

MGM INSTITUTE OF HEALTH SCIENCES

(Deemed University u/s 3 of UGC Act, 1956)

Grade 'A' Accredited by NAAC

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MGM 04 MD Biochemistry

Program Outcomes:

At the end of the MD training programme in Biochemistry, the post graduate student should have acquired competencies in the following areas, as detailed below.

PO1. **Acquisition of knowledge:** The student should be able to explain clearly concepts and principles of biochemistry and cell biology, including correlations of these with cellular and molecular processes involved in health and disease.

PO2. **Teaching and training:** The student should be able to effectively teach undergraduate students in medicine and allied health science courses so they become competent health care professionals and able to contribute to training of postgraduate post graduate students.

PO3. **Diagnostic services:** The student should be able to set up/supervise/manage a diagnostic laboratory in Biochemistry in a hospital, ensuring quality control, and providing a reliable support service. The student should be able to provide clinicians with consultation services for diagnostic tests in biochemistry and in interpretation of laboratory results.

PO4. **Research:** The student should be able to carry out a research project from planning to publication and be able to pursue academic interests and continue life-long learning to become more experienced in all the above areas and to eventually be able to guide postgraduates in their thesis work.

SUBJECT SPECIFIC COMPETENCIES

The student during the training programme should acquire the following competencies:

A. Cognitive domain

1. Describe and apply biochemical principles to explain the normal state, abnormal disease conditions and mechanism of action used in the perception, diagnosis and

- treatment of diseases.
- 2. Explain energy transactions in a living system, and describe importance of biomolecules in sustaining the life process.
- 3. Describe pathways of the intermediary metabolism along with their individual and integrated regulation and apply that in understanding the functioning of the body.
- 4. Describe and apply the concept of nutrition in health and disease, micro- and macronutrition and essential nutrients, and interlinks of nutrients with metabolism and functions of a living system.
- 5. Apply and integrate knowledge of molecular and metabolic conditions in normal and disease states for clinical problem solving and research
- Acquire knowledge on application of various aspects of genetic engineering in medicine
- 7. Acquire knowledge and apply the principle of statistics, biostatistics and epidemiology to the evaluation and interpretation of molecular and metabolic disease states.
- 8. Evaluate, analyze and monitor disease states by applying relevant biochemical investigations and interpreting the clinical and laboratory data.
- 9. Able to integrate principles of immunology in biochemistry.
- 10. Demonstrate knowledge of basics of research methodology, develop a research protocol, analyse data using currently available statistical software, interpret results and disseminate these results and to have the potential ability to pursue further specializations and eventually be competent to guide students.
- 11. Describe the principles of teaching learning technology towards application and take interactive classroom lectures, prepare modules for PBL, organize and conduct PBLs, case discussions, small group discussions, Seminars, Journal club and research presentations
- 12. Demonstrate knowledge of principles of Instrumentation.
- 13. Demonstrate knowledge about recent advances and trends in research in the field of clinical biochemistry.

B. Affective domain

- 1. Effectively explain to patients from a variety of backgrounds, the molecular and metabolic basis of disease states and lifestyle modifications.
- 2. Communicate biochemical reasoning effectively with peers, staff and faculty, and other members of the health care team.
- 3. Demonstrate empathy and respect towards patients regardless of the biochemical nature of their disease.

- 4. Demonstrate respect in interactions with patients, families, peers, and other healthcare professionals.
- 5. Demonstrate ethical behavior and integrity in one's work.
- 6. Demonstrate effective use of nutrition, lifestyle and genetic counseling.
- 7. Be aware of the cost of diagnostic tests and economic status of patients.
- 8. Acquire skills for self-directed learning to keep up with developments in the field and to continuously build to improve on skills and expertise

C. Psychomotor domain

- 1. Able to select, justify, and interpret the results of clinical tests in biochemistry.
- 2. Develop differential diagnoses for molecular and metabolic causes of diseases.
- Suggest preventive, curative, and/or palliative strategies for the management of disease.
- 4. Predict effectiveness and adverse effects associated with disease intervention.
- 5. Demonstrate skills for clinical diagnosis, testing, understanding of biochemical conditions and diagnostic service.
- 6. Perform important biochemical, immunological and molecular biology techniques.
- 7. Observed working of important advanced techniques.
- 8. Demonstrate standard operating procedures of various methods and techniques used in clinical biochemistry.
- Determination of enzyme activity and study of enzyme kinetics. Ideally it should be
 accompanied by purification (partial) of the enzyme from a crude homogenate to
 emphasise the concepts of specific activity, yield and fold purification
- 10. Demonstrate and report routine investigations in hematology and microbiology
- 11. Demonstrate presentation skills at academic meetings and publications.

By the end of the course, the post graduate student should have acquired practical skills in the following:

- Performance of reactions of carbohydrates, amino acids and proteins, and lipids
- Experiments to demonstrate constituents of milk
- Experiments to demonstrate normal and abnormal constituents of urine
- Determination of iodine number and saponification number of fats
- Estimation of ammonia and amino acids by Sorenson formal titration

- Estimation of nitrogen estimation in a given amino acid solution by micro Kjeldahl method
- Estimation of phosphorus by Fiske Subbarao method
- Estimation of ascorbic acid in lime
- Estimation of calcium content in milk
- Estimation of proteins by Folin's method and dye binding method.
- Two-dimensional paper chromatography for separation of amino acids
- Preparation and estimation of starch, glycogen, cholesterol, casein (phosphorus in casein) and hemoglobin from biological samples Determination of enzyme activity and study of enzyme kinetics, using any 2 suitable enzymes (eg, catalase from rat liver and acid phosphatase from potatoes).
- Estimation of clinical analytes as detailed below:
 - blood glucose, glycated haemoglobin; performance of glucose tolerance test
 - o electrolytes, arterial blood gas analysis
 - o cholesterol, triglycerides, free fatty acids, phospholipids, Lp (a), urea, creatinine, uric acid, ammonia, microalbuminuria
 - o parameters of liver function tests (bilirubin, hepato-biliary enzymes such as AST, ALT, ALP, GGT, serum proteins/albumin and prothrombin time)
 - Calcium, magnesium, copper (and ceruloplasmin), serum iron, TIBC and ferritin
 - o markers of myocardial damage (CK, CK MB, troponins, LDH)
 - o other enzymes of diagnostic relevance (eg. phosphatases, amylase etc)
 - o vitamins D and B₁₂ and folate
- Electrophoresis of serum proteins
- Electrophoresis of lipoprotein (Optional)
- Electrophoretic separation of LDH isozymes or any other isoenzymes
- Clearance tests
- CSF analysis
- Thyroid function tests and other hormone assays by ELISA/RIA
- Preparation of buffers.

Clinical Laboratory

- Taking any one parameter, students should prepare a Levy Jennings chart and plot inter-assay and intra-assay variation for the laboratory.
- Implementation of Westgard rules.

Optional:

 Determination of reference values for any one parameter for the clinical laboratory

In addition, all efforts should be made to ensure that students at least see a demonstration of the following techniques.

- Separation of peripheral blood lymphocytes using Ficoll Hypaque
- Subcellular fractionation/marker enzymes for organelles to demonstrate fractionation
- Ultracentrifugation
- Isolation of high molecular weight DNA from tissues/blood
- Isolation of RNA; synthesis of cDNA by reverse transcription; PCR (both conventional and real-time)
- Isolation of plasmids and agarose gel electrophoresis for proteins and nucleic acids
- Basic techniques in cell culture
- High performance liquid chromatography (HPLC)

COURSES OUTCOME

SYLLABUS

The course contents are outlined below:

Paper I

Biomolecules, cell biology, biochemical techniques, biostatistics and research methodology, basics of medical education in teaching and assessment of biochemistry.

Biomolecules:

Properties of water

Concept of an acid, a base, pH, pK, buffer and buffering capacity

Classification, structure and functions of amino acids and peptides

Structural organization of proteins and relationship with their functions

- o primary, secondary, tertiary and quarternary structure of proteins
- o protein folding and denaturation

Structure-function relationship of proteins

- o Structure and functions of hemoglobin and myoglobin
- o Structure and function of collagen
- Structure and function of immunoglobulins

