UNIVERSITÀ DEGLI STUDI DI MILANO

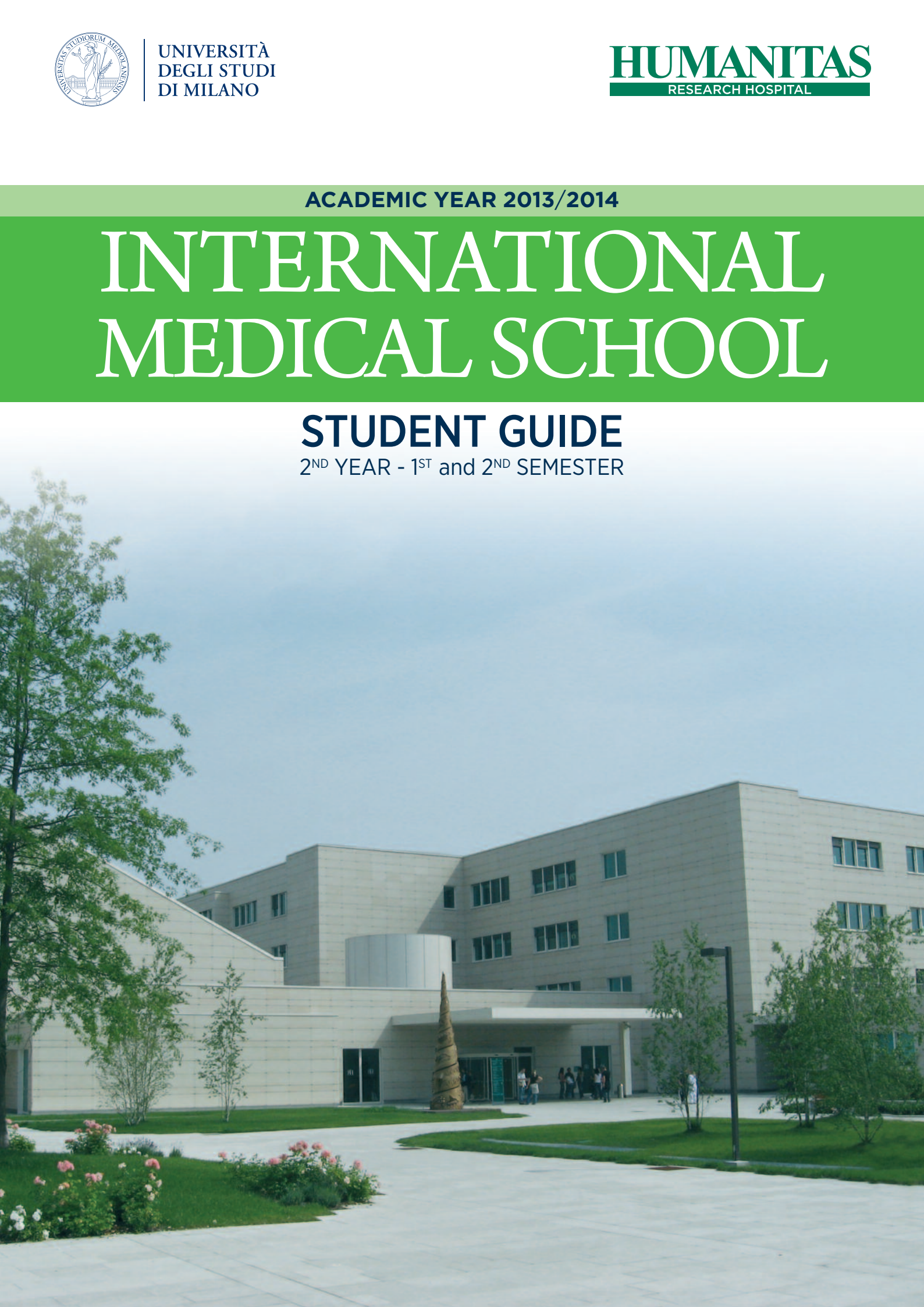
HUMANITAS RESEARCH HOSPITAL

ACADEMIC YEAR 2013/2014

INTERNATIONAL MEDICAL SCHOOL

STUDENT GUIDE

2ND YEAR - 1ST and 2ND SEMESTER



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1. MECHANISMS OF DISEASES – GENERAL OVERVIEW

MECHANISMS OF DISEASES

Professors
Bonecchi, Borghi, Del Bue, Della Bella, Duga, Ferrante, Kallikourdis, Locati, Mantovani, Mavilio

Year/Semester
2nd year (1st and 2nd semester)

Credits
22

Text books
- Cellular and molecular immunology
  7th edition, 2011; Elsevier
- Robbins and Cotran, Pathologic Basis of Diseases
  8th edition, 2009; Elsevier
- Murray, Medical Microbiology
  7th edition, Elsevier

Overview
The course will offer an integrated introduction to causes of cell, tissue and organ injury (general pathology) and the major groups of microbial pathogens that cause human diseases (microbiology), the principal mechanisms of responses to injury and defense (inflammation and immunity), and the general processes of the most relevant causes of human diseases (vascular pathology and oncology).
At the end of the course students will gain understanding of:
- how the body reacts to physical and biological agents to recover homeostasis
- general pathological mechanisms leading to cell injury and death, thrombosis, atherosclerosis, ischemia, infarction, and neoplasia
- molecular and cellular basis for inflammatory disease states
- normal and abnormal functions of the innate and adaptive immune system
- body's immune reactions to infections
- molecular basis for neoplastic diseases

Modules
A – Causes of cell stress/tissue damage and consequences
B - Inflammation and innate immunity
C - Microbiology
D - Adaptive immunity and immunopathology
E - Oncology
F - Vascular pathology
G - Genetic diseases

Teaching methods

lectures, seminars, webinars, small group activities.
Two collections of webinars are made available to the students with free access:

- the Humanitas Lectures Collection is freely available at http://humanitas.axenso.com/ after registration.
- the Henry Stewart Talks Collection is available at http://hstalks.com/main/index_category.php?id=252&.

Independently from the course, students are encouraged to browse these collections and attend on their own lectures of their choice as personal insights into specific arguments of their particular interest.
Some specific lectures have been integrated in the course program and are considered integral part of the course. These lectures will be attended and discussed in class in the presence of a tutor:

- Atherosclerosis is an inflammatory disease

Peter Libby; Harvard Medical School, Boston, USA
Humanitas Lectures Collection (http://humanitas.axenso.com/?p=16)

- Pentraxins: From proteins to drugs by design

Marc Pepys; University College London Medical School, London, UK
Humanitas Lectures Collection (http://humanitas.axenso.com/?p=1033)

- Apoptotic pathways in mammals

Douglas Green; St. Jude Children's Research Hospital, Memphis, USA
Henry Stewart Talks Collection
(http://hstalks.com/main/browse_talk_view.php?t=278&s=278&s_id=12&c=252)

- Oxidative stress and aging

Jose Vina, University of Valencia, Spain
Henry Stewart Talks Collection
(http://hstalks.com/lib.php?t=HST28.1635_1_2&c=252)

Exams

Students' evaluation will be assessed through two multiple choice examinations at the end of each semester (each focused on topics developed during the corresponding semester) and a final oral examination.
Only students who pass the two written exams are eligible for the oral session.
The final score will be assigned on the basis of the final oral examination only.
Intermediate written exams Each of the two written examinations will deal with the topics and activities covered in one semester. The threshold score of each of these multiple choice tests is 75% or better.
Students can takes both the exams in a single session or in separate sessions with no mandatory order.
Final oral exams During the final exams, the students will be challenged to apply the concepts acquired during the course on pathological or clinical problems.
Registration to final exams through SIFA is mandatory for each session.

2. MECHANISMS OF DISEASES – 1ST SEMESTER

Lessons from October, 1st to December, 12th
Two multiple choice tests in January and February

Modules

0 – Introduction to the course
A - Causes of cell stress/tissue damage and consequences
B - Inflammation and innate immunity
C - Microbiology

Introduction to Mechanisms Of Diseases and its organization

1. Introduction to the course (all teachers)

2. Overview of the inflammatory response (Mantovani)

3. Overview of the adaptive immunity (Locati)

4. Introduction to microbiology (Ferrante)

5. General properties of prokaryotic organisms (Borghi)
   Bacterial structure, function, and classification
   The protective and teaching role of the normal microbiome
   Bacterial genetics
6. Introduction to oncology (Della Bella)

Module A - Causes of cell stress/tissue damage and consequences

Content of this part of the course will be acquired by the student through personal activity.
For content refer to Chapter 1 of Robbins and Cotran, Pathologic Basis of Diseases.

