Syllabus Master's Degree Course in Medicine and Surgery

THE CELL: FUNCTIONS AND REGULATIONS

First year, second semester (9 academic credits [CFU])

Teachers

Subject	Academic credits (CFU)	Lecturer
Cellular physiology	4	PUZZO Daniela CIRANNA Lucia
Biochemistry	5	AMORINI Angela Maria

Learning outcomes

Subject	Learning outcomes
Cellular physiology	By the end of the course, students are expected to: • Understand the biophysical laws involved in body function regulation. • Understand basic neurophysiology, with particular reference to cellular excitability mechanisms and neurotransmission. • Be able to apply the acquired knowledge to clinical practice (pathophysiological implications).
Biochemistry	By the end of the course, students are expected to: • Understand the correlation between structure and function of macromolecules for cellular function. • Understand the strategy and the mechanisms of metabolic pathways. • Understand the biochemical alterations in pathological conditions.

Prerequisites

Subject	
Cellular physiology	Propaedeutic subjects as per the study plan.
Biochemistry	Propaedeutic subjects as per the study plan.

Course contents

Subject	
Cellular physiology	THE CELL AS AN INTEGRATED SYSTEM • Dynamic balance, cell functions, the cell as a thermodynamic system, energy and entropy, the cell as a chemical system. • Gas and solute exchanges through cell membranes (Fick's law, passive diffusion, facilitated diffusion, controlled diffusion, primary and secondary active transport). • Homeostasis, steady state, regulation of cellular functions. GAS LAWS AND THEIR APPLICATIONS • Ideal gas law, Boyle's law, Charles and Gay-Lussac's law, second law of Gay-Lussac, Avogadro's law, Dalton's law, Graham's Law, Henry's Law, Laplace's law. Applications in physiology and pathophysiology (physiological polycythemia, high-altitude sickness, decompression sickness). FLUID COMPARTEMENTS AND HOMEOSTASIS • Human body fluid compartments: intracellular and extracellular compartments, compartments volumes and methods for their measurements. Sources and removal of body fluids. Water and salts balance. • Exchanges of water and electrolytes through biological membranes. Concentration and electrochemical gradients. Saline, isotonic and iso-osmotic solutions, and their use. Osmotic pressure: definition, units of measurements, plasma values. Van't Hoff's law, Gibbs-Donnan equilibrium. Hydrostatic pressure. Colloid osmotic and oncotic pressure: plasmas value and fluctuations. Consequences of oncotic pressure modifications. Starling's law and capillary exchanges. Pathophysiology: edema. PRINCIPLES OF HEMODYNAMICS AND HEMORHEOLOGY • Systemic circulation: generalities. Blood volume and velocity in different areas of the vascular system. Morphological and physiological characteristics of vessels: arteries, capillaries and veins. • Blood flow: physical factors affecting blood flow. Bernoulli's principle. Pressure, flow and resistance: Hagen-Poiseuille Law. Blood viscosity: relationship between viscosity and haematocrit. Turbulent blood flow. Laplace's law applied to vessels. • Vascular tone: nervous, hormonal and humoral control. ION CHANNELS AND MEMBRANE POTENTIAL • Cell excitability: cell membrane polarization, depolarisation and hyperpolarization. Ion channels: voltage-gated ion channels for sodium, potassium, calcium, chloride (characteristics, functions, main agonist and antagonists), electrophysiological techniques (patch clamp), Pathophysiology: canalopathies.

	• Electric potentials: membrane potential, electrochemical potential, Nernst equation, Goldman equation. Genesis and characteristics of an action potential. All-or-none law. Refractory period. Membrane repolarization. Graded potentials. • Excitability conduction along cell membranes. Propagation velocity. Saltatory or continuous conduction, myelin sheath. SYNAPTIC TRANSMISSION • Excitable cells communication. Electric and chemical synapses. Synaptic types. • Neurotransmitters and neuropeptides: synthesis, transport, release and secretion, neurotransmitter release cycle, vesicle cycle (trafficking). • Neuromuscular junction. Endplate potential, miniature potential, quantal neurotransmitter release. • Synaptic integration and transmission in CNS (EPSP, IPSP, spatial and temporal summation). • Ionotropic and metabotropic receptors. • Synaptic plasticity, Hebbian theory, long-term and short-term plasticity (long-term potentiation e long-term depression). NEUROTRANSMITTERS AND RECEPTORS • Acetylcholine, nicotinic receptors, muscarinic receptors, cholinergic synapses, main agonists and antagonists, pathophysiology: Miastenia gravis. • Glutamate glutamine cycle, NMDA, AMPA and Kainate receptors, metabotropic receptors, involvement in synaptic plasticity (LTP), main agonists and antagonists, Pathophysiology: glutamate excitotoxicity, notes on related diseases (Alzheimer's disease, glutamate hypothesis of schizophrenia). • GABA, Ionotropic and metabotropic receptors, Notes on benzodiazepine, barbiturate and alcohol mechanism of action. Pathophysiology: Anxiety, Epilepsy. • Catecholamine and their receptors, Role in SNA, Notes on stress and catecholamine. • Dopamine and its receptors. Pathophysiology: Addiction, Parkinson's disease, Schizophrenia. • Serotonin and its receptors, Drugs acting on serotonin receptors. Pathophysiology: mood disorders. • Endocannabinoids and opioids, notes on drug abuse (cocaine, amphetamine, heroine, hallucinogens, etc.) • Nitric oxide pathway and retrograde transmission. MUSCLE CONTRACTION • Skeletal muscles: structure, myofibrils, sarcomere and mechanisms of contraction, Sliding filament theory of muscle contraction, Neuromuscular junction, Excitation-Contraction Coupling, single muscle twitch and tetanus, isometric and isotonic contraction, length-tension curve, force-velocity curve, muscle energetics, oxygen consumption, muscle work, performance, and fatigue. Muscle fibers. Skeletal muscle innervation. Electromyogram. • Smooth muscle: generalities, unitary and multiunit muscles, structure, contraction mechanisms, contraction regulation (arteriolar tone), biomechanics.

	• Cardiac muscle: generalities, structure, contraction mechanisms, contraction regulation, biomechanics. NERVOUS SYSTEM: GENERALITIES • Neuron: morphologic, functional, biochemical and trophic unit of the nervous system. • Glia functions.
Biochemistry	PROTEINS • Structure, general properties and classification of amino acids. Peptide bond and its properties. Definition of primary, secondary, tertiary, quaternary structure. Ramachandran chart. Secondary structure: alpha-helix; beta strand, parallel, antiparallel. Denaturation and renaturation. Protein folding and denaturation. Protein misfolding and human pathologies. Classification: fibrous proteins and globular proteins. • Fibrous proteins: keratins, silk fibroin, collagen, elastin. Collagen: primary structure, secondary structure (elongated triple helix); summary e post-translational modifications (hydroxylation of prolines and lysine; role of the acid ascorbic; glycosylations; transformation of pro-collagen into collagen; oxidation of lysines and cross-link formation). • Globular proteins and globin chains. Hemoproteins involved in the transport of gases (O2, CO2). Porphyrins and heme group. Structure of myoglobin, hemoglobin and globinic chains. Oxygen saturation curve of hemoglobin and myoglobin. Hemoglobin as an allosteric protein, T and R states. Molecular structure of oxyhemoglobin and deoxyhemoglobin. Bohr effect, cooperativity, the effect of 2,3-DPG. Hemoglobin and regulation of acid-base balance. Methemoglobin reductase, reduced glutathione (GSH) and NADPH for the maintenance of hemoglobin functions. Deficit of G-6 PDH, oxidation of hemoglobin, malaria. Fetal hemoglobin. Molecular bases of hemoglobinopathies and thalassemias. ENZYMES • Classification. Mechanism of action of enzymes and thermodynamics. Coenzymes and vitamins. Thiamine, riboflavin (vitamin B2), pyridoxine, nicotinamide (vitamin PP), pantothenic acid, coenzyme A, biotin, folic acid, retinol, calciferol, ascorbic acid, vitamin B12. • Structure and function of hydrogen transporters: pyridine-nucleotide coenzymes: NAD and NADP, flavin coenzymes: FMN and FAD); ferrosulfoproteins; structure and function of cytochromes. Avitaminosis and related pathologies. • Enzymatic catalysis and regulation. The Michaelis-Menten equation, kinetics parameters: Km, Vmax, Kcat. Reversible and irreversible inhibition. Regulation of enzymatic activity. Inner and external mitochondrial membrane; mitochondrial electron transport chain: potential redox standards of transport chain components of electrons. • High-energy compounds: ATP structure and role in bioenergetics. Relationship between variation of standard free energy and standard oxidation-reduction potential difference. Organization of the electron transport chain in complexes lipoproteins of the internal membrane (complex I-

	II-III-IV) and mobile components (ubiquinone and cytochrome C).; Structure and functions of: Complex I (NADH-ubiquinone oxide reductase), Complex II (succinate-ubiquinone oxide reductase), Complex III (ubiquinol-cytochrome C oxide reductase); Complex IV (cytochrome oxidase). Electron transport inhibitors. Oxidative phosphorylation: mitochondrial ATP synthase (complex V): structure and function. P/O ratio; chemiosmosis coupling hypothesis; respiratory control; decoupling. METABOLIC BIOCHEMISTRY (PART 1) • Introduction to metabolism – general organization. Understanding pathways and metabolic maps. Catabolism and anabolism. • Saccharides of biological importance: glycogen, starch, disaccharides, monosaccharides. Glucose metabolism. Aerobic and anaerobic glycolysis: chemical reactions, enzymes and functional significance. • Origin of lactic acid and lactic dehydrogenase (LDH). Alcoholic fermentation. Energy balance of glycolysis. • Oxidative decarboxylation of pyruvic acid. The tricarboxylic acid cycle or Krebs cycle: reactions and energy balance. Mitochondrial localization of enzymes. • Glycogen synthesis and degradation. Regulation of hepatic and muscular glycogen metabolism. • Gluconeogenesis. Mechanism of action of adrenaline, glucagon and insulin. Metabolism of fructose, lactose and galactose. Pentose phosphate pathway: role of NADPH in metabolism. Malic enzyme and NADP+ reduction. Favism.

Assessment methods

Subject	Assessment methods
Cellular physiology	The assessment of acquired knowledge is carried out through a written exam consisting of 60 true/false questions covering 15 topics from the curriculum. Each correct answer is awarded 1 point, each incorrect answer deducts 1 point, and unanswered questions receive zero points. The minimum passing score for the assessment is 27 out of 60. This score is then converted on a scale of thirty, up to a maximum of 30/30 cum laude (with honors). The final grade is determined by the weighted average of the scores obtained in cellular physiology and biochemistry subjects.
Biochemistry	

Examples of common questions and/or exercises

Subject	Examples of common questions and/or exercises
Cellular physiology	1. They are mostly found in the intracellular compartment: • sodium (True/False) • chloride (True/False)

	• bicarbonate (True/False) • proteins (True/False) 2. The following mechanisms are involved in long-term potentiation: • Phosphorylation of AMPA receptors (True/False) • Activation of CaMKII (True/False) • Activation of the CREB transcription factor (True/False) • Protein neosynthesis (True/False)
Biochemistry	1. Hemoglobin and myoglobin: • Myoglobin has a quaternary structure (True/False) • Saturation curve of hemoglobin is a sigmoid (True/False) • Bohr effect positively modulates oxygen transport (True/False) • Iron is completely oxidized during oxygen transport (True/False) 2. Glucose metabolism: • Glycolysis occurs in the mitochondria (True/False) • Gluconeogenesis requires CO2 (True/False) • Glycogen synthesis is stimulated by insulin (True/False) • Pentose phosphate pathway produces NADH (True/False)

Reference texts

Subject	Textbooks
Cellular physiology	• Kandel ER et al. Principles of Neural Science, The McGraw-Hill Companies, Inc. • Hall, J. E. Guyton and hall textbook of medical physiology. W B Saunders. Any additional educational material (slides, videos, handouts, etc.) will be distributed or indicated during the lessons.
Biochemistry	• Devlin, T. M. Textbook of Biochemistry With Clinical Correlations, John Wiley and Sons. • David L. Nelson; Michael M. Cox. “Lehninger Principles of Biochemistry”, W. H. Freeman & Co. • Voet D, Voet JG, Pratt CW. “Voet's Principles of Biochemistry, Global Edition”, Wiley. Any additional educational material (slides, videos, handouts, etc.) will be distributed or indicated during the lessons.

Course format

Subject	Textbooks
Cellular physiology	The teaching will primarily be conducted through in-person lectures with a blend of theory and practical exercises. In the event that teaching is delivered in a blended or remote mode, necessary adjustments may be introduced compared to what has been previously stated, in order to adhere to the planned program as outlined in the Syllabus.
Biochemistry	

Attendance

Subject	Textbooks
Cellular physiology	Mandatory attendance.
Biochemistry	

Course schedule

Subject	Textbooks
Cellular physiology	Program topics from recommended textbooks and handouts provided by the teachers.
Biochemistry	Program topics from recommended textbooks and handouts provided by the teachers.