Classification, functions, properties and reactions of carbohydrates

Classification, properties and importance of lipids

- o Fatty acids nomenclature, classification, properties, reactions
- o Mono, di- and triacylglycerols
- o Trans fats
- Cholesterol structure, properties and functions
- o Phospholipids definition, types, properties, s and importance
- o Glycolipids definition, types, functions, examples.
- Lipoproteins definition, structure, types, functions, role of apoproteins, importance in health and disease.
- o Biological membranes structure, function, properties and importance.
- Micelles and liposomes

Nucleotides and nucleic acids

- o purine and pyrimidine bases in DNA and RNA
- o nucleosides and nucleotides
- o physiologically important nucleotides
- synthetic analogues of purine/pyrimidine bases and nucleosides used as therapeutic agents (anti-cancer drugs, anti-viral drugs)
- Watson and Crick model of DNA structure
- o Structure and functions of different types of RNA.

Cell biology

- Structure of the cell and different subcellular organelles
- Structure and functions of cell membrane, solute transport across biological membranes
- Intracellular traffic and sorting of proteins

- Intracellular signaling pathways, membrane receptors and second messengers
 Extracellular matrix: composition, importance and biomedical importance,
 cellular adhesion molecules and intercellular communication
- Cytoskeleton, muscle contraction and cell motility
- Cell cycle, mitosis, meiosis and mechanisms of cell death
- Red and white blood cells

Analytical techniques in biochemistry

- o Spectrophotometry (UV and visible spectrophotometry),
- o atomic absorption spectrophotometry
- o Flame photometry
- Fluorometry
- o Turbidimetry and nephelometry
- Gravimetry
- Electrochemistry (pH electrodes, ion-selective electrodes, gas-sensing electrodes)
- Chemiluminescence
- Water testing
- Electrophoresis (principle, types, applications; isoelectric focusing capillary electrophoresis; 2-D electrophoresis)
- Chromatography (principle, types [including high performance liquid chromatography and gas chromatography])
- Techniques in molecular biology: Blotting techniques, polymerase chain reaction (PCR), DNA and protein sequencing, microarrays and DNA chip technology, cloning techniques, genomics, proteomics and metabolomics

Nanotechnology and microfabrication
Techniques to study in vivo metabolism - NMR, SPECT, PET scans, etc
Radioisotope-based techniques and its applications
Biostatistics and research methodology

• Basic concepts of biostatistics as applied to health science

• Statistical tests: t-test, analysis of variance, chi-square test, non-parametric tests, correlation and regression

Statistical methods of validation of diagnostic tests

Basics of epidemiological study designs and sampling methodologies

• Meta-analysis and systematic reviews

Basics of medical education in teaching and assessment of biochemistry

Principles of adult learning, taxonomy of learning, educational objectives, principles of assessment and question paper setting, methods of assessing knowledge, appropriate use of

media, microteaching, small group teaching.

Environmental Biochemistry:

Health and pollution.

Paper II:

Enzymes, bioenergetics, biological oxidation, intermediary metabolism and regulation,

inborn errors of metabolism and nutrition

Enzymes:

Properties, classification, mechanism of action, coenzymes and cofactors, kinetics of enzyme activity, regulation of enzyme activity, isoenzymes, diagnostic and therapeutic enzymes, principles of assays of enzymes, enzymes as therapeutic targets of drugs.

Biological oxidation

Basic concepts of thermodynamics and its laws, as applied to living systems,

Exergonic and endergonic reactions and coupled reactions, redox potential

High energy compounds

Classification and role of oxidoreductases

Cytochromes; cytochrome P450 system

Respiratory chain and oxidative phosphorylation

• Components, complexes and functioning of the respiratory chain

Process of oxidative phosphorylation

• Mechanisms of ATP synthesis and regulation

Mitochondrial transport systems and shuttles

Inhibitors, uncouplers and ionophores

OXPHOS diseases

Overview of metabolism and intermediary metabolism

Metabolism of carbohydrates

- Digestion and absorption
- Glycolysis and TCA cycle, including regulation
- Glycogen metabolism and its regulation
- Cori cycle, gluconeogenesis and control of blood glucose
- Metabolism of fructose and galactose
- Pentose phosphate and uronic acid pathways and their significance
- · Polyol pathway
- Regulation of blood glucose levels
- Diabetes mellitus (including gestational diabetes mellitus) classification, pathogenesis, metabolic abnormalities, diagnostic criteria, principles of treatment, pathogenesis of complications, laboratory tests
- Metabolism of ethanol

Metabolism of lipids

- Digestion and absorption, including role of bile salts
- Biosynthesis and oxidation of fatty acids
- Ketone bodies formation, utilisation and regulation
- Metabolism of unsaturated fatty acids and eicosanoids
- Metabolism of triacylglycerol; storage and mobilisation of fats
- Metabolism of cholesterol
- Metabolism of lipoproteins
- Metabolism in adipose tissue
- Role of liver in lipid metabolism
- Role of lipids in atherogenesis
- Metabolism of phospholipids and associated disorders

Metabolism of amino acids and proteins

- Digestion and absorption
- Pathways of amino acid degradation transamination, oxidative deamination
- Transport and metabolism of ammonia
- · Metabolism of individual amino acids.
- Plasma proteins

Metabolism of nucleotides

- De novo synthesis of purine nucleotides
- Salvage pathway for purines
- Degradation of purines
- De novo synthesis of pyrimidine nucleotides
- Degradation of pyrimidine
- Synthetic analogues of purine/pyrimidine bases and nucleosides used as therapeutic agents

Metabolism of haem

- Biosynthesis of heme and associated disorders
- Degradation of heme and associated disorders

Metabolism in individual tissues and in the fed and fasting states

Liver, adipose tissue, brain, RBCs

Nutrition

- Principal food components
- General nutritional requirements
- Energy requirements
- Biological value of proteins
- Thermogenic effect of food
- Balanced diet, diet formulations in health and disease, mixed diet
- Nutritional supplements
- Food toxins and additives
- Parenteral nutrition
- Disorders of nutrition, obesity, protein and protein energy malnutrition, dietary fibers, under-nutrition, laboratory diagnosis of nutritional disorders
- National Nutrition Programme.

Vitamins

Classification, biochemical role, sources, RDA and deficiency state of each vitamin (including diagnostic tests for deficiency and treatment)

Minerals

Classification, biochemical role, sources, requirement and deficiency state of each mineral (including diagnostic tests for deficiency and treatment)

Metabolism of xenobiotics

Free radicals and anti-oxidant defence systems in the bodyand associations with disease processes

Paper III:

Molecular biology, molecular and genetic aspects of cancer, immunology and effects of environmental pollutants on the body

Structure and organization of chromosomes and chromatin re-modelling DNA replication

- DNA replication in prokaryotes and eukaryotes (including important differences between the two):
- Roles of DNA polymerase, helicase, primase, topoisomerase and DNA ligase
- · Replication fork
- Okazaki fragments and its importance in replication.
- Overview of role of major DNA repair mechanisms mismatch repair, base excision repair, nucleotide excision repair and double strand break repair.
- Diseases associated with abnormalities of DNA repair systems
- DNA recombination

Transcription

- Structure of a gene exons and introns, promoter, enhancers/repressors and response elements.
- Process of transcription in prokaryotes and eukaryotes initiation, elongation and termination (including important differences).
- Post-transcriptional processing capping, tailing and splicing.

Genetic code and mutations

Characteristics of the genetic code

- Molecular basis of degeneracy of the genetic code (Wobble hypothesis)
- Mutagens- examples of physical, chemical and biological mutagens.
- Types of mutations point mutations and chromosomal mutations
- Relationship of mutations with specific diseases

Translation

- Basic structure of prokaryotic and eukaryotic ribosomes.
- Structure of tRNA (diagram of clover leaf model of tRNA structure) and its function in protein synthesis.

- Function of aminoacyl tRNA synthase.
- Process of protein synthesis (translation) initiation, elongation and termination (including important differences between prokaryotic and eukaryotic translation).
- Inhibition of prokaryotic translation by antibiotics.
- Post-translational modifications

Regulation of gene expression in prokaryotes and eukaryotes

- The operon concept in prokaryotes
- Role of general and gene specific transcription factors
- Small interference RNA (siRNA) and micro RNA (miRNA).
- Other modes of regulation of gene expression: alternative splicing, alternative promoter usage, DNA methylation, Histone acetylation / deacetylation, RNA editing, alterations of RNA stability

Recombinant DNA technology and its applications in modern medicine

- Concepts of recombinant DNA, genetic engineering, biotechnology and cloning.
- Restriction endonucleases.
- Vectors for cloning plasmids and phages.
- Genomic and cDNA libraries.
- Applications of recombinant DNA technology in medicine.
- Gene therapy
- Diagnosis of genetic diseases and genetic counseling
- DNA fingerprinting
- DNA sequencing
- Microarrays
- Fluorescent in situ hybridization (FISH)
- DNA vaccines
- Transgenic animals
- Application of molecular techniques in forensic investigation and medicolegal cases

Overview of Human Genome Project

Basics of bioinformatics

Principles of human genetics

- Alleles, genotypes and phenotypes
- Patterns of inheritance: monogenic and polygenic inheritance
- Population genetics
- Genetic factors in causation of diseases
- Types of genetic diseases: Chromosomal, monogenic and polygenic disorders, mitochondrial disorders, nucleotide repeat expansion disorders, imprinting disorders
- Screening for genetic diseases and prenatal testing
- Ethical and legal issues related to medical genetics

Stem cells in clinical medicine

- Basic concepts regarding stem cells
- Types of stem cells: embryonic and induced pleuripotent stem cells (IPSC)
- Potential applications in the clinical medicine
- Ethical and legal issues related to use of stem cells in medicine

Cancer

- Carcinogens: physical, chemical and biological
- Clonal origin of cancers

Genetic basis of carcinogenesis

- Role of oncogenes and tumour suppressor genes
- Familial cancer syndromes
- Cancer stem cells
- Epigenetic regulation in cancer
- Gene expression profiling in cancer
- Cancer cell biology: cell cycle abnormalities, telomerase activity, proliferative capacity and decreased apoptosis
- Metastasis
- Tumor markers
- Biochemical basis of cancer chemotherapy and drug resistance
- New methods of anti-cancer therapy: targeted cancer therapy, cancer immunotherapy.

Immunology

- Innate and acquired immunity
- Humoral and cell-mediated immunity
- Cells and organs of the immune system T and B cells, macrophages, dendritic cells, NK cells, granulocytes
- Antigens, epitopes and haptens
- Immunoglobulin classes, isotypes, allotypes, idiotypes, monoclonal antibodies, organization and expression of immunoglobulin genes, immunoglobulin gene rearrangement, class switching
- · Antigen-antibody interaction immunochemical techniques
- Major histocompatibility complex, antigen processing and presentation,
- T cell and B cell receptor, toll like receptors
- T cell maturation/activation/differentiation
- B cell generation/activation/differentiation
- Cytokines
- Complement system, cell
- Immune response to infections
- Hypersensitivity reactions
- Vaccines
- Immuno-deficiency syndromes
- Autoimmunity
- Transplantation immunology
- Cancer and immune system,
- Immunodiagnostics
- Immunotherapy

Paper IV

Clinical biochemistry and molecular diagnostics related to different body systems/organs, endocrinology, and recent advances in biochemistry

Basic principles and practice of clinical biochemistry

Units of measure, reagents, clinical laboratory supplies, basic separation techniques, laboratory calculations, specimen collection and processing, safety in the laboratory, clinical utility of laboratory tests (including sensitivity, specificity, ROC curves, etc), analysis in the laboratory, selection and evaluation of methods (including statistical techniques), evidence-

based laboratory medicine, establishment and use of reference values, pre-analytical variables and biological variations, quality management, clinical laboratory informatics

Analytical techniques and instrumentation

Principles of basic techniques used in a clinical biochemistry laboratory (spectrophotometry, electrochemistry, electrophoresis, osmometry, chromatography, mass spectrometry, immunochemical techniques, molecular techniques, automation, point of care testing,

Clinical correlates and analytical procedures

- Amino acids, peptides and proteins; non-protein nitrogenous compounds
- enzymes
- carbohydrates
- lipids, lipoproteins and apolipoproteins and other cardiovascular risk factors
- electrolytes
- blood gases and pH
- hormones and associated disorders
- · catecholamines and serotonin
- vitamins; trace and toxic elements
- hemoglobin, and bilirubin

- porphyrins and associated disorders
- bone and mineral metabolism
- tumour markers
- assessment of organ functions (hypothalamus and pituitary, adrenal glands, gonads, thyroid, parathyroid, liver, kidney, heart, stomach, pancreas, intestine, etc) and associated disorders
- pregnancy and maternal and fetal health
- reproduction related disorders infertility
- newborn screening
- inborn errors of metabolism
- hemostasis
- therapeutic drug monitoring
- clinical toxicology
- molecular diagnostics
- body fluid analyses

Regulation of fluid and electrolyte balance and associated disorders

Regulation of acid-base balance and associated disorders

Biochemistry of the endocrine system

- Classification and general mechanism of action of hormones
- Biosynthesis, secretion, regulation, transport and mode of action of hypothalamic peptides, adenohypophyseal and neurohypophyseal hormones, thyroid and parathyroid hormones, calcitonin, pancreatic hormones, adrenocortical and medullary hormones, gonadal hormones, gastrointestinal hormones, opioid peptides, parahormones.
- Biochemistry of conception, reproduction and contraception
- Endocrine interrelationship and their involvement in metabolic regulation
- Neuro-modulators and their mechanism of action and physiological significance
- Biochemical aspects of diagnosis and treatment of endocrinal disorders:

Hematopoietic disorders

Iron deficiency and other hypoproliferativeanaemias - iron metabolism, laboratory

tests of iron status, iron therapy

- Anaemia of chronic disease, anaemia of renal disease
- Hemoglobinopathies sickle cell anaemia, methaemoglobinemias, thalassemia syndromes, Megaloblastic anaemia
- RBC membrane and metabolism
- Hemolytic anaemia inherited defects in RBC membrane and enzymes (G6PD deficiency), immunologic causes of hemolysis
- ABO blood group system biochemical basis, transfusion biology.
- Plasma cell disorders multiple myeloma.

Hemostasis and thrombosis

Biochemical mechanisms, related laboratory tests, antiplatelet/anticoagulant/fibrinolytic therapy

Cardiovascular system

Atherosclerosis - pathogenesis, risk factors, prevention and treatment Cardiac failure, acute coronary syndrome, cardiac biomarkers

Respiratory system

Gaseous exchange in lungs - physiological features and disturbances, arterial blood gases Pathogenesis of cystic emphysema, alpha-1 anti-trypsin deficiency

Kidney

Kidney function tests; pathophysiology, biochemistry, laboratory findings and management in acute kidney injury and chronic kidney disease; estimation of GFR; glomerular diseases - pathogenesis and mechanisms of glomerular injury, nephrotic syndrome, diabetic nephropathy; tubular disorders - renal tubular acidosis, proteinuria, nephrolithiasis, kidney transplant; biochemical aspects of renal stones.

Gastrointestinal system

- Gastric physiology
- Pathophysiology of peptic ulcer disease, including role of *H. pylori*; gastric function tests; Zollinger-Ellison syndrome
- Digestion and absorption of nutrients; evaluation of malabsorption (steatorrhea, lactose intolerance)

- · Celiac disease
- · Inflammatory bowel disease
- Protein losing enteropathy
- Regulatory peptides in the gut
- Neuroendocrine tumours

Liver

- Liver function tests
- Hyperbilirubinemias
- Viral hepatitis
- Serologic/virologic markers
- Alcoholic liver disease, fatty liver, chronic liver disease, cirrhosis and its complications
- Pathogenesis of ascites
- Hepatic encephalopathy
- Metabolic diseases affecting liver
- Reye's syndrome
- Diseases of gall bladder/bile ducts pathogenesis of gallstones
- Pancreas acute and chronic pancreatitis, cystic fibrosis, pancreatic function tests.

Bone and mineral metabolism

Bone structure and metabolism; metabolism of calcium, phosphate and magnesium; regulation and abnormalities of bone metabolism; vitamin D; parathyroid hormone; calcitonin; parathyroid hormone-related (PTHrP); osteoporosis – pathophysiology; markers of bone turnover

Nervous system

- Neurotransmitters and their receptors
- Ion channels and channelopathies
- Neurotrophic factors
- Protein aggregation and neurodegeneration
- Alzheimer's disease, Parkinson's disease, Huntington's disease, multiple sclerosis
- Prions and prion diseases
- Guillain-Barre syndrome immunopathogenesis

- Myasthenia gravis pathophysiology
- Hereditary myopathies Duchenne muscular dystrophy
- Inherited disorders of muscle energy metabolism
- Mitochondrial myopathies
- Pathophysiology of psychiatric disorders such as anxiety, depression and schizophrenia

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