resources
• act as a resource for colleagues
• recognise personal gaps in professional knowledge, and use appropriate resources to resolve those gaps
• identify and use appropriate references for further understanding of laboratory results and clinical findings.

**Theme 2.2: Genetic Testing**

**Learning Objective: Apply appropriate diagnostic procedures and interpret results of genetic tests**
**Knowledge**
• understand the principles of informed consent in adults and assent in children
• describe the indications for performing procedures
• distinguish between screening and diagnostic tests
• define and explain techniques of the procedure, including risks, limitations and benefits
• describe the special considerations in predictive genetic testing and such testing in children
• define techniques for chromosomal analysis in different tissues
• describe laboratory techniques in conventional and molecular cytogenetics
• describe molecular genetic techniques of common use
• describe application and advances of new DNA technologies, e.g. microarrays, next generation sequencing, PGD
• use common methodologies for a biochemical diagnosis of inborn errors of metabolism
• describe the applications of pharmacogenetic testing

**Skills**
• obtain informed and specific consent for genetic testing
• perform procedures related to clinical genetics before genetic testing
• perform blood and cheek swab collection, hair root extraction, and skin biopsy
• apply standard precautions in dealing with blood or body fluids
• interpret laboratory tests taking into account sensitivity and specificity
• use the International System for Human Cytogenetic Nomenclature and standard mutation nomenclature
• apply DNA based testing for mutation detection and linkage

• interpret clinical consequences of abnormal karyotypes, abnormal nucleotide variant profiles and enzyme deficiencies
• interpret clinical results of pharmacogenetics testing
• analyse test results in a clinical diagnostic context, in contact with molecular and cytogenetic scientists (if needed)
• conduct Bayesian calculations to estimate genetic risk, using information from different sources
• evaluate the efficacy and appropriate application of new technologies
• explain the uncertainties and limitations of genetic testing for both screening and diagnostic tests
• discuss with colleagues the interpretation of test results
• explain genetic test results to patients and discuss the implications of the results for them and their relatives

**Theme 2.3: Genetic Screening Programs and Registers**

**Learning Objective: Explain the processes to establish and operate genetic screening programs**
**Knowledge**
• define World Health Organisation recommendations for requirements to implement a screening program and its limitations
• describe potential applications of screening for conditions that do not meet the criteria
• describe the genetic characteristics in local populations, including mutation spectra and frequencies and disease prevalence
• describe contributing factors for the establishment of population screening programs for genetic diseases
• identify current screening programs, including prenatal, neonatal, and postnatal screening
• describe the operation of national genetic disease screening programs
• discuss the counselling support needed for screening programs
• discuss the public health outcomes and benefits of screening programs, including the costs
• identify population-based genetic registers and their practical issues
• describe the methods of data collection and their limitations
• describe the principles of prevention and screening
• discuss ethical, legal, social, and cultural issues associated with genetic screening programs

**Skills**
• assess an individual patient's risk factors
• interpret the sensitivity, specificity, and predictive values of screening tests
• explain the benefits and consequences of screening programs
• contribute to the operation of screening programs for common carrier states
• encourage participation in appropriate disease prevention or screening programs
• educate patients efficiently about epidemiological screening.

**Theme 2.4: Genetic Counselling**

**Learning Objective: Provide genetic counselling as part of a multidisciplinary team**
**Knowledge**
• describe the role of a genetic counsellor
• identify patient's reactions to grief and loss and their effects on decision making regarding genetic risks
• recognise and discuss factors that will impact on a genetic counselling process, including patient and family anxieties, experiences, cultural, religious and ethnic background and specificities such as consanguinity, arranged marriages, non-paternity, views on prenatal diagnosis and assisted reproduction techniques

• prepare counseling questions to identify the patient's concerns, problems and priorities, expectations, understanding, and acceptance
• describe communication strategies to:
    • facilitate and engage in realistic discussion with respect, empathy, and sensitivity
    • assist patients to consider their available choices and to make decisions
    • identify role of family of genetic diagnosis
• identify skills required for 'non-directive' counselling, including active listening, using and encouraging questions in simple language.