Module B - Inflammation and innate immunity

1. Hematopoiesis (Bonecchi)
   - The hematopoietic niche
   - The hematopoietic stem cell
   - Hematopoietic lineages
   - Cytokines and growth factors

2. The acute inflammatory response (Bonecchi)
   - Biological and physical barriers of innate immunity
   - Cardinal signs of (acute) inflammation
   - Vascular and cellular reaction
   - Mechanisms of increased vascular permeability

3. Virulence factors that trigger pathology (Borghi)

4. Cells of the innate immune system: neutrophils (Bonecchi)

5. Cells of the innate immune system: macrophages (Mantovani)

6. Cells of the innate immune system: NK cells (Mavilio)

7. Primary inflammatory cytokines (Mantovani)

8. Soluble mediators of inflammation (Bonecchi)
    - Circulating mediators
    - Cell-derived mediators
    - Notes on complement cascade

9. Chemokines and leukocyte recruitment (Bonecchi)
    - Cell adhesion and migration
    - Adhesion molecules and chemoattractants

10. Pathogen recognition (Bonecchi & Borghi)
    - Pathogen-Associated Molecular Patterns
    - Structure and signalling properties of Pattern Recognition Receptors
    - Structure and signalling properties of opsonic receptors
    - Pentraxins (HL from Marc Pepys)

11. Exudate and pyogenic bacteria (Borghi)
    - Introduction to streptococci, staphylococci and neisseriae
    - Primary agents of acute inflammatory respiratory tract infections
    - Primary agents of acute inflammatory CNS infections
    - Primary agents of acute inflammatory genito-urinary tract infections

12. Toxigenic bacteria (Borghi)
    - Etiological agents of toxin-mediated infections
    - Spore-forming bacteria

13. Pathogen killing (Bonecchi)
    - Opsonization, phagocytosis and degranulation
    - Oxygen-dependent mechanisms
    - Oxygen-independent mechanisms
    - Mechanisms of cell cytotoxicity

14. Exudate and pathogenic bacteria (Borghi)

15. Resolution of the inflammatory response (Locati)
    - Negative regulators of the inflammatory response
    - The inflammatory response as a genetic program
    - The hypothalamic-pituitary-adrenal axis
    - Anti-inflammatory cytokines
    - Anti-inflammatory eicosanoids

16. Chronic inflammation, fibrosis and tissue renewal (Mantovani)

- Causes, cellular and molecular effectors
- Polarization of the immune response
- Fibrosis and sclerosis
- Stem cells and tissue renewal
- Growth factors and tissue regeneration

17. Granulomatous infections (Borghi and Mantovani)
    - Granulomata reactions
    - Mycobacteria
    - Fungi

18. Acute phase reaction and systemic inflammation (Mantovani)
    - Fever
    - Leukocytosis
    - Acute phase protein production in liver
    - Septic shock

Module C – Microbiology

1. Fungal structure, function, and pathogenesis (Borghi)
    - The eukaryotic nature of fungi and their classification
    - The opportunistic relationship with humans

2. Viruses: introduction, morphology and classification (Ferrante)
    - Definition of structures of the virus particles and to describe the classification of the human viruses, based on their genome organization and their morphology

3. Viruses: replication and pathogenesis (Ferrante)

4. RNA positive viruses: picornaviruses (Ferrante)
    - Definition of structures, genome organization, and replication properties of the RNA viruses associated to human diseases (picornaviridae, flaviviridae, togaviridae, orthomixoviridae, paramixoviridae, filoviridae, rhabdoviridae, bunyaviridae)

5. RNA positive viruses: flaviviridae, togaviridae (Ferrante)

6. Viral hepatitis: HAV, HBV, HDV (Ferrante)

7. Viral hepatitis: HCV, HEV, HGV (Ferrante)

8. RNA negative viruses: hortomixoviridae, paramixoviridae (Ferrante)

9. Other RNA viruses: filoviridae, arenaviridae

10. Retroviruses: human immunodeficiency viruses (Ferrante)

- Definition of structures, genome organization, the replication properties of the human viruses belonging to the retroviridae family and retroviruses associated with human diseases

11. Deltaretrovirus, retroids, prions (Ferrante)

12. DNA viruses: herpesviridae, parvoviridae (Ferrante)

13. DNA viruses: papillomaviridae, polyomaviridae (Ferrante)

Small group activities

The functional consequences of point mutations (Duga)

This activity will be developed in the computer room, with the following objectives:

- Understand how nucleotide variations impact on RNA metabolism and on protein structure and function
- Critically evaluate the consequences of a nucleotide substitution in a DNA sequence
- Visualize a protein 3D structure by the Swiss-Pdb viewer software and to predict the possible consequences of a missense mutations in a protein structure
- Analysis of nucleotide sequence and of the functional consequences of point mutations

Seminars

The stem cell (Vezzoni)

- Define a stem cell and the concept of pluripotency
- Define main properties of embryonic and adult stem cells
- The hematopoietic stem cell as a paradigm of adult stem cells
- Reprogrammed cells and induced pluripotency
- Somatic cell reprogramming by nuclear transfer (“therapeutic cloning”)

3. MECHANISMS OF DISEASES 2ND SEMESTER

Lessons from March, 1st to May, 24th
Two multiple choice tests in June and July

Modules

D - Adaptive immunity and immunopathology
E - Oncology
F - Vascular pathology
G – Genetic diseases

Module D – Adaptive immunity and immunopathology

1. Overview of the adaptive immune system (Locati)
    - Features of acquired immune response: specificity, memory, tolerance
    - Primary and secondary lymphoid tissues
    - Lymphatic vessels

2. Antigen processing and presentation (Locati)
    - Antigen structure and processing
    - Thymus-dependent and thymus-independent antigens
    - MHC-I and MHC-II loci organization
    - Structure and function of Major Histocompatibility Complex class I and II
    - Superantigens
    - Antigen presenting cells

3. T cells development and functions (Locati)
    - Intrathymic development
    - TCR structure and repertoire generation
    - The TCR/CD3 signalling complex and signal transduction pathways
    - Costimulatory molecules
    - Cytotoxic T lymphocytes

4. B cells development and functions (Locati)
    - Generation of B cell repertoire and selection
    - Antibody classes: structure and functions
    - Isotype switch
    - Antibody classes in primary and secondary immune responses

5. The complement system (Locati)
    - Activation pathways
    - Functions and regulation

6. Central and peripheral tolerance (Locati)
    - Positive and negative selection of T lymphocytes
    - Peripheral tolerance

7. Immune response polarization (Locati)
    - Type 1 and type 2 immune rsponses
    - New types of polarizing T cells

8. Immune response memory (Locati)
    - Vaccines and their development

9. Negative regulators of the immune response (Kallikourdis)
    - Regulatory T cells
    - Myeloid regulatory cells

10. Immune response to viruses (Locati)
    - Strategies for viral entry, evasion of the immune system, and subversion of host-cell machinery

11. Immune response to intracellular pathogens (Locati)
    - Strategies for microbial evasion of the immune system and subversion of host-cell machinery

12. Immune response to extracellular bacteria (Locati)
    - Strategies for microbial evasion of the immune system and subversion of host-cell machinery

13. Hypersensitivity reactions (Locati)
    - Immediate ipersensitivity
    - Antibody-mediated hypersensitivity reactions
    - Delayed-type hypersensitivity

14. Autoimmunity (Kallikourdis & Della Bella)
    - Failure mechanisms of the central and peripheral tolerance

15. Congenital immunodeficiencies (Mavilio)

16. Acquired immunodeficiencies (Mavilio)
    - Iatrogenic immunodeficiencies
    - HIV

Module E – Oncology

1. Introduction to tumors (Della Bella)
    - Definition
    - Epidemiology
    - Tumor nomenclature
    - TNM classification

2. Distinctive features of benign, precancerous and malignant growth (Della Bella)
    - Differentiation and cell grading
    - Rate of growth
    - Local invasion
    - Metastasis, pathways of spread

3. Metabolic derangements in cancer cells (Riboni)
    - Describe tumor microenvironment in selection for altered metabolism
    - Discuss tumor sensing and adaptations to hypoxia and nutrient deprivation
    - Describe oncogene activation and hypoxia-inducible factor in cancer metabolic changes
    - Discuss cancer metabolic alterations
    - Compare advantages and liabilities of tumor cell metabolism

4. Molecular basis of cancer: oncogenes and oncosuppressors (Della Bella)
    - Proto-oncogenes and oncogenes
    - Functional properties of oncogenes
    - Oncogene products
    - Mutations affecting oncosuppressor genes
    - Functional properties of oncosuppressor genes
    - Genomic instability and tumor progression

5. Carcinogenesis: physical and chemical agents (Della Bella & Corti)
    - Describe UV and ionizing radiations
    - Chemical carcinogenesis: compare initiation, promotion and progression
    - Dexcribe metabolic activation of chemical compounds in vivo
    - Describe factors that control chemical carcinogenesis
    - Discuss genotoxic and non-genotoxic effects of carcinogens

6. Carcinogenesis: infective agents (Della Bella & Ferrante)
    - Describe oncogenic DNA and RNA viruses
    - Discuss genetic mechanisms underlying the oncogenic process
    - Discuss host interaction with oncogenic viruses
    - Discuss pathogenic role of viruses into the oncogenic process
    - Analyze the role of bacteria into the oncogenic process: Helicobacter pylori case

7. The host response: immune responses to cancer (Della Bella)
    - Discuss the immunosurveillance hypothesis
    - Describe lessons from the animal models: TSTA antigens
    - Discuss tumor-specific and tumor-associated antigens
    - Compare defensive mechanisms against tumors
    - Compare mechanisms of immune evasion

8. Metabolic changes in patients with tumors (Della Bella & Riboni)
    - Neoplastic cachexia
        - Discuss clinical characteristics

  - Describe tumor factors contributing to cancer cachexia
  - Analyze metabolic changes induced by cancer and leading to cachexia
- Analyze paraneoplastic syndromes

9. Angiogenesis (Bonecchi)
   - Multipotent endothelial cells
   - Angiogenesis and vasculogenesis
   - Angiogenetic cytokines and their receptors

10. The host response: adaptive immunity (Della Bella)

11. The host response: inflammation and cancer (Mantovani)

12. The host response: tumor angiogenesis (Della Bella & Bonecchi)
    - Compare critical role of angiogenesis to tumor survival and growth
    - Discuss the contribution of TAM and tumor microenvironment
    - Analyze soluble angiogenic factors and chemokines
    - Describe endothelial progenitor cells and other bone-marrow-derived cell populations

Module F - Vascular pathology

1. Thrombotic diseases (Bonecchi)
   - Thrombus formation and evolution
   - Clinical manifestations

2. Hemostasis and coagulation (Bonecchi)
   - Platelets
   - Primary and secondary emostasis
   - Coagulation cascate
   - Fibrinolitic system

3. Bleeding disorders (Bonecchi)
   - Vessel alterations
   - Platelet alterations
   - Coagulation system alterations
   - Clinical manifestations

4. Atherosclerosis (Bonecchi)
   - Mechanisms of plaque generation
   - Risk factors
   - Complications
   - Clinical manifestations
   - Atherosclerosis (HL from Peter Libby)

Module G – Genetic diseases

Content of this part of the course will be acquired by the student through personal activity.

For content refer to Chapter 5 of Robbins and Cotran, Pathologic Basis of Diseases.

4. FUNCTIONS

FUNCTIONS

Professors
Barajon, Cerri,Cerbino, Riboni, Pecchiari

Year/Semester:
2nd year (1st and 2nd semester)

Credits: 29

Overview
The course focuses on the mechanisms of body functions from cell to system and is organised around the central theme of homeostasis, i.e. how the body maintains the constancy of the internal environment needed for all cells and organs to function properly despite continuously changing external and internal demands. In order to accomplish this goal the course integrates different disciplines including Physiology, Neuro-anatomy, Biochemistry and Physics providing the students the view of the complex interplay between macro- and micro functional levels acting in life processes.
The course is designed to highlight the integration between the different functional systems of the human body. To this aim, lectures or groups of lectures devoted to one specific topic, will conclude with the "*Focus on Homeostasis*", helping the students to put in perspective how the functions related to the part of the body just discussed contribute to the homeostasis and, whenever possible, with "*Clinical Point*", i.e. clinical examples illustrating the pathological effects of the disarrangement of a physiological function. During the course, the message of the lectures will be reinforced and expanded by *Practical Activities* and *Seminars.*
The course is designed in 2 blocks. The first block will focus on the mechanisms adopted by the human body to maintain the homeostasis. The second block will address the structure and function, in body's homeostasis, of cardiovascular, respiratory, renal, and digestive systems, liver and adipose tissue.

Exams

Students' evaluation will be assessed through two multiple choice examinations at the end of each semester (each focused on topic developed during the corresponding semester) and a final oral examination.
Only students who pass the two written exams are eligible for the oral session.
The final score will be assigned on the basis of the final oral examination only.

Intermediate written exams Each of the two written examinations will deal with the topics and activities covered in one semester (lectures, labs and assigned

readings). The threshold score of each of these multiple choice tests is 75% or better.
Students can takes both the exams in a single session or in separate sessions with no mandatory order.

Final oral exams During the final exams, the students will be challenged to apply the concepts acquired during the course on physiological or clinical problems.

Registration to final exams through SIFA is mandatory for each session.

5. FUNCTIONS 1ST SEMESTER

Functions Part I

Description:
The first part of the course is devoted to understand the mechanisms adopted by the human body in order to perceive and adapt to the challenges induced by the interactions with the external environment. To this aim lectures will be focused on the nervous and the endocrine systems illustrating, in details, how these constantly interacting systems coordinate and regulate tissue and organs functions, in order to build up adaptation responses, from the most simple and involuntary reflex reactions to the most complex and behavioural motivational and emotional responses. In order to optimize the interdisciplinary integration some of the topic will be presented with interdisciplinary lecture involving more then one discipline.

Block 1 will include 52 (6 physics, 25 neurophysiology, 9 neuro-anatomy and 7 biochemistry, 4 multidisciplinary) lectures, 3 seminars and 7 practical activities.

CONCEPT OF HOMEOSTASIS

Lecture n1- P Internal environment and the cell: maintenance of the homeostasis.

Objectives:
Recall the general concept of homeostasis.
Describe interrelationships between external and internal environment.
Define essential homeostatic parameters.
Describe the homeostatic circuit: sensory input -integrative centre- efferent action at different levels of complexity.
Describe the two main monitoring systems and the general principles of control responses: neural and endocrine systems.

Lecture n2- Phy Electricity I: Charges, Forces and Fields

Objectives:
Describe the charge and forces between charges (Coulomb's law).
Define electric dipoles and charge distributions
Describe conductors and insulators
Define the electric field

Lecture n3- Phy Electricity II: Energy, potential and currents

Objectives:
Define the electric potential energy and the electric potential
Define capacitors and their use to model membranes
Describe currents and the resistance of conductors (Ohm's law)
Define the magnetic field and its basic properties (Ampere's law, Lorentz force, Faraday's law)
Desribe em waves

NERVOUS SYSTEM: A WIRED SYSTEM

Lecture n4- Phy Bioelectricity

Objectives:
Explain the electrical model of axons

Define the typical amplitude of bioelectric signals
Explain how to electrically map the human body: EMG, EEG, ECG

Lecture n5- B The ins and outs of ions in the nervous system.
Objectives:
Describe properties and types of ion channels and active transporters in neurons.
Explain how ion channels are controlled.
Outline the role of trans-membrane ion movements in electrical excitability, signal propagation, and neurotransmission.
Describe myelin composition and structure, and explain the role of myelin lipids and proteins.
Describe the channel distribution in the different compartments of a myelinated axon.
Focus on homeostasis
Clinical point
Neurotoxins acting on ion channels

Lecture n6- P Electrical signalling in the excitable cells I.
Objectives:
Describe ion movements across the membrane of excitable cells: Na^+, K^+, Ca^{++}, Cl^- ion channels, the electrochemical gradient and the equilibrium potential of different ions.
Describe the resting membrane potential: ions and currents.
Describe the contribution of each of the different ions and of the Na^+/K^+ ATP transport in establishing and maintaining the resting membrane potential.
The Clinical Point
Ions disorders: altered neuromuscular excitability

Lecture n7- P Electrical signalling in the excitable cells II.
Objectives:
Define the depolarizing and hyperpolarizing currents.
Describe the passive responses of the plasma membrane: the local sub-threshold responses and the electrotonic conduction.
Describe the active responses of the plasma membrane: the action potential. Time course, ion fluxes underlying action potential and its conduction along the axon.
Describe the transduction mechanisms: the receptor potential, tonic and phasic receptors.
Focus on homeostasis
The Clinical Point
Alteration of nerve conduction

Lecture n8- B Neurotransmitters: special molecules in the nervous system.
Objectives:
Define neurotransmitters and describe differences and similarities with hormones.
Describe the different types of excitatory and inhibitory neurotransmitters.
Recognize the key role of amino acids in neurotransmitter synthesis.
Describe the key steps of neurotransmitter metabolism and their regulation.
Describe neurotransmitter receptors, their types and action mechanisms.
Focus on homeostasis
Clinical point
Botulism

Lecture n9- P Neuronal target actions: neural integration; contraction; secretion.

Objectives:

Describe the Electric synapse: gap junctions, ion currents, synaptic modulation and bi-directionality.

Describe the Chemical synapse: role of the action potential in the neurotransmitter release.

Describe how the chemical binding to post synaptic receptors triggers the post synaptic changes in membrane potentials giving rise to the "excitatory" and "inhibitory" responses.

Describe the synaptic integration, the current-to-frequency coding and the mechanisms underlying the modulation of the synaptic gain .

List the different neuronal target actions by means of synapsis: neuronal communication, contraction and secretion

Focus on homeostasis

The Clinical Point

Neurotransmitters hypothesis of depression

Lecture n10- P Electrical signalling: is it exclusive language of the nervous system?

Objectives:

Describe the events across the neuromuscular junction, the end plate potential, the striate muscle action potential and the current-to-frequency coding.

Describe the smooth muscle action potential and the functional syncytia.

Describe the heart action potentials: ion fluxes underlying pace maker and contractile cells action potential; the spread of cardiac excitation.

Focus on homeostasis

The Clinical Point

Myasthenia Gravis

ENDOCRINE SYSTEM: A WIRELESS SYSTEM

Lecture n11- P Chemical signalling: endocrine glands, the metabolic chemical controllers.

Objectives:

Recall the chemical classification of hormones, the functional properties of steroid and peptidic hormones.

Classify hormones dependent and independent from hypophyseal control

List the anterior pituitary trophic hormones.

Describe the individual functions of the endocrine glands under the hypophyseal control: focus on thyroid gland and adrenal gland.

Describe the individual functions the endocrine glands outside the hypophyseal control.

Examples of integrated responses.

Focus on homeostasis

The Clinical Point

Goiter

DO ENDOCRINE AND NERVOUS SYSTEM INTERACT WITH EACH OTHER?

Lecture n12- P Hypotalamus-hypophysis axis: master and commander.

Objectives:

Describe the Hypothalamus and Posterior Pituitary gland as a neuroendocrine unit.

Describe the Hypothalamus and Anterior Pituitary gland as a functional unit: the hypothalamus-hypophyseal portal system.
List the Hypothalamic releasing and inhibiting hormones acting on the anterior pituitary gland.
Describe mechanism underlying control of hormonal secretion.
Describe the time course of hormone secretion: pulsatile vs episodic secretion.
Compare the action of the nervous and endocrine system in controlling body functions.
Focus on homeostasis
The Clinical Point
Pituitary Adenoma

BUILDING UP ADAPTATION RESPONSE: ENVIRONMENTAL PERCEPTION. WHAT'S GOING ON OUT THERE? WHERE CAN I FIND FOOD? ARE YOU A FRIEND OR AN ENEMY?

SOMATOSENSORY INTERACTION WITH THE EXTERNAL ENVIRONMENT
Lecture n13-B The skin: our boundary and brain on the outside
Objectives:
Describe the stages and molecular mechanisms of skin cell differentiation
Illustrate the properties of the vital barrier function of the skin
Describe molecules and functional properties of the cornified envelope
Explain the mechanisms of the epidermal strength and skin permeability
Describe the molecular pathways of skin pigmentation and their control
Describe the structure and function of dermal proteins
Describe the skin role in temperature regulation
Describe the detection of different incoming stimuli by skin receptors and skin interrelationships with other organs/tissues
Focus on homeostasis
Clinical point:
Photoaging

Lecture n14-A Sensory receptors, sensory modalities, and sensory pathways: man in energyland.
Objectives:
Describe the general features of afferent (sensory) pathways.
Classify sensory modalities.
Classify sensory fibers.
Illustrate the structure and location of sensory receptors in relation to the transduction of different forms of energy.
Illustrate the location of sensory ganglia and describe primary sensory neurons.
Describe the medial division and the lateral division of the dorsal root as the origin of ascending pathways in the spinal cord: the conscious and non conscious pathways.
The Clinical Point:
The axon reflex and neurogenic inflammation

Lecture n15-A Ascending pathways : to feel or not to feel?
Objectives:
Describe the pathways of the anterolateral system: pain, touch and temperature.
Describe the dorsal column pathway: conscious proprioception and discriminative touch.

Describe the trigeminal pathway: information from the head.
Describe the pathways to the cerebellum: the non conscious pathways of somatosensory information.
Describe the routes of visceral information.
Clinical Point:
sensory loss

Lecture n16-A Thalamus and Somatosensory cortex: beam me up, Scotty.
Objectives:
Classify the thalamic nuclei in relation to their target.
Localize primary and secondary somatosensory areas.
Describe the structure of the somatosensory cortex.
The Clinical Point
Central pain syndrome

Lecture n17-P Coding sensory information: sensing the difference!
Objectives:
Define the sense of touch.
Describe the receptive field, the functional and adaptation properties of mechanoreceptors in the skin.
Define the processing of afferents through the dorsal column system to the sensory cortices.
Describe the cell properties and the functional organization of the primary sensory cortex.
Describe the mechanisms underlying the ability of coding of spatial characteristic of objects.
Describe the main psicophysical laws.
Focus on homeostasis
The Clinical Point
The Phantom Limb

Practical activities
Electrical nerve stimulation and Electroneurography
2 hours x 4 (groups 10 students)

Lecture n18-P Coding sensory information: danger area: stay alert!
Objectives:
Describe the functional and adaptation properties of the thermal warm and cold receptors.
Define the processing of thermal afferents through the anterolateral system to the sensory cortices.
Describe the functional properties of the specific, polymodal and silent nociceptors.
Define the mechanisms underlying Pain: acute vs slow pain, afferents processing in the dorsal horn and mechanisms underlying sensitization and hyperalgesia.
Describe the major ascending pathways mediating specific and diffuse pain, autonomic, endocrinal and emotional reactions.
Describe the non-opioid and opioid central mechanisms controlling pain.
Focus on homeostasis

The Clinical Point
Referred pain: the heart attack

Practical activities
Somatosensory perception
2 hours x 2 (groups 20 students)

SENSING THE INTERNAL ENVIRONMENT:
Lecture n20-P The body's knowledge of itself: the seventh sense.
Objectives:
Define proprioception: limb position sense and kinaesthesia.
Describe functional and adaptation properties of joint receptors and the central coding of the angular excursion.
Describe Muscle spindles structure: afferent and efferent innervations; functional and adaptation properties.
Describe functional and adaptation properties of the Golgi tendon organs and their afferent innervations.
Define the role of the skin receptors as proprioreceptors.
Define the functional processing of proprioceptive information through ascending systems and the body schema representation in parietal cortex
Describe the properties of the mechanoreceptors and chemosensory receptors innervating viscera and modalities of visceral perception.
Focus on homeostasis
The Clinical Point
Sacks' syndrome: the disembodied woman

THE WORLD THROUGH OUR SPECIAL SENSES
Lecture n20- Phy Sound waves
Objectives:
Define wave pulses, periodic waves, sinusoidal waves
Define wavelength, amplitude, phase, velocity, frequency, polarization
Explain the basics of sound waves (speed of sound, intensity and other properties)
Standing sound waves

Lecture n21-A Special senses: hearing. If a tree falls into a forest, does it make a sound?
Objectives:
Give and overview of the three compartments of the ear: external, middle and inner.
Describe the component of the middle ear relevant to sound transduction.
Describe the acoustic labyrinth: the cochlea
Describe the acoustic pathway.
The Clinical Point:
conductive hearing loss

Lecture n22-P and Phy Sounds familiar…or not?
Objectives:
Describe the functional role of the middle ear: amplification of sound and muscular reflexes.
Describe the functional role of the inner ear: 1) Detecting sound waves. 2) The ear as a spectrum analyser. 3) Auditory response
Describe the coclear mechano-electrical transduction

Describe the neural processing of auditory input.
Memory for sounds.
Focus on homeostasis
The Clinical Point
Tinnitus

Lecture n23- Phy Lenses: focusing and imaging
Objectives
Explain refraction, reflection and transmission
Describe lenses, image formation and magnification
Describe the eye as a compound lens

Lecture n24-A and P Special Senses: the eye. How the brain pictures the world.
Objectives:
Describe the organization of the eyeball: layers, chambers, dioptric devices
Extraocular muscles.
Describe the lens of the eye, accommodation and common vision disorders.
Illustrate the inversion of the visual field in the retinal image.
The Clinical Point:
Pupillary and corneal Reflexes

Lecture n25- A,B,P, PHY The world upside-down: the eye and the brain.
Objectives:
Describe the organization of the retina: a piece of brain in the periphery.
Describe the different types of photoreceptors and their biochemical properties.
Describe the role and metabolism of vitamin A in vision.
Describe the molecular mechanism of vision and differences between rods and cones.
Define the role of rods and cones in the foveal and peripheral retina.
Describe mechanisms underlying dark and light adaptation.
Describe functional properties of the ganglion and bipolar cells: the center-surround organization of receptive fields.
Explain the eye as the "perfect" performance-limited detector : the retina and its "pixels"
Describe the effects of the wave nature of light on vision: diffraction and aberrations
Describe the effects of the particle nature of light on vision: counting single photons
The Clinical Point
Optic neuritis

Lecture n26-A Pathways from the retina: the optic pathways. Man as a visual creature.
Objectives:
Describe the course of the optic nerve.
Describe the optic chiasm and its surrounding.
Describe the medial and lateral component of the optic tract.
Describe the pathway of the lateral optic tract to the visual cortex: lateral geniculate body and optic radiation.
Describe the visual cortex.
The Clinical Point:
In a long travel many things can go wrong

Lecture n27-P What's wrong in this picture?
Objectives:
Describe the neural processing of visual inputs: functional models in primary visual cortex.
Describe the "computational" differences between the foveal and the peripheral vision: do we use information coming from the different part of the retina in different ways?
Overview of transcortical pathways fed by visual cortex: visuomotor transformation and objects-face and space recognition.
Illustrate the mechanisms underlying the colour vision.
Focus on homeostasis
The Clinical Point
colour blindness

Practical activities
Special senses II: vision
2 hours all students

Lecture n28-A Special senses: position sense. Where is my head?
Objectives:
Describe the vestibular labyrinth.
Describe the vestibular pathways.
Describe the medial longitudinal fasciculus.
The Clinical Point:
vertigo

Lecture n29- P Spinning around.. jumping...on the lift: thank you vestibular system!
Objectives:
Describe the receptors in the vestibular labyrinth: functional properties in mechano-electrical transduction.
Describe movements eliciting complex pattern of vestibular stimulation: the macular system
Describe movements eliciting complex pattern of vestibular stimulation: the semicircular canals system
The neural processing of vestibular inputs feeding the body schema
Premises for the functional interaction with cerebellum and spinal cord.
Focus on homeostasis
The Clinical Point
Ménière's desease

Lecture n30- P Look around
Objectives:
Define the two main mechanisms of gaze control: the mechanisms for gaze stabilization and the mechanisms for gaze shifting.
Describe the gaze stabilization mechanisms: the vestibulo-ocular system and the optocinetc system
Describe the gaze shifting mechanisms: the saccadic system and the smooth pursuit system
Describe the Vergence movements and the Hering's law of equal innervation
Focus on homeostasis

The Clinical Point
The lesion of the III cranial nerve

Lecture n31-A,B and P Perceiving the environment: the mechanisms of olfaction and taste.
Objectives:
Neuroanatony of taste and olfaction
Explain how chemical stimuli are perceived and transformed.
Describe olfactory receptors and associated signalling mechanisms.
Describe molecular mechanisms for detection and transduction of taste and connections between taste cells and gustatory fibers.
Describe regulatory mechanisms of taste information at peripheral taste organs
Describe the processing of afferent information form taste and olfactory receptors in the central olfactory and taste pathways
Describe the functional interaction between taste and olfactory pathway in perception.
Insular lobe: a multisensory cortex.
Focus on homeostasis
Clinical point:
Insular lobe seizures

Practical activities
Special senses I: Taste-olfaction-acustic-vestibular
2 hours x 2 (groups 20 students)

BUILDING UP ADAPTATION RESPONSE: HUMAN ACTION IN THE ENVIRONMENT
HUMAN MOTION: THE MUSCLE AND FORCE RECRUITMENT
Lecture n32- B Motors and energy in the skeletal muscle.
Objectives:
Delineate structure and, properties of molecular motors and associated proteins, and explain their interactions.
Describe neuronal signals to skeletal muscle and the sliding filament model of muscle contraction.
Integrate skeletal muscle contraction and metabolism, and explain their coordinated regulation.
Describe the role of myoglobin, phosphocreatine and glycogen during exercise.
Describe metabolic integrations in aerobic and anaerobic exercise.
Explain the role of muscle proteins in glucose homeostasis.
Focus on homeostasis:
Clinical point:
Muscular dystrophies

Lecture n33-P Muscle mechanics: the isometric force-length diagram.
Objectives:
Describe the experimental approach to the study of the mechanical properties of the skeletal muscle: from the anatomical organization of the parts of the skeletal muscle to its biomechanical model.
Describe the functional behaviour of the muscle during relaxation and contraction (total, active and passive force) in isometric condition.

Lecture n34-P Muscle mechanics: the isotonic force-velocity diagram.

Objectives:

Describe the modalities of skeletal muscle activation in experimental conditions and in situ: twitch, incomplete and complete tetanus and their relations with the active state.

Describe the functional behaviour of the skeletal muscle in dynamical condition. Velocity of skeletal muscle shortening and lengthening as a function of the load.

Explain the skeletal muscle as a motor and as a brake.

Lecture n35-P Moving eyes and building houses: different force requests.

Objectives:

Define the Motor Unit: innervation ratio in different muscles.

Define the three types of motor units and based on the functional properties of different muscular fibres.

Describe the motoneurones properties: synaptic current to frequency coding; the rate match.

Describe the neural mechanisms controlling muscular force: recruitment order of motor units, the size principle and tetanic activation.

Outline the role of agonist and antagonist muscles at joint level, the coordinated work of different muscles on skeletal joints and the role of muscles in determining joint stiffness.

Focus on homeostasis

The Clinical Point

Lou Gehrig's disease

BUILDING UP ADAPTATION RESPONSES: FROM REFLEX TO BEHAVIOUR

1. SIMPLE ACTION-INTERACTIONS REFLEX AND LOCOMOTION

Lecture n36-P The hierarchical motor system and the "independent" spinal cord. Reflexes

Objectives:

Illustrate the hierarchical organization of motor system.

Define the reflex arc components: and outline the somatic and visceral reflexes in the spinal cord/brain stem.

Describe: the main spinal reflexes in adults and in neonates.

Focus on homeostasis

The Clinical Point

Spinal cord injury

LOCOMOTION THE NERVOUS SYSTEM DRIVES A COMPLEX MACHINE

Lecture n37-P Let's go for a walk

Define Spinal automatism: general neural network underlying automatic functions.

Describe phases of human locomotion: sequence of muscle contraction required for stepping.

Describe the spinal rhythm generating system, the neural control of locomotion and the processes active in learning locomotion.

Lecture n38- Phy Elastic properties of biomaterials

Define (tensional and compressional) stress and strain
Define elasticity and Young's modulus
Explain the Hooke's law
Explain the energy storage in elastic materials such tendons and bones
Define plasticity, fracture, ductility and brittleness of materials.
Define bending, shear and torsion

Lecture n39- B Strengthening and shaping the human body: connective tissues.
Objectives:
Describe the molecular composition of connective tissue extracellular matrix and its interactions with cells
Describe collagen biosynthesis, assembly and factor requirement
Explain how collagen fibrils interact to form macro-aggregates and confer tissue specific characteristics
Explain the biochemical mechanisms underlying alterations associated to connective tissue disorders
Describe structure features of elastin and proteoglycans and relate them to their functional properties
Focus on homeostasis:
Clinical point:
Scurvy

Lecture n40- B Sustaining, the human body: bone, cartilages and tendons
Objectives:
Describe the molecular composition of bone and explain what bone mineral is
Describe the molecular mechanisms underlying bone remodelling, and its regulation
Know molecular markers of bone turnover and explain their roles
Describe the structure, properties and metabolism of tendons and cartilages
Focus on homeostasis:
Clinical point:
Brittle bone disease

Practical activities
Biomechanics of locomotion: force platforms as ergometers.
2 hours all students

2. COMPLEX ACTION-INTERACTIONS
2a VOLUNTARY MOVEMENT: HUMAN HIGH SKILL:
Lecture n41-A Descending pathways: I like to move it, move it.
Objectives:
Give a general overview of the descending pathways: the medial and lateral system.
Describe the origin and course of the pyramidal tract.
Describe the location of the primary and secondary motor areas.
Describe the structural features of the motor cortex.
Describe the pathways from the reticular formation, red nucleus, tectum and vestibular nuclei.
The Clinical Point:
absence of movement (paralysis)

Lecture n42-P Use of the hand: from tool use to playing piano.

Objectives:

Describe the functional properties acquired during evolution by the cerebral cortex and the corticospinal tract.

Describe the influence exerted by the brain stem descending pathways on spinal cord.

Describe the corticospinal influences on spinal cord machinery for movement control.

Illustrate the relation between the sensation and movement and the descending control of afferent inputs to sensory cortex.

Describe output functions of the motor cortices: primary, premotor and supplementary motor cortices.

Describe the dynamic nature of cortical organization: dynamic changes after lesion and in learning.

Focus on homeostasis

The Clinical Point

Consequences of cortical lesions

SEMINAR-P: The grasping circuit: neural circuits underlying visuomotor transformation

Practical activities

Electromyography, tetanus, spinal reflexes, corticospinal conditioning, fatigue

2 hours x 4 (groups 10 students)

Lecture n43-A e P Cerebellum: coordination and planning. The smooth one.

Objectives:

Describe the organization of the cerebellum into different regions.

Describe how the cerebellum receives sensory inputs from several regions of the brain and spinal cord.

Describe the cerebellar output pathways.

Describe the microcircuitry of the cerebellar cortex.

Describe the functional properties of the basic cerebellar circuit module: the simple spikes and complex spikes.

Describe the control exerted by the Vestibulocerebellum on balance and eye movement: interaction with the vestibular pathways

Describe the control exerted by the Spinocerebellum on body and limb movements:interaction with thevestibular system and with the spinal cord

Describe the control exerted by the Cerebrocerebellum on the cortical motor program: interaction with the cortex.

Describe the functional role of the afferents from the Inferior olive and the role of cerebellum in motor learning

Describe the role of the cerebellum in cognition, mood and non motor behaviour.

The Clinical Point:

lack of order (ataxia)

Lecture n44-A Basal ganglia: controlling, selecting, behaving, timing, planning ...The controversial one.

Objectives:

Describe the structures belonging to the basal ganglia circuitry.
Describe the inputs to the basal ganglia.
Describe the outputs from the basal ganglia.
Describe the intrinsic connections.
Give a general outline of the four parallel channels passing through the basal ganglia.
Describe functional properties of the basal ganglia-thalamocortical circuitry.
Describe the skeletomotor, the oculomotor, the prefrontal and the limbic circuit.
Describe the role of the basal ganglia in cognition, mood and non motor behaviour.
The Clinical Point:
too much or too little movement (disikinesia)

Lecture n45-P Growing dizzy..and falling down!
Objectives:
Define posture and its biomechanical constraints.
Define the different components of the postural control: spinal, vestibular and visual components.
Describe the Spinal mechanisms acting in postural control and the main role of the stretch reflex.
Describe the Vestibular mechanisms acting in postural control: the vestibulospinal and tonic neck reflexes. Describe the Visual action in postural control: closed vs opened eyes, lateral shift of retinal images and optocinetic nistagmus.
Focus on homeostasis
The Clinical Point
Conflicting visual, proprioceptive and vestibular inputs: vertigo and motion sickness

SEMINAR-P: Acquisition of motor schemas during development. Disruption in cerebral palsy.

Lecture 46-A Vascular supply to the cerebral hemispheres and brainstem. I depend on yO_2u.
Objectives
Describe the circle of Willis: anterior and posterior circulation.
Describe the course and territory of supply of the three main cerebral arteries and revise main functional areas of the cerebral cortex.
Describe the most important penetrating vessels and their territory of supply.
Describe the vascular supply to the brainstem and revise internal structure.
Describe the superficial and deep venous drainage of the cerebral hemispheres.
The Clinical Point:
The heart attack of the brain (TIA and stroke)

Lecture n47-P Access Denied: the Brain barriers.
Objectives:
Define the Blood and Cerebrospinal fluid (CSF) Barrier.
Describe the Cerebrospinal Fluid amount, composition, production, circulation, reabsorbtion and functions.
Describe the structural and functional relationships between the intracranial compartments and blood-brain and blood-CSF barriers.
Define the Blood- Brain Barrier.

Focus on homeostasis:
Clinical point:
Meningitis

Lecture n48- B The energetic side of the nervous system: glia and neurons in dialogue.
Objectives:
Describe the molecular composition of the nervous system and differences between the grey and white matter.
Outline the energy requirements and fuels of the nervous system.
Explain why glucose is the obligatory energy substrate for the nervous system.
Describe how local brain energy metabolism can be studied in humans.
Describe the metabolic and functional cross-talk between astrocytes and neurons
Describe the role of amino acid metabolism in neuronal properties.
Explain ammonia neurotoxicity.
Outline the role and metabolism of cholesterol in the nervous system.
Focus on homeostasis
Clinical Point:
Metabolic encephalopaties

Practical activities
Principles of EEG recording: Sleep and awake state: evoked potentials; event related potentials;
3 hours all students

2b BEHAVIOURAL RESPONSE/ACTIVITIES: THE ROLE OF HYPOTHALAMUS

Lecture 49P From the autonomic actions to motivational states
Objectives:
Describe the "driving" role of the hypothalamus in controlling the autonomic system.
Describe the visceral reflexes: slow and rapid visceral responses and the neuroendocrine reflexes.
Introduction to the "driving" role of the hypothalamus in integrating endocrinal and autonomic functions with behaviour.
Define the motivational states and their neural control

Lecture n50-P Thinkering with our biological clocks.
Objectives:
Describe the "driving" role of the hypothalamus in integrating endocrinal and autonomic functions with the environment.
Describe the circadian rhythms and nervous structure underlying them.
Illustrate the functional properties of the clock proteins and of the pineal gland (melatonine).
Describe the role of the sovrachiasmatic nucleus in synchronization of biological rhythms with external environmental cues.
Focus on homeostasis
The Clinical Point
Jet lag

THE MOST COMPLEX NEURO-ENDOCRINE INTERACTIONS: GROWTH AND REPRODUCTION

Lecture n51-P Drop the child: I'm adult.

Objectives:

Define tissutal and metabolic events underlying physiological growth.

Describe the factors affecting growth, the growth curves and growth rate at different ages.

Describe events occurring in the skeletal growth.

Describe the Growth Hormone production, its direct and indirect action by means of somatomedine and the regulation of GH secretion: role of GHRH, Somatostatin and IGFs.

Describe the role of the "permissive hormones" in growth: thyroid hormones, cortisol, insulin and gonadal hormones.

The Clinical Point

Cretinism

Lecture n52-P Reproduction: does it really contribute to homeostasis?

Objectives:

Illustrate the hormonal control of male reproduction: maturation of male seminal cells and role of LH, FSH and testosterone in spermatogenesis.

Describe the functional properties of the male reproductive tract and of the accessory sex glands.

Illustrate the hormonal control of female reproduction: role of FSH, LH and ovarian estrogen and progesterone. on the ovarian cycle and on the events occurring in the menstrual cycle.

Describe the feedback control of the hypotalamus-hypophysis-gonads axis on male and female, the puberty and GnRH activity.

Define menopause.

Outline of principal pregnancy, parturition and post-pregnancy events.

The Clinical Point

Amenorrhoea

6. FUNCTIONS 2ND SEMESTER

Functions Part II

Description:
The second part of the course deals with the functions of cardiovascular, gastrointestinal, respiratory and renal systems, relating to the maintenance of the homeostasis of the body composition and energy balance. A particular attention will be paid to the complex interplay between the different organs of each system and between the different systems. Given the non linearity of many of the biological systems considered, a semiquantitative description will be provided using graphical analyses.

Block 2 will include 47 (5 physics, 27 physiology, 1 anatomy, 14 biochemistry) lectures, 3 seminars and 9 practical activities.

THE CARDIOVASCULAR SYSTEM

Lecture n1-Phy Nonviscous fluids

Objectives:
Define pressure and relative pressure. Define shear stresses. Explain Pascal's principle.
Explain the effect of gravity: Stevino's law, Archimede's principle
Define mmHg: blood pressure and characteristic pressures in the body (min, max, delta)
Explain how to measure pressure (I): barometer and manometer
Explain fluid dynamics and conservation laws: continuity equation and Bernoulli's principle

Lecture n2,3-Phy Viscous fluids

Objectives:
Define rate of strain and viscosity
Explain Poiseuille law and fluid circuits
Explain Stokes law, sedimentation and centrifugation
Explain blood as complex fluid and its circulation in the human body
Explain how to measure pressure (II): turbulence and the sphygmomanometer

Lecture n4-B The dynamic composition and multifunctional role of blood plasma.

Objectives:
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
Overview plasmatic carbohydrates and lipids: types, roles and turnover
Describe the different classes of plasma proteins, their turnover and functional properties
Describe plasma proteins of diagnostic importance
Focus on homeostasis
Clinical point:
α1-antitrypsin deficiency

Lecture n5-P Effects of gravity on the cardiovascular system.

Objectives:

Define the hydrostatic indifference point and describe its relation with the changes of intravascular pressure and volume distribution due to the postural changes.

Describe the compensatory mechanisms for the maintenance of cardiac output during changes in posture and the role of the lower limb muscles and veins as auxiliary pumps.

Clinical point:

Orthostatic hypotension, varicose veins

Lecture n6-B Hemostasis: protecting vascular integrity

Objectives:

Describe megakaryocyte maturation, platelet release and their control

Delineate structure and properties of the major proteins involved in blood coagulation, and clot dissolution

Describe the mechanisms of coagulation, anticoagulation and fibrinolytic phases of hemostasis

Recognize the role of vitamin K in blood coagulation

Explain how natural anticoagulants exert their action, and describe the anticoagulant functions of the microvasculature

Focus on homeostasis

Clinical point:

Protein C deficiency

Lecture n7,8-Phy Adding complexity: diffusion and molecular forces

Objectives:

Explain undirected molecular motion: thermal kicks and Brownian motion

Explain diffusion processes in the human body

Explain surface tension and the Laplace law

Explain the role of surfactants in the lungs: infant respiratory distress syndrome

Explain capillarity and the Jurin law

Define osmotic pressure. Explain dialysis and the kidney

Lecture n9-P Blood flow.

Objectives:

By applying of the equation of continuity to the cardiovascular system, describe the relation between blood velocity and section in the different parts of the cardiovascular system.

Combine Bernoulli and Poiseuille equations and describe the relation between pressure and flow in the different parts of the cardiovascular system.

Explain how turbulence can arise due to pathological changes of the cardiovascular system and its hemodynamic consequences

Clinical point:

Carotid stenosis

Lecture n10- B Erythropoiesis and mature erythrocytes.

Objectives:

Describe erythropoiesis and control mechanisms.

Outline the synthesis of heme, factor requirement, regulation, and explain how its defects lead to porphyries.
Describe heme, catabolism of bilirubin, conjugation and excretion.
Correlate the erythrocyte membrane and its unique cytoskeletal structure with cell properties.
Explain how the erythrocyte metabolism is related to oxygen transport.
Describe the roles of iron in humans and how its homeostasis is maintained.
Explain the toxicity of free iron, its consequences, and the body defenses against it.
Focus on homeostasis:
Clinical point:
Spherocytosis

Lecture n11- B The red blood cells: transport of oxygen (and more)
Objectives:
Delineate structure and function of hemoglobin and their relationships.
Describe the cooperative oxygen binding to heme and the physiological factors that influence it.
Know the physiological variants of hemoglobin.
Describe hemoglobin switching in human development, its control and role.
Explain how hemoglobin can transport carbon dioxide and nitric oxide besides oxygen.
Overview the buffer role of hemoglobin.
Focus on homeostasis:
Clinical point:
CO intoxication

Lecture n12-P Rheology of the blood and blood flow through elastic tubes.
Objectives:
Define blood viscosity and describe its dependence on the hematocrit value and on temperature.
Explain the role of vessel diameter and blood velocity in the non newtonian behavior of the blood, and the consequences of pathological changes in the microcirculation.
Describe the critical closing pressure and vascular instability which can take place during vasoconstriction.
Clinical point:
Polycythemia

Lecture n13-P Electrical properties of the heart and electrocardiography.
Objectives:
Describe the physiological sequence of the cardiac action potentials propagation from its formation in the sinoatrial node to the ventricular muscle.
Explain how the conduction system can change in pathological condition.
Describe how the pathological changes of the electrical properties of the heart can be investigated with electrocardiography.
Clinical point:
Describe the most common alterations of sinoatrial rhythms, atrioventricular conduction blocks, premature depolarizations, ectopic tachycardias and fibrillation.

Lecture n14-P Cardiac cycle.

Objectives:
Describe the mechanical events of the cardiac cycle in terms of the main hemodynamic parameters, and the relations between these mechanical events and the electrocardiogram.
Describe what relevant information can be obtained from the auscultation of the heart (sounds and murmurs).
Apply the notions acquired to the major valvular heart diseases.
Clinical point:
Aortic stenosis

Lecture n15-P Mechanics of the heart.
Objectives:
Explain how to represent the cardiac cycle on the pressure-volume diagram, and use it to estimate cardiac work.
Define isovolumic and isobaric maxima curves, and explain how these curves reflect the mechanical properties of the heart.
Define preload and afterload, and use the pressure-volume plane to explain the Frank Starling law of the heart and its relevance in the physiology of the cardiovascular system.
Describe how a Frank starling curve can be obtained from the pressure-volume representation of the cardiac cycle.
Using the pressure-volume plane, describe the effects of contractility changes and how they are estimated in the clinical settings. Describe the cardiovascular responses to physical exercise.
Define the determinants of myocardial oxygen consumption, and how the coronary blood flow is regulated.

Lecture n16-B The heart: energy for beating.
Objectives:
Describe how contractile proteins and ion channels differ in heart and skeletal muscle.
Overview the cardiac metabolism, and describe the energetic fuels of the heart, and their metabolic fates.
Explain cardiac metabolic adaptation to different physiological conditions and hypoxia.
Explain why fatty acids are the privileged substrate of the heart and how this process is regulated by insulin.
Describe the role and control of lipoprotein lipase and carnitine in the heart.
Describe the mechanism and role of cardiac CPK and know its diagnostic implication.
Describe the effect of conditions/stimuli leading to heart remodeling, and explain its consequences.
Delineate structure and action mechanism of natriuretic peptides and the control of their secretion by the heart.
Focus on homeostasis:
Clinical point:
Heart failure

Lecture n17-P Cardiac output.
Objectives:
Define cardiac output and describe the methods of its measurement (indicator dilution methods, Fick's method and echocardiography). Describe the determinants of heart rate and contractility. Explain how the orthosympathetic and parasympathetic systems can modify heart rate and contractility and in which regulatory loops they are involved.

Clinical point:
Carotid synus syndrome

Lecture n18-P Arterial pressure.
Objectives:
Define systolic, diastolic, pulse and mean arterial pressure.
Describe the mechanical behaviour of arterial compartment using a simple hydraulic model, and the relation between the model's parameters (compliance and resistance) and the arterial pressure.
Describe the changes of arterial compliance with age.
Explain how the pulse wave travels along the arterial walls and how its shape changes from the ascending aorta to the peripheral arteries.
Clinical point:
Radial pulse

Lecture n19-P Microcirculation.
Objectives:
Describe the role of arterial compliance and peripheral resistances in the genesis of a continuous capillary blood flow.
Describe some mechanisms of transcapillary exchange: diffusion, filtration, pinocytosis. Use the Starling hypothesis to predict how filtration changes in physiological and pathological situations and the role of lymphatics in the removal of plasma proteins in the interstitium.
Explain how the microcirculation is regulated by several mechanisms and their relative importance in the different parts of the body.
Focus on homeostasis:
Hypovolemia compensation
Clinical point:
Edema

Lecture n20-P Mechanical coupling between the heart and the vessels: one pump model.
Objectives:
Use the analysis of a cardiac arrest to understand the relations between cardiac output and central venous pressure. Explain the dependence of vascular function curves on intravascular volume, arterial and venous compliance and peripheral resistance.
Combine vascular function and cardiac function curves to build a one pump model of the cardiovascular system and use it to describe the physiology of the cardiovascular system in physiological and pathological situations.
Clinical point:
Cardiovascular responses to hypo and hypervolemia

Lecture n21-P Mechanical coupling between the heart and the vessels: two pumps model. Cardiopulmonary integration.
Objectives:
Expand the one pump model previously described into a two pumps model to predict the cardiovascular effects of right ventricle failure. Explain the role of the right ventricle in maintaining a low systemic capillary pressure.
Describe the interactions between the respiratory and the cardiovascular system.
Clinical point:
Valsalva manoeuvre

Practical activities
ECG
1.5 hours X 4 (groups 13 students)

Practical activities
Measurement of arterial blood pressure at rest and during exercise.
1.5 hours X 4 (groups 13 students)

GASTROINTESTINAL SYSTEM
Lecture n22-P Motility of the gastrointestinal system.
Objectives:
Describe the mechanical properties of smooth muscle.
Describe the motility of esophagus, stomach, small and large intestine.
Clinical point:
Gastroesophageal reflux

Lecture n23-24-B Secreting into opposite sides: the exocrine and endocrine properties of the gastro-intestinal system.
Objectives
Describe the composition, elaboration, and control mechanisms of the digestive secretions.
Describe the digestive and absorption processes
Describe the role of the digestive apparatus in the hydro-electrolytic balance and in the metabolic homeostasis.
Delineate the structural properties, regulation, local and systemic effects of gastro-enteric hormones.
Focus on homeostasis:
Clinical point:
Cystic fibrosis

THE REGULATION OF ORGANIC METABOLISM AND ENERGY BALANCE
SEMINAR-B Eating for health

Lecture n25-B The integrative role of the CNS in caloric homeostasis and food intake
Objectives:
Overview nutritional requirements, and the role of nutrition in homeostasis
Describe factors influencing food intake and energy expenditure.
Explain caloric balance and caloric homeostasis.
Describe fuel-sensing mechanisms and their function in homeostasis: “hunger” and “satiety”.
Describe the influence of body weight on food intake.
Outline the hormonal mechanism of eating behavior
Explain how the interplay among hormones and the autonomic nervous system allows for the control of caloric homeostasis and appetite.
Focus on homeostasis:
Clinical point:
Diabetic hyperphagia

Lecture n26-B The liver I: the body's receiving and recycling central.

Objectives:

Overview the key properties and molecular specialization of the liver .

Explain how the liver coordinates its use of fuels versus that of the body.

Describe the role of the liver in the maintenance of blood glucose and the mechanisms of this regulation.

Describe the role of hepatic lipid metabolism in homeostasis and how its derangement results in a fatty liver.

Overview the essential role of the liver in the amino acid and protein metabolism.

Explain why diseases of the liver can be biochemically and clinically devastating.

Focus on homeostasis:

Clinical point:

Liver cirrhosis

Lecture n27-B The liver II: detoxifying and waste disposing properties.

Objectives:

Describe phase I reactions, and explain the role of the microsomal electron transport chain.

Overview the inducible properties of phase I enzymes and explain clinical consequences arising from this.

Explain how phase II reactions proceed, and detoxifying compounds used to favor urine excretion of waste compounds.

Describe ethanol absorption, tissue distribution, and metabolism.

Describe the metabolic interrelationships of tissues after ethanol consumption.

Explain ethanol toxicity and its clinical consequences.

Focus on homeostasis:

Clinical point:

Chronic alcohol consumption

Lecture n28-B There is more in the adipose tissue than fat: the white and brown sides of adipocytes.

Objectives:

Explain the key storage role of adipose tissue and its crucial functions in body's homeostasis.

Describe lipogenesis and lipolysis in the adipose tissue, and their hormonal control of adipocyte.

Describe the endocrine properties of adipose tissue, and he different compounds secreted by adipocytes.

Describe the biochemical and functional differences between white and brown adipocytes.

Explain how brown adipocytes contribute to thermogenesis, and describe their nervous control.

Focus on homeostasis:

Clinical point:

Obesity

THE RESPIRATORY SYSTEM

Practical activities
Spirometric and plethismographic measurements.
1.5 hours all students

Lecture n29-P Quasi-static properties of the respiratory system: pressure-volume curves.
Objectives:
Describe the quasi-static behaviour of the respiratory system using a simple one compartment model. Characterize the compliance of the model by building the quasi-static pressure-volume curve of the respiratory system.
Use the quasi-static pressure-volume curve to estimate the elastic work done by the respiratory muscles to increase or decrease the volume of the respiratory system.
Implement the model of the respiratory system by subdividing it into two compartments (lungs and chest wall) and describe the quasi-static pressure-volume curves of each.

Lecture n30-P Quasi-static properties of the lungs and of the chest wall.
Objectives:
Explain how the quasi-static characteristics of the lungs depend on the presence of surface phenomena. Describe the role of surfactant and pulmonary interdependence in reducing the heterogeneity of alveolar volume.
Describe the effects of gravity on the pressure-volume curve of the chest wall, on pulmonary volumes and how the regional pleural surface pressure changes with a change in posture. Use the onion skin diagram to predict the effect of gravity on regional ventilation.
Clinical point:
Respiratory distress syndrome in the newborn

Lecture n31-P Dynamics of the respiratory system. The Campbell diagram.
Objectives:
Describe the organization of the airways. Describe the peculiar characteristics of upper and lower airways. Explain how the airways of each generation contribute to total airway resistance and the effect of pulmonary interdependence on airway diameter. Describe the mechanisms for removal of foreign particles in the lungs.
Use Campbell diagram to describe respiratory mechanics during spontaneous ventilation and how the total respiratory work can be computed and subdivided into elastic and resistive work.
Explain how pleural surface pressure changes during mechanical ventilation and its cardiovascular effects.
Describe the phenomenon of expiratory flow limitation and discuss its relevance in health and disease.
Clinical point:
Obstructive and restrictive syndromes

Lecture n32-P Pleural space. Respiratory muscles.
Objectives:
Describe the mechanics of the pleural space and the mechanisms of gases and fluids removal.

Describe the organization of the respiratory muscles and use the force-length and the force-velocity diagrams to predict their mechanical actions on the respiratory system.
Clinical point:
Pneumothorax

Practical activities
Pulmonary volumes and lung mechanics.
1.5 hours X 4 (groups 13 students)

Lecture n33-P Distribution of ventilation and of perfusion in the lungs.
Objectives:
Describe how the intravascular pressure changes inside the pulmonary circulation and underline the differences between pulmonary and systemic circulation.
Explain the effects of gravity on the pulmonary circulation and how the vessels are affected by alveolar pressure and lung recoil according to their anatomical position.
Describe the dependence of overall pulmonary vascular resistance on lung volume.
Describe the distribution of pulmonary blood flow and ventilation-perfusion ratio according to body position.
Clinical point:
Pulmonary hypertension

Lecture n34-P Gas exchange: the alveolar-capillary barrier.
Objectives:
Define anatomical and physiological dead space and describe how they can be measured (Fowler's and Bohr's methods).
Define total, dead space and alveolar ventilation and the differences in gas composition of inspired, alveolar and expired air.
Explain how respiratory gases diffuse across the alveolar-capillary barrier during rest and exercise and how blood gases are carried by the blood to the peripheral tissues.
Clinical point:
Diffusion capacity for oxygen

Lecture n35-P Gas exchange: alveolar gases equations and ventilation perfusion ratio.
Objectives:
Describe how oxygen consumption, carbon dioxide production and respiratory exchange ratio are measured during indirect calorimetry. Explain the relation between respiratory exchange ratio and the metabolism, and how oxygen production and respiratory exchange ratio can be used to estimate energy consumption.
Considering an ideal lung, describe the determinants of alveolar air composition (barometric pressure, inspired air composition, carbon dioxide production and oxygen consumption, alveolar ventilation) and use the alveolar gases equations to predict carbon dioxide and oxygen alveolar partial pressures in physiological and pathological conditions.
Define the ventilation perfusion ratio and describe how its value changes in the different parts of the lungs. Define the ideal, arterial and alveolar point in the carbon dioxide and oxygen partial pressures plane and explain the mechanisms responsible for the production of an alveolar arterial oxygen gradient in health and disease.
Focus on homeostasis:
Hypoxic vasoconstriction and hypercapnic bronchodilation in the lungs

Clinical point:
ARDS

Lecture n36-P Control of breathing.
Objectives:
Describe the neural mechanisms responsible for the generation of the breathing pattern. Explain how the output of the central pattern generator can be modulated by information from central and peripheral chemoreceptors, slow adapting, fast adapting, irritant and J pulmonary receptors, muscle and joints proprioceptors and temperature.
Describe the ventilatory response to changes of arterial carbon dioxide and oxygen partial pressures.
Clinical point:
Ventilatory adaptation to high altitude

Practical activities
Oxygen consumption and carbon dioxide production. Dead space.
1.5 hours X 4 (groups 13 students)

Practical activities:
Mechanical ventilation.
1.5 hours X 2 (groups 26 students)

THE URINARY SYSTEM
Lecture n37-A The Nephron
To describe the structural and ultrastructural aspects of renal corpuscle and glomerular filtration barrier
Clinical drops: glomerular filtration defects
To describe to structural and ultrastructural features of the tubular segment of the nephron and of the collecting tubule in relation to their contribution to the modification of the glomerular ultrafiltrate
Clinical point:
polycystic kidney
To describe the structure of the different component of the iuxtaglomerular apparatus in relation to their contribution to the regulation of systemic blood pressure
Clinical point:
hypertension

Lecture n38-P Renal blood flow and glomerular filtration.
Objectives:
Explain the characteristics of the renal circulation and their relations with renal blood flow distribution between the cortical and medullary part of the kidneys. Define glomerular filtration rate, net filtration pressure and coefficient of ultrafiltration and their determinants.
Explain the relations between glomerular blood flow, the resistances of the afferent and efferent arterioles and the pressure in the peritubular capillaries.
Describe intrarenal and extrarenal mechanisms of blood flow and glomerular filtration rate regulation.
Focus on homeostasis:

Tubuloglomerular feedback
Clinical point:
Nephrotic syndrome

Lecture n39-P Renal Clearance.
Objectives:
Define the renal clearance of a substance.
Explain why the clearance of inulin corresponds to glomerular filtration rate and the clearance of p-amino-hyppuric acid to effective renal plasma flow.
Compare the clearance of a freely filtered substance with that of inulin in order to gain information about net secretion or absorption of that substance.
Clinical point:
Clinical indexes of the glomerular filtration rate: clearance of creatinin and plasma creatinin concentration

Lecture n40- B There is more than excretion in the kidney.
Objectives:
Overview the renal functions and role in the body's homeostasis.
Describe the functional properties of the kidney in relation to specific molecular compartmentalization.
List the major components of the urine and explain the importance of their excretion.
Outline the energy requirements of the kidney, and explain its adaptations in physio-pathological conditions.
Describe the role of the kidney in glucose homeostasis during starvation, and its hormonal regulation.
Describe the renal metabolism of amino acids, and its role in starvation and acidosis.
Overview the endocrine role of the kidney.
Focus on homeostasis:
Clinical point:
Uremia

Lecture n41-P Proximal tubule, Henle's loop and distal tubule.
Objectives:
Describe how osmolarity and ultrafiltrate volume change along the nephron.
Describe for each segment of the nephron the main processes of reabsorption and secretion, in particular the renal treatment of organic substances (proteins, aminoacids, glucose), electrolytes (sodium, chloride, bicarbonates, potassium, calcium and magnesium), , inorganic phosphorus, urea and ammonia.
Explain how the kidneys play a role in drugs elimination and the influence of luminal pH on the excretion of organic acids and bases.
Clinical point:
Diuretics

Lecture n42-P Regulation of sodium and water balance.
Objectives:
Describe the sodium balance and the role of the kidneys in its maintenance.
Explain how the reabsorption of sodium is regulated by intrarenal and extrarenal factors.
Describe the renin-angiotensin-aldosterone system and its renal and systemic actions.
Describe how aldosteron can increase the reabsorption of sodium in the distal collecting duct.

Describe the water balance and the role of antidiuretic hormone in its maintenance.
Explain how osmoreceptors and baroreceptors regulate antidiuretic hormone secretion.
Sum up the regulatory mechanisms of arterial pressure in short, middle and long term.
Clinical point:
Primary aldosteronism

Lecture n43-P Potassium homeostasis.
Objectives:
Describe the distribution of potassium in the body compartments and how redistribution of potassium can maintain a constant plasma concentration or cause hypo or hypokalemia.
Describe the role of the kidneys in the maintenance of the potassium balance and explain which are the determinants of potassium secretion in the cortical collecting duct.
Clinical point:
Clinical symptoms of hyper or hypokalemia. Iatrogenic effects of diuretics administration.

SEMINAR-P Homeostasis of body temperature.

SEMINAR-P Should I stay or should I go? The Stress response.

Practical activities :
Cardiac failure.
2 hours all students

Lecture n44-P Acid-base balance.
Objectives:
Describe the intracellular and extracellular buffer systems of the body.
Represent the acid base status on the Davenport diagram and use it to describe the acid-base disorders and their compensations.
Describe the respiratory and renal compensation for acid-base disorders.
Describe the mechanisms used by the kidneys to reabsorb filtered bicarbonates and to add new bicarbonates to plasma. Explain how these mechanisms are regulated.
Clinical point:
Acid-base disorders.

Lecture n45- B Calcium and phosphorus homeostasis.
Objectives:
Define calcium balance and explain the importance of calcium homeostasis.
Recognize the importance of dietary calcium, describe its absorption and factors influencing it.
Explain physiological conditions influencing calcium requirements (including age, sex, and pregnancy).
Know different forms of calcium distribution in plasma and their functional roles.
Describe the properties and mechanism of action of calcitonin, parathyroid hormone, and calcitriol
Descxribe the role of intestine, bone and kidney in calcium homeostasis.
Explain the role of phosphate as major intracellular ion and how phosphate homeostasis is maintained.
Explain consequences of alterations in calcium and phosphate homeostasis .

Focus on homeostasis:
Clinical point:
Rickets

Practical activities:
Arterial blood gases analysis and acid-base disorders.
1.5 hours all students

Practical activities:
Loss of consciousness.
2 hours all students

7. FACULTY

ISABELLA BARