HUMANITAS MEDICAL SCHOOL

Course: **BODY AT WORK 2**

Year **2nd (second)**

Period **2ndst semester**

Credits: **13 (Anatomy 1, Physics 1, Biochemistry 3, Physiology 8)**

Objectives

This second part of the *Body at Work* course faces the mechanisms and processes that sustain the survival and proper functioning of the organism. The students will understand the ***neural and endocrine*** regulation of bodily functions; They will learn how substrates and gases are distributed in the organism, by studying the ***heart*** and ***circulatory*** system.). They will know the processes of nutrient absorption and metabolism by the ***digestive system***; the elimination of substances from the body and the regulation of extracellular fluid volume, pH and composition by the ***kidney***; and the exchanges of ***gases at the lung*** and at peripheral tissues. The students will acquire a comprehensive view of the complex interaction of neural, hormonal, visceral, cardiac, renal, hepatic and somatic factors in controlling blood pressure, respiration, extracellular fluid volume, cardiac output and regional distribution of blood, blood pH, glycemia, body temperature and feeding. Finally, they will understand the main functions of the ***central nervous system***, from vegetative control and ***emotional*** responses to the various types of ***memory***, and from pleasure and ***motivation*** to planning, strategical ***control of behaviour*** and consciousness.

Key physical, biochemical and anatomical aspects will be addressed, either in specific lectures or in joint lectures, in a functional and Pathophysiological perspective, to help the student to acquire a comprehensive, interdisciplinary perspective.

The course is organized at three distinct levels:

1. ***knowledge transfer:*** Lectures, slide-sets, written lecture, suggested textbooks, scientific articles and other studying material will offer the students the *notions* needed to master the topics at hand.
2. ***active knowledge mastering*** will be stimulated through self-assessment tests, small-group assignments and didactic material for ***flipped classrooms***
3. ***knowledge activation –*** will be pursued through interactive lectures, joint interdisciplinary seminars, question and answer sessions, discussions of group assignments and the actual flipped classrooms.

The objective of this organization is to lead the student to fully understand, assimilate and frame the acquired notions in an organized general perspective; the student should then be able to clearly and linearly explain the complex issues of the functions of organs and systems and their integration.

Collaborative Learning sessions and integrated lectures on specific Priority Presenting Problems are aimed at promoting meaningful learning: conceptual maps (CMap) are used to organize complex sets of facts into a hierarchy and link information from different domains. Such training in sharing and discussing clinical problems should help the students reach better learning and understanding.

The course also includes PhysioLab experiences to practice with physiological measurements (electrocardiogram, spirometry and electroencephalogram).

Professionalizing activity: two practical activities on the physical examination of the abdomen, thorax and heart are offered during the course. These activities build on the knowledge acquired during previous courses and the anatomical and functional content of this course, and help the students to further proceed in acquiring the basic skills of the general physical examination.

Prerequisites

In order to be able to take the exam the students must have passed the following 1st year exams:

- Building Bodies: from gametes to organs
- Principles of the living matter
- Body architecture
- The Cell: Functions and control.

Apart from the access to the exam, in order to profitably attend the course the students must absolutely have acquired the main concepts of cellular function and regulation, the basis of neurobiology (cell excitability, receptors, transduction mechanisms, synaptic functions, neuronal processing and plasticity), they must know the gross anatomy of the body and the structure of the tissues; they should master the principles of embryology, cellular biochemistry and control of gene expression.

Contents

SPECIFIC LEARNING GOALS

For each module, learning goals will be achieved through activities in class and personal study at home (lectures, readings, off-campus personal and group assignments), while **knowledge activation goals** will be achieved through interactive and collaborative work: problem based learning, joint seminars, question time, revision of assignments, flipped classrooms and supervised small group activity

1 - The endocrine system
Learning goals:

- *Describe the general organization of the endocrine system, the main categories of hormones*
- *Re-examine the main signal transduction pathways and the principles of homeostasis*
- *Know the hormones produced by the hypothalamus and neurohypophysis, and their functions*
- *Discuss the neural control of endocrine function and the effects of hormones on neural systems*
- *Describe the genetic feedback loops that sustain periodic gene expression patterns in SCN neurons (circadian clock) and in peripheral tissue, and the environmental and metabolic factors that "entrain" endogenous clocks*
- *Summarize growth hormone and somatostatin release; describe the effects of GH: dwarfism and gigantism*
- *Classify the main hormones involved in sexual maturation and describe their functions: the menstrual cycle*
- *Understand the regulation of adreno-cortical hormones; describe the metabolic and anti-inflammatory effects of cortisol and how they are produced; understand the features of hyper- and hypo-corticalism*
- *Illustrate the synthesis, storage, release, transport, processing of thyroid hormones (TH), their cellular actions and effects on organs and systems: understand hyper- and hypothyroidism, and goiter*
- *Examine the many hormones that influence glycemia and understand the "rationale" of their actions*
- *Discuss the synthesis, storage, metabolism and metabolic effects of thyroid hormones and corticosteroids*
- *Understand the function of nuclear receptors and their role in lipid metabolism*

2 - The cardiovascular system

Learning goals:

Mechanical activity of the heart

- *Understand the properties of fluids and the principles of fluid-dynamics (pressure, force, flux rate and velocity)*
- *Understand Pascal's principle with reference to flow, Archimedes' principle with reference to fluid density; the law of Laplace and superficial tension (and capillarity)*
- *Explain the concepts of viscosity, laminar flow according to Poiseuille's law and turbulence (Reynolds number)*
- *Discuss flow resistance and compliance of blood vessels and anomalies in blood viscosity*
- *Describe the mechanical events of the cardiac cycle; explain Frank-Starling's law.*
- *Define preload, afterload, isovolumic and isobaric curves; locate these entities on pressure-volume diagrams*
- *Define systolic and cardiac output, and model the cardiocirculatory system to illustrate the roles of central venous pressure, blood pressure, end-diastolic volume, peripheral resistance*
- *Understand the relations among heart volume, pressure and work: the triple product and oxygen consumption*
- *Illustrate the compensatory changes in the face of reduced heart contractility; examine their haemodynamic and energetic costs, and long-term consequences*

Muscle and Heart metabolism

- *Overview the cardiac metabolism, the fuels for the heart and their metabolic fates*
- *Explain cardiac metabolic adaptation to different physiological conditions and hypoxia*
- *Explain the privileged use of fatty acids by the heart and its regulation by insulin.*
- *Describe role and control of lipoprotein lipase and carnitine, and the role of CPK, and its diagnostic value*
- *Describe the mechanisms of heart remodelling, and discuss structure and action of natriuretic peptides*

Electric activity of the heart

- *Describe the cellular bioelectric properties of "slow" and "fast" cells in the heart*
- *Define the absolute, effective and relative refractory and their relevance to action potential propagation*
- *Explain how the action potentials are generated by pacemaker cells and possible anomalies in the process*
- *Describe action potentials propagation to the myocardium and possible anomalies in the process*
- *Understand the principles of extracorporeal electrophysiological recording*

Electrocardiogram

- *Analyse the path of myocardial depolarization and repolarization during the cardiac cycle and the resulting electrocardiographic signal in Einthoven's, unipolar, and thoracic derivations; discuss the cardiac vector*
- *Examine the changes in the ECG in the presence of rhythm disturbances*

Regulation by the autonomic nervous system

- *Describe the determinants of heart rate and contractility, examine how the autonomic nervous system controls heart rate, conduction velocity and contractility, and discuss the haemodynamic changes produced by the ANS*

The circulatory system

- *Distinguish resistance vs. capacitance vessels; define systolic, diastolic, pulse and mean arterial pressure.*
- *Explain the relations among intravascular volume, arterial and venous compliance, peripheral resistance and arterial pressure; explain how the pulse shape changes along the circulatory tree*
- *Analyse the origin of turbulence, the determinants of blood viscosity, and the consequence of he latter*
- *Describe the mechanisms of transcapillary exchange: diffusion, filtration, pinocytosis, "Starling's forces"*
- *Explain how the microcirculation is regulated (locally, directly, indirectly) at the various vascular beds*

Plasma proteins

- *Define plasma, and list its major ions and organic components*
- *Describe similarities and differences among plasma, extracellular and intracellular fluids*
- *List the major plasma components and recognize their functional role*

3 - The digestive system

Learning goals:

GI motility and secretions

- *Describe the mechanical properties of smooth muscle, the motility of oesophagus, stomach, and intestine*
- *Analyse the mechanics of swallowing*
- *Understand the principles of nutrient absorption by the gut*
- *Examine the concerted exocrine secretory activity of stomach, intestine, pancreas and liver*
- *Analyse the many endocrine secretions from the GI system*
- *Discuss the neural and hormonal coordination of GI motility and secretion*

Metabolic functions of the liver

- *Overview the key properties and molecular specialization of the liver and its role in glucose regulation*
- *Describe the role of hepatic lipid metabolism in homeostasis and how its derangement results in a fatty liver*
- *Explain the biochemical and clinical impact of liver diseases*
- *Describe phase I reactions and enzyme induction, explain the role of the microsomal electron transport chain*
- *Explain how phase II reactions proceed and how detoxifying compounds may favour urinary excretion*
- *Describe ethanol absorption, tissue distribution, and metabolism; metabolic interactions among tissues*

Metabolic adaptation to stress / exercise /fasting

- *Describe metabolism of fed state (focus on liver, muscle and adipose tissue)*
- *Describe metabolic adaptations to fasting (focus on liver, muscle, adipose tissue and brain)*

Nutritional biochemistry and dietary interventions

- *Overview dietary macronutrients*
- *Describe the benefits of intermittent fasting on metabolic health and explain how time-restricted feeding prevents obesity*

4 - The kidney and the regulation of plasma and fluid volume and composition

Learning goals:

Body fluids and the principles of renal functioning

- *Examine the distribution of water and electrolytes in the body and analyse kidneys and bladder mechanics*
- *Discuss diffusion vs. filtration mechanisms and understand the concept of clearance*
- *Understand how the kidney selectively disposes of endogenous and exogenous substances*
- *Explain the regulation o of renal circulation and the function of the glomerulus*
- *Explain the general relation between blood pressure and urinary volume*

Glomerular filtration

- *Examine the organization and functioning of the glomerulus and discuss the principles of glomerular filtration*
- *Define glomerular filtration rate, net filtration pressure, ultrafiltration coefficient*

The proximal tubule

- *Describe how the proximal tubule operates to reabsorb precious substance*
- *Examine the contribution of active secretion or reabsorption of a substance in determining its clearance*
- *Explain the use of inulin and para-ammino hyppurate to estimate GFR and effective renal plasma flux*

Henle's loop, distal and collecting tubule

- *Discuss the principle of counter-current flow and counter-current multiplication*
- *Describe regulated sodium reabsorption, bicarbonate production and proton secretion at the distal tubule*

The regulation of sodium & water balance – The kidney & blood pressure – Micturition and thirst

- *Describe the regulated transport of water (and urea) at the collecting tubule and duct*
- *Describe the renin-angiotensin-aldosterone system and its renal and systemic actions*
- *Understand how sodium and water elimination regulate body fluid volume, plasma osmolarity and effectively control blood pressure in the long term: sum up short, middle and long term arterial pressure regulation*
- *Understand the regulation of micturition and the control of thirst*

Acid-base balance and the regulation of body pH

- *Describe the intra- and extracellular pH-buffer systems of the body, and grasp the concept of alkaline reserve*
- *Draw a quantitative picture of overall body intake and elimination of protons*
- *Dissect the roles of proximal and distal tubules in handling bicarbonate and protons*
- *Understand the distinction between plasma pH values and respiratory or metabolic acidosis / alkalosis*

5 – The respiratory system

Learning goals:

Respiratory mechanics

- *Understand the physics of breathing; review the concepts of compliance and resistance in this domain*
- *Define pulmonary "volumes" and "capacities"*
- *Review Laplace's law in its application to the alveolus, and discuss the role of surfactants*
- *Examine pulmonary compliance and pressure-volume curve, and the mechanics of lungs and chest wall*
- *Estimate the work performed by the respiratory muscles; familiarize with spirometry and understand the main functional measurements of respiratory function (explain the phenomenon of expiratory flow limitation)*

Gas exchanges, ventilation / perfusion

- *Examine the differences in gas composition of inspired, alveolar and expired air.*
- *Describe gas exchanges at the alveoli and tissues*
- *Understand the differential ventilation and perfusion of the various parts of the lungs*
- *Explain the relation between respiratory exchange ratio and metabolism*

Control of breathing

- *Describe the neural mechanisms responsible for the generation of the breathing pattern*
- *Discuss the roles of central and peripheral chemoreceptors and ventilatory response to CO_2 and O_2 saturation*

Placental circulation and gas exchanges with the foetus

- *Re-examine the structure of the placenta and discuss the principles of placental circulation*
- *Analyse the exchanges of gas (and other substances) at the placenta, and oxygen balance in the foetus*