**Skills**
• identify patients at-risk and make appropriate referrals
• plan a genetic counselling case in an appropriate setting
• present genetic information to a patient in a sensitive and understanding manner
• discuss the features, natural history, genetic basis, and risks of patients developing or passing on genetic disorders
• explain genetic information and risks to patients and family members both verbally and written, according to the patient's age, education, cultural background
• provide clear information and feedback to patients and share information with relatives when necessary
• support patients to share information with their relatives
• discuss the patient's and family members' understanding of the information received
• discuss strategies to assist patients and/or family members to "adapt" to the disorder and/or to minimise the risk of recurrence of the disorder
• identify and support patients in distress and refer to a specialist
• reflect on own genetic counselling style and effectiveness, and identify strategies for improvement.
• provide genetic counselling to families with affected children identified by genetic screening
• use clinical and counselling supervision

# MODULE 3: GENETIC DISEASES AND DISORDERS

## Theme 3.1: Neurogenetics

**Learning Objective: Assess, diagnose and treat patients with neurogenetic disorders, including:**

**neuromuscular disorders**
- muscular dystrophies
- myotonic disorders
- spinal muscular atrophies
- mitochondrial myopathies

**neurodegenerative disorders of**
- basal ganglia (Huntington disease, torsion dystonia, Fahr disease, hereditary tremor, Tourette syndrome)
- cerebellum, brainstem, and spinal cord (multiple sclerosis, Friedreich ataxia, spinocerebellar ataxias, familial spastic paraplegia)
- peripheral and cranial nerves (Charcot-Marie-Tooth disease, other types of hereditary motor, sensory and autonomic neuropathies)
- extrapyramidal and movement disorders (Parkinson's disease)
- other degenerative diseases of the nervous system (Alzheimer's disease, etc.)

**epilepsy**

**mental and behavioral disorders**
- schizophrenia
- mood disorders (bipolar disease, depression)
- intellectual disabilities
- autism spectrum disorders

**neurocutaneous disorders**
- tuberous sclerosis
- neurofibromatosis

**Knowledge**
- overview epidemiological data of neurogenetic based diseases
- describe the molecular basis of neurogenetic disorders
- describe premutation, anticipation, hypermethylation, toxic RNA and loss of protein function in neurologic disorders
- describe the natural history of childhood and adult onset genetic neuromuscular conditions, including clinical and genetic correlations
- define genetic and syndromic classification of hereditary spastic paraplegias, inherited epilepsies
- define common clinical presentations of neurogenetic conditions, such as:
- hypotonic neonate/infant ("floppy baby")
- developmental delay (motor, cognitive and/or speech; global)
- progressive weakness and/or ataxia
- other movement disorders (dystonia, dyskinesia, tics, etc)
- dementia/cognitive decline
- intellectual disabilities
- identify appropriate investigations for suspected neurogenetic disorders, such as:
- indications for serum and liquor biochemistry (CK, lactate, etc)
- electroneuromyography (incl. nerve conduction studies) and electrocardiogram (ECG)
- neuroimaging (MRI, CT)
- muscle biopsy
- molecular genetic analyses, including predictive testing (such as Huntington's disease)

- describe the management options available for childhood and adult onset genetic neuromuscular conditions

**Skills**

- recognise the medical presentations and family histories that indicate a risk of familial neurological disease
- conduct a neurological examination of the patient
- recognise the different features of neuromuscular diseases in adults, children, infants, and neonates
- formulate a differential diagnosis and appropriate genetic testing, including prenatal testing
- apply protocols for pre-symptomatic predictive testing of late-onset neurodegenerative disorders
- refer appropriately to specialists
- recognize the correlation of trinucleotide repeat expansion size with disease penetrance and severity
- recognize phacomatoses as neurocutaneous disorder
- evaluate genetic risk and prognosis of the development of Duchenne&Becker muscular dystrophy based on mutational spectrum
- discuss possibilities of and provide multidisciplinary rehabilitation, management, and care for neurogenetic disorders

**Theme 3.2: Dysmorphology and skeletal dysplasia**

**Learning objectives: Assess, diagnose and treat patients with dysmorphic syndromes, including**

- congenital malformations (major and minor; single and multiple anomalies)
- chromosomal abnormality syndromes
- skeletal dysplasia
- single gene mutations

**Knowledge**

- define teratogenicity and related causes of dysmorphology
- understand of normal and abnormal development in embryogenesis
- define specific terms, expand vocabulary used in the diagnosis of human congenital malformation
- describe different ways of structural defects classification
- determine morphogenesis in terms of: malformation, deformation, disruption, or dysplasia
- explain the difference between a syndrome, sequence, and association
- understand the phenotypic spectrum of dysmorphic syndromes
- define the approach to evaluation, diagnosis, and management of individuals with a wide variety of birth defects
- define normal standards of measurement for a variety of features
- understand the relevance of major and minor anomalies
- recognize heterogeneity, variability, critically reflect on the wide variation in phenotype within a syndrome and genotype-phenotype correlations
- define common chromosomal abnormality syndromes as a cause of dysmorphology
- understand the uses, limitations, interpretation, and significance of specialized laboratory and clinical procedure for accurate diagnoses
- describe indications for investigation of children with developmental delay and malformations
- describe the natural history, prognosis and risks of inheritance of skeletal dysplasia
- recognise common clinical presentations and basic radiographic signs of skeletal dysplasia
- describe the management options for common skeletal dysplasia at specialized centers

**Skills**

- examination of an individual with multiple defects

- use the skills required in interviewing and counseling
- take a family history for diagnosis of given anomaly
- perform a complete physical examination and assess dysmorphic features for 12 key body area in patient (short stature, hair growth patterns, ear structure, size and placement, nose size, face size and structure, philtrum, mouth and lip, teeth, hand size, fingers and thumbs, nails, feet structure and size)
- diagnose developmental delay based on normal parameters
- use both clinic-based technologies (compilation of medical pedigrees, photographs and family history) and laboratory-based methods and register case report
- demonstrate an ability to create a differential diagnosis for particular syndrome
- understand the uses, limitations, interpretation, and significance of specialized laboratory and clinical procedures
- apply appropriate analysis to risk and probability calculations. Outline the essential features of techniques used for genetic assessments
- use relevant online resources and computer databases to aid diagnosis
- identify key radiographic features of skeletal dysplasia
- demonstrate interpersonal and communication skills with patients and other health care professionals
- assess, diagnose and contribute to the multidisciplinary management of patient with dysmorphology
- transmit pertinent information in a way that is comprehensible to the individual or family
- help families and individuals recognize and cope with their emotional and psychological needs
- provide a prognosis and plan of management for the affected child as well as genetic counselling for the parents
- provide education on preventable issues for dysmorphic syndromes (folic treatment)

**Theme 3.3: Reproductive Genetics and Prenatal Diagnostics**

**Learning objectives: To assess, diagnose and manage patients with reproductive health concerns including male and female infertility, multiple miscarriages, and those considering prenatal diagnosis.**

**Knowledge**

- describe normal and abnormal gametogenesis
- describe common genetic factors of male infertility resulting in oligo- or azoospermia
- describe common genetic causes of female infertility resulting in primary amenorrhea
- define genetic causes of recurrent pregnancy losses
- distinguish between teratogenic and genetic factors of infertility and reproductive loss
- understand laboratory assessment in the context of reproductive genetics
- understand the difference between screening and testing for gentic conditions in pregnancy
- describe the range of normal variation in fetal ultrasound images, the association of soft markers with the risk of chromosome and gene disorders, and the limitations of ultrasound as a screening modality
- describe the indications for prenatal diagnostics in women at risk for genetic disorders
- understand prenatal screening and procedures at several stages of pregnancy
- understand the use of PGD in assisted reproductive technology
- be aware of the ethical and legal aspects of use of reproductive technologies, prenatal testing and prenatal screening
- be aware of the psychological and social impact of reproductive health issues on the patients as an individual and the couple.

**Skills**

- provide patient and family with appropriate genetic counselling and take accurate family history
- sensitively offer counselling that is appropriate to the couples' values and beliefs
- assess, diagnose and contribute to the multidisciplinary management of patient with infertility
- apply strategies and management plans for patients with infertility and reproductive disorders.
- interpret specialized laboratory testing information and manage genetic disorders in cases of male and female infertility
- provide genetic risk assessment for prenatal, pediatric and adult-onset genetic disorders;
- achieve competency in interpretation of prenatal diagnostic results
- be able to accept and support all parental decisions regarding the management of an abnormal fetus
- interpret ultrasound exam data
- identify factors that place in couples at increased reproductive risk through careful pedigree construction and pregnancy risk assessment
- recognize the benefits and limitations of each diagnostic methodology and present the information to patients in a non-directive and culturally sensitive way
- present couples (or individuals) with options to manage the reproductive risk through genetic counselling, prenatal diagnostic testing, and/or assisted reproductive technology
- interpret the results of maternal serum and ultrasound screenings and provide counselling for normal and abnormal results.

**Theme 3.4: Autoinflammatory syndromes**

Autoinflammatory hereditary syndromes including:
- Hereditary Periodic Fever Syndromes
- Familial Mediterranean fever (FMF)
- TNF receptor-associated periodic syndrome (TRAPS)
- Hyperimmunoglobulinemia D with periodic fever syndrome (HIDS)
- Cryopyrin-associated periodic syndromes (CAPS)
- Other monogenic autoinflammatory syndromes
- Multifactorial autoinflammatory disorders

**Learning Objectives: Assess, diagnose and multidisciplinary management of patients with autoinflammatory syndromes.**

**Knowledge**
- define autoinflammatory and autoimmune disorders
- describe the inflammasome – a pivotal structure in the pathogenicity of autoinflammatory diseases
- define Mendelian and multifactorial autoinflammatory disorders
- describe clinical and genetic features of TRAPS, HIDS, Cryopyrin-associated periodic syndromes (FCAS, MWS, CINCA)
- describe MEFV gene mutations as the genetic factor for development of FMF.
- recognise the diagnostic value of MEFV mutations
- describe genetic factors influencing the risk of amyloidosis.
- discuss Tel Hashomer clinical criteria for diagnosis of FMF and new diagnostic criteria for children.
- describe the typical and atypical course and complications of FMF
- define the necessity of genetic testing and counselling in clinical practice of FMF
- discuss the main indication for genetic testing to evaluate the carrier status in at-risk relatives
- discuss the genotype-phenotype correlations and the effect of other possible modifiers such as other genes, gender and/or environmental factors
- describe the FMF and comorbidity conditions, and genetically related disorders

- discuss the management, treatment and surveillance of patients with FMF and FMF-like syndromes, including colchicine resistance cases

**Skills**

• recognise clinical features of periodic fever syndromes
• complete past medical history, including pedigree analysis
• explain difficulties in clinical diagnosis in the cases with atypical course and complex phenotypes
• use diagnostic algorithm for differential diagnosis of patients with suspected autoinflammatory conditions
• recognise molecular diagnosis of HRF: clinical entities, genes and types of inheritance
• offer molecular genetic testing to all first-degree and other family members (regardless of symptoms)
• offer genetic counselling for patients with FMF, carriers and at-risk asymptomatic family members
• be able to manage, treat and follow up patients with FMF
• educate patients about their behaviour and social life
• use genetic register of autoinflammatory disorders
• offer psychological support for FMF patients and family members

**Theme 3.5: Inborn Errors of Metabolism**

**Learning Objective: general clinical and genetic aspects, diagnosis, and screening of Inborn Errors of Metabolism (IEMs), including:**

- Organic acidemias
- Fatty acid oxidation defects
- Primary lactic acidoses
- Aminoacidopathies (phenylketonuria, hereditary tyrosinemia, nonketotic hyperglycinemia, maple syrup urine disease and homocystinuria)
- Urea cycle defects (citrullinemia, ornithine transcarbamylase deficiency, and arginosuccinic aciduria)
- Disorders of carbohydrate metabolism (galactosemia, hereditary fructose intolerance, fructose 1,6-diphosphatase deficiency and the glycogen storage diseases)
- Lysosomal storage disorders (mucopolysaccharidosis, Tay-Sachs disease, Niemann-Pick disease, Gaucher's disease)

**Knowledge**

• define metabolism of the amino acids phenylalanine and tyrosine (metabolic block: albinism, alkaptonuria, phenylketonuria)
• describe inborn errors of metabolic pathways
• recognize early signs of inborn errors of metabolism: neurologic, ophthalmologic, cardiac, gastrointestinal, dermatologic
• describe group of disorders caused by defects in the metabolism of simple intermediary metabolites, like amino acids and monosaccharides
• define the types of inheritance of IEMs (autosomal recessive; X-linked; autosomal dominant; mitochondrial inheritance)
• describe the signs and symptoms of IEMs as the result of metabolic disturbances caused by: deficiency of catalytic or transport proteins; accumulation of substrate or minor metabolite.
• describe the signs and symptoms of lysosomal storage disorders
• recognize the neonatal screening strategy and protocols for IEMs including lysosomal storage disorders
• describe congenital adrenal dysplasia as a result of metabolic block for production of steroid hormones
• understand the impact of diagnsosis of an IEM on the patient and the family
• understand the need to offer carrier testing to relevant family members after diagnosis of an IEM.

**Skills:**
• identify clues to the presence of IEMs: physical examination - failure to thrive, dysmorphic features; abnormalities of hair, skin, skeleton; abnormal odor; organomegaly; abnormal muscle tone
• identify the correlation of metabolic abnormalities with prognosis based on individual IEMs which may differ for different forms of particular IEMs
• promote early diagnosis and lifesaving rapid treatment of IEMs
• interpret clinical findings in older children, adolescents, and adults
• interpret main laboratory findings
• explain treatment modalities according to two general categories: disease-specific therapy (ie, treatment that addresses the biochemical basis of the disease) and nonspecific medical management (including symptom management and medical or surgical interventions)
• educate parents of the child with IEM about clinical problems in adult age and reproductive issues
• provide counselling (dietary, genetic, psychosocial) as appropriate to discuss prognosis, recurrence risks, screening of other family members, prenatal diagnosis, and support groups

**Theme 3.6: Cancer Genetics**

Genetic cancer syndromes including:
- Breast and ovarian cancer arising from BRCA1 and BRCA2 mutations
- Colorectal cancer arising from familial adenomatous polyposis (FAP) or hereditary non-polyposis colorectal cancer (HNPCC)
- Multiple endocrine neoplasia type 1 and 2 (MEN1 and MEN2)
- Melanoma arising from CDKN2A or CDK4 mutations
- Neurofibromatosis types 1 and 2
- Li-Fraumeni syndrome (TP53)

**Learning Objectives: Assess, diagnose and contribute to the multidisciplinary management of patients with genetic cancer syndromes**

**Knowledge**
• identify genetic and environmental factors that affect cancer risk
• describe current recommendations concerning tumor surveillance in cancer prone families
• define clinical features of genetic cancer syndromes
• describe medical and family history features of inherited cancers
• describe genetic mechanisms in cancer, including Knudson's two-hit hypothesis• describe mechanisms of oncogenesis, the role of tumor supressor genes, onco genes, driver mutations, passenger mutations)
• discuss the impact of inherited cancer on the individual and their at-risk family
• discuss current recommendations concerning tumor surveillance and genetic testing in families at risk of cancer
• discuss surveillance recommendations for those at low to moderate risk of cancer
• discuss the impact of cancer risk on individuals and families
• discuss the impact of mutation positive diagnosis on individuals and their families
• describe the roles primary care physicians and genetic counsellors play in assessing families where relatives are at risk of developing cancer

**Skills**
• recognise when a monogenic familial predisposition to cancer is likely to be present in a family
• verify a reported cancer history
• evaluate and prioritize gene testing for cancer diagnosis
• detection and genetic assay of circulating tumor cells in the bloodstream
• use genetic and disease registers to support follow-up of affected and at-risk patients
• assess screening protocols for at-risk relatives

• recommend appropriate interventions for individuals who are identified as being at increased risk of cancer
• identify at-risk patients and relatives who are eligible to participate in trials of cancer prevention strategies
• educate patients about lifestyle factors that affect cancer risk, emphasizing risk factor avoidance and promoting behaviors that reduce the risk of developing disease
• support general practitioners with the long-term management of selected patients with familial cancer syndromes
• liaise with other specialists regarding cancer screening and treatment options
• order and evaluate genetic testing results to inform cancer management
• attend multidisciplinary cancer genetic meetings.

**Theme 3.7: Haematological Disorders**

**Learning Objectives: Assess, diagnose and contribute to the multidisciplinary management of patients with haematological disorders with genetic alterations including:**

- red cell disorders (haemoglobinopathies, red blood cell enzymopathy, other congenital anemias, haemochromatosis)
- congenital platelet disorders (Bernard-Soulier syndrome)
- congenital bleeding disorders (Hemophilia A&B, von Willebrand disease, other bleeding disorders - deficiency of factor XIII, XI, X, VII, V and II, and hypofibrinogenaemia)
- thrombotic disorders (thrombophilia - F V Leiden, II G20210A; acquired thrombotic tendency)
- bone marrow failure syndromes (acquired aplastic anemia, Fanconi's anemia, other inherited bone marrow failure syndromes)
- myeloid malignancies
    - ✓ myeloproliferative and myelodysplastic neoplasms
    - ✓ acute myeloid leukemia and leukemia's of ambiguous lineage – AML with recurrent genetic abnormalities, AML with MDS related changes, therapy related AML and MDS, other AML, Myeloid proliferations related to Down syndrome, Acute leukemia of ambiguous lineage)
- lymphoid malignancies and plasma cell disorders
    - ✓ B-cell neoplasms – Acute lymphoblastic leukemia/lymphoblastic lymphoma of B-cell origin, Burkitt's lymphoma, Chronic lymphocytic leukemia/small lymphocytic lymphoma/monoclonal B cell lymphocytosis
    - ✓ T-cell lymphomas and NK-cell Neoplasms - Acute lymphoblastic leukemia /lymphoblastic lymphoma of T-cell origin, other T-and NK-cell lymphomas
    - ✓ Hodgkin lymphoma

**Knowledge**

- Knowledge of clinical features of haematological disorders
- Genetic mechanisms in leukemias
- The genetic and environmental factors that affect risk of developing haematological disorder
- Current recommendations concerning tumor surveillance in cancer – prone families

**Skills**

- Taking a relevant bleeding history (previous challenges and family history) with a focused clinical examination
- Considerations in carriers of hemophilia in relation to pregnancy

- Perform an appropriate examination and undertake risk estimation using a variety of methods
- Use a haematological disease registers and other sources to verify diagnoses, to support follow-up of affected and at-risk patients
- Assessment of screening protocols for at-risk relatives.

**Theme 3.8: Other Genetic Disorders and Diseases**

**Learning Objective: Assess, diagnose and treat patients with other genetic disorders and diseases**

Relatively common genetic disorders, including:
Marfan syndrome
Cystic Fibrosis
Polycystic kidney disease
Inherited cardiac disorders
Hypercholesterolemias
Hereditary deafness
Hereditary ophtalmological disorders

Diseases with genetic predisposition include:
Cleft lip/palate
Diabetes mellitus
Metabolic syndrome
Asthma and allergy
Vascular disorders
Amyloidosis

**Knowledge**
• describe clinical, biochemical, metabolic, and genetic features of the diseases
• discuss the diagnosis and management of the diseases
• understand the relevant inheritance patterns
• understand the psychological and social impact of an inherited condition on the individual and family.

**Skills**
• identify family history data that suggest inherited disease
• verify the diagnoses of genetic disorders and diseases from hospital records
• confirm clinical signs of genetic disorders and diseases in affected individuals
• interpret the results of genetic disorder investigations, including molecular tests, computer tomography and MRI scans
• refer patients to appropriate specialists
• refer patients for relevant health and social care support.

# MODULE 4: PROFESSIONAL QUALITIES

## Theme 4.1: Ethics

**Learning Objective:** Identify, understand and apply appropriately the principles, guidance and laws regarding medical ethics and confidentiality

**Knowledge**

• discuss relevant strategies to ensure confidentiality
• identify situations where confidentiality might be broken
• discuss different cultural attitudes to genetic disorders and genetic testing and their impact on individuals, families and cultural groups
• recognise the factors influencing ethical decision making: including religion, personal and moral beliefs, cultural practices
• discuss privacy, consent and access issues in relation to the creation and use of genetic registers
• discuss the importance of genetic registers in research and management of genetic conditions
• differentiate between the legal and personal requirements of the patient's medical record and that of the genetic register
• discuss issues relevant to consent for post mortem examinations
• discuss the ethical basis of needing approval and consent prior to commencing a research project
• identify the key sources of advice on the responsibilities of medical practitioners in serious criminal matters
• discuss the legal issues related to criminal matters that may arise during the management of patients with genetic disorders, e.g. discovery of an incestuous relationship between parents of a patient
• outline the issues involved in the genetic testing of minors
• discuss the need for equity of services
• outline situations where patient consent, while desirable, is not required for disclosure e.g. serious communicable diseases, public interest
• outline the procedures for seeking a patient's consent for disclosure of identifiable information
• summarise the diversity of public opinion on ethical and moral aspects of the practice of clinical genetics

**Skills**

• consult with patients before distribution of information within members of the immediate healthcare team
• respect patient's requests for information not to be disclosed
• adapt counselling considering specific cultural beliefs and attitudes
• provide 'non-directive' genetic advice to patients and their families
• appropriately use and share information with the highest regard for confidentiality
• disseminate appropriate information in lay terms and gain informed consent from patients
• communicate the value of genetic registers to colleagues, patients and their families
• provide patient details to the appropriate genetic registers
• establish or maintain genetic registers
• obtain suitable evidence when criminal matters arise and consult with appropriate bodies when necessary
• discuss with patients, colleagues and the public the ethical issues concerning:
    assisted reproduction
    confidentiality
    informed consent
    genetic testing of children
    late termination of pregnancy
    population screening for genetic disease

potential impact of testing an individual on other family members, employment/life insurance
predictive genetic testing
prenatal/pre-implantation diagnosis
• refer cases when conflict exists between personal values and those of the patient
• show willingness to seek advice of peers/experts in the event of ethical dilemmas

**Theme 4.2: Informed Consent**

**Learning Objective:** Ensure the trainee has the knowledge and skills to deal appropriately with ethical and legal issues that arise during the management of patients with genetic disorders

**Knowledge**
• discuss the process for gaining informed consent
• understand process of consent for tissue/sample storage and use
• understand the process of consent for non-invasive activities, such as sharing information with relatives
• understand how to gain consent in a research context

**Skills**
• present all information to patients (and careers) in a format they understand and allow time for reflection on the decision to give consent
• provide a balanced view of all care options
• respect a patient's rights of autonomy
• do not withhold information relevant to proposed care or treatment in a competent patient
• refrain from undertaking procedures the practitioner is not competent to perform
• show willingness and ability to obtain a second opinion, senior opinion, and legal advice in difficult situations of consent or capacity
• inform a patient and seek alternative care where personal, moral or religious belief prevents a usual professional action

**Theme 4.3: Dealing with Medical Uncertainty**

**Learning Objective:** Identify and discuss factors contributing to uncertainty in clinical genetics practice

**Knowledge**
• identify uncertainty as an integral part of all medical practice, including clinical genetics
• identify that uncertainty is a limitation of current knowledge and not a professional failure
• develop a solid basis of accurate and up to date knowledge, including literature search and consultations with colleagues
• recognise that uncertainty in current clinical genetic knowledge can provoke anxiety in the patient and the clinician
• discuss many types of uncertainty in clinical genetics, including:
antenatal detection of abnormality with uncertain consequences for the fetus
lack of diagnosis, particularly in person with intellectual disability, malformations or dysmorphism leading to uncertainty about cause, prognosis and recurrence risks
known diagnosis but uncertain prognosis
absence of prenatal tests leading to uncertain outcome for current or future pregnancy

**Skills**
• disclose and openly acknowledge areas of uncertainty to patients

• communicate to a patient and support decision making in cases where uncertainty exists as to the diagnosis or appropriate screening, prevention or management
• reframe uncertainty by breaking it down into manageable parts
• assist in the patient's decision making process to reach an acceptable conclusion
• consult with appropriate colleagues regarding best practice in cases where uncertainty exists

**Theme 4.4: Working with Colleagues and Medical Agencies**

**Learning Objective:** To demonstrate effective working relationships with colleagues relevant to practice issues of clinical genetics

**Knowledge**
• know the roles and responsibilities of team members and know how a team works effectively
• know the role of multidisciplinary management in genetic disorders
• know the principles of effective inter-professional collaboration to optimize patient or population care
• demonstrate knowledge of facilitation and conflict resolution methods

**Skills**
• show leadership, delegate and supervise safely
• develop effective working relationships with colleagues and other staff
• recognise when input from another specialty is required for individual patients
• employ behavioural management skills with colleagues to enhance collaboration and prevent/resolve conflict
• demonstrate the ability to facilitate, chair, and contribute to meetings
• foster a supportive and respectful environment where there is open and transparent communication between all team members
• ensure appropriate confidentiality unrelated to medical management is maintained during communication with any member of the team

**Theme 4.5: Patient Education**

**Learning Objective:** To have the knowledge, skills and attitudes to be able to educate patients effectively about genetic disease

**Knowledge**
• understand the genetic factors that influence the incidence and prevalence of common conditions
• understand the factors which influence health and illness (psychological, biological, social, cultural, and economic)
• understand the influence of lifestyle and lifestyle therapeutic factors on health
• understand the purpose of screening programmes and know the available common programmes
• understand the positive and negative effects of screening on the individual

**Skills**
• demonstrate in practice an appropriate knowledge of the influences of environment and behaviour on health
• identify opportunities to promote changes in lifestyle and other actions which will positively improve health and/or disease outcomes
• identify the interaction between mental, physical and social wellbeing in relation to health
• counsel patients appropriately on the benefits and risks of screening and health promotion activities

• identify patient's ideas, concerns and health beliefs regarding screening and health promotions programmes and be capable of appropriately responding to these
• provide the means for patients to access further information and patient support groups
• engage in effective team-working around the improvement of health
• offer screening, where appropriate, to facilitate early intervention