PhysioLab: Spirometry

- *Learn to measure respiratory volumes and capacities and to compute the FEV1 index*

6 – Cancer metabolism – Notions about Personalized Medicine and the microbiota

Learning goals:

Cancer metabolism

- *Understand key metabolic properties and the principles of metabolic reprogramming of cancer cells*
- *Understand role and mechanisms of action of oncometabolites, and the principles of One-carbon metabolism*

Personalized medicine

- *Understand principles of personalized medicine and the main technological approaches to it*
- *Understand practical issues and limitations of personalized medicine*

Microbiota and microbiome

- *Understand the principles of microbiota composition and development from birth to adult age*
- *Understand the main metabolic pathways occurring in the microbiota, and host and microbiota cometabolism*

7 – Integrated controls

Learning goals:

The autonomic nervous system (ANS) and the hypothalamus

- *Recall the structure and organization of the autonomic nervous system and describe the actions mediated by the para- and ortho-sympathetic nerves, and by systemically released adrenaline*
- *Understand the balance among heat production, input, and output, in maintaining body core temperature*
- *Discuss the hormones involved in the regulation of feeding behaviour and the integration by the hypothalamus*

Ascending aminergic projections from the brainstem (ARAS)

- *Describe the two main input paths to the cortex: information vs. arousal control*
- *Examine the main aminergic projections from the brainstem to the cortex and their specific roles*
- *Understand the regulation of arousal, cognitive performance, exam of reality and motivational control*

The sleep/waking cycle – Coma and cortical arousal

- *Describe the regulation of the sleep-wake cycle and the role of thalamus and subcortical structures*
- *Discuss the role of cortex-thalamus dialogue in determining the mode of information processing by the cortex*

Limbic circuits, emotions and feelings

- *Describe the circuit of Papez and the structures involved in the limbic circuits*
- *Understand the role of the amygdala, hypothalamus, hippocampus and dopaminergic systems in emotions*
- *Understand the concept of "body marker", its functions and its relation with "feelings"*

The hippocampus: memory and contextualization

- *Classify the various "types" of memory :implicit and explicit memory, associative learning (and not)*
- *Discuss the role of hippocampus and contextualization; discuss memory encoding, recall, consolidation*

Mesencephalic dopamine: pleasure and motivation – Serotonin in the CNS

- *Discuss the motor, behavioural, motivational and plastic functions of dopamine on striatal circuits*
- *Understand the general function of the VTA in pleasure and motivation: the mesocortical-mesolimbic balance*
- *Discuss the multiple roles of serotonergic projections from the raphe*

The Electro-Encephalogram

- *Understand the origin of the EEG signals at the scalp and discuss the spectral decomposition of EEG signals*
- *Learn to read an EEG, recognize the various bands and see how they appear in different mental activities*

Working memory and planning – Primary and extended consciousness

- *Examine the concept of "working memory", the circuits involved in it, and its relation with conscious thought*
- *Examine the neurophysiological basis of "primary consciousness" (here and now)*
- *Discuss neural handling of time and examine the neurophysiological basis of extended consciousness*
- *Examine inherent subjectivity (relational aspects and self-referenced interpretation) of cortical elaboration*

The "external" and the "internal" paths of behavioural control

- *Examine the concept of "affordance" and describe the regulation of behaviour oriented by external clues*
- *Explain the role of basal ganglia in behaviour initiation, choice, conciliation, shifting*
- *Understand the inhibitory and directive function of the supplementary motor area (the "stop-go" paradigm)*
- *Understand the role of the prefrontal cortex in conscious control and endogenously programmed behaviour*

8 – Multidisciplinary workshops

Learning goals:

Understanding the heart through congenital defects (Anatomy / Physiology Joint Lecture)

- *Classify and describe the most important congenital heart defects and reason on the functional impairments*

Integrated workshop on Shock

- *Understand the clinical picture of shock and the mechanisms that may lead to shock*

Integrated workshop on pain

- *Revise the organization of nociceptors, their transduction mechanisms, the transmitters they release*
- *Examine the mutual interaction between nociception and inflammation*
- *Revise the ascending nociceptive paths and descending control path and locate the sites of modulation*

Obesity and metabolic syndromes (a pathophysiological approach):

- *Revise the biochemical and physiological mechanisms related to feeding and energy consumption*
- *Discuss the possible reasons for a gain of weight and difficulty in losing weight*
- *Examine the problems and risks (cardiovascular, metabolic, inflammatory) connected to excessive body weight*
- *Discuss the clinical outcome of relevant weight gain and "the metabolic syndrome"*

Understanding the kidney through the nephrotic and nephritic syndromes

- *Examine the structural, functional, and pathological processes implied in disturbances of glomerular filtration*

Shortness of breath: understanding the respiratory system through COPD

- *Revise and connect anatomical, immunological and physiological features of the respiratory system to the physiopathology of COPD and Asthma*

Integrated workshop on Altered mental status

- *Understand the possible sources of a quantitative or qualitative alteration in mental status*
- *Discuss anatomical, the neurophysiological, pathophysiological, endocrine and metabolic causes*

Integrated workshop on Substance abuse

- *Review the most common drugs of abuse and discuss the basis of compulsive behaviours in general*

Teaching Methods

Lectures, Outlines and Slides – aim at offering the student all needed support to help understanding the information contained in textbooks: students are encouraged to actively participate to the lectures with questions and comments, in order to assimilate the matter being discussed and make it their own.
Indication of readings – aim at offering the student all the needed information and the possibility of critically and autonomously deepening their knowledge
Interactive and multidisciplinary re-elaborations – aimed at involving the students in an active handling of the knowledge material at hand, and showing them the profit of discussion in grasping difficult concepts
Personal and group assignments: quizzes, research assignments, open questions, self-evaluation – aimed at letting the students evaluate their own knowledge and competence and to encourage students toward group work, discussion and confrontation (to improve their capability of explaining)
Flipped classrooms – Question time – Collaborative learning and use of conceptual maps (Cmaps), all oriented to stimulate discussion
Practicals (Neurological examination) – PhysioLab (Electrooculogram, Electromyogram)

Assessment

The exam is comprised of three parts:

1. Evaluation of the skills on the physical examination of the abdomen, thorax and heart
2. Written examination: Multiple Choice Questions or similar tests
3. Oral examination

1. Physical examination: this part of the exam consists in a pass-or- fail evaluation. Students will be asked to perform part of the checklist they have learned during the Practicals. This part or the exam ***must be passed*** to proceed to the written part.

2. Written part: 60 questions of variable kind (multiple choice – only one or more than one possible correct answers, – drag & drop, matching, ordering): 8 for Physics, 20 for Biochemistry, 32 for Physiology-Pathophysiology-Anatomy-PPPportfolio. Time allotted: 90 minutes.

In order to pass the written test, 2/3 of the questions must be answered correctly (40/60); 60% of the correct answers must also be given for each discipline (5/8 Physics, 12/20 Biochemistry, 20/32 Physiology). Occasionally, thresholds might be lowered, in case of anomalous average, best and worst performances. Only students who pass the written test will access the oral examination.

The mark obtained in the written test will be given by the formula { $18 + 0.75 \cdot (\text{correct answers} - 40)$ }. Students who passed the written test do not need to repeat it if they take the oral during the same exam session.

3. The oral exam consists in an interview to assess the overall knowledge on the matter dealt with in the course (Physics, Biochemistry and Anatomy / Physiology / Pathophysiology) and to *verify the competence of the student in* ***explaining*** how the structural aspects, the biophysical and biochemical mechanisms and the physiological processes contribute to the functions of organs and systems in the body and to the integrated control of physiological parameters and behaviour.

Obtaining a successful mark in the written test does not grant success. The mark will be modified (generally by no more than 3 points), based on the performance in the oral interview, also taking into consideration the attendance and active participation to the classes as well as the results of formative tests possibly held during the course.

Since failing this exam implies repeating the second year, an extra-session will be set up in the last days before the beginning of next academic year to give a final opportunity to students who failed all previous sessions. On this exam session only, the students will be given the opportunity of an oral interview even if they failed the written test, to confirm the judgement and discuss their learning performance and possible problems for tutoring. Only students who did attend (and failed) the last session in September will be admitted to this extra session.

Texts

Anatomy, Physics, Biochemistry: refer to 1st year textbooks

Physiology:

Guyton and Hall – Textbook of Medical Physiology, 13th ed. Elsevier, 2016.
W.F. Boron, E.L. Boulpaep – Medical Physiology, 3rd ed. Elsevier, 2017.
E.R. Kandel, J.H. Schwartz et al. – Principles of neural science. McGraw Hill 2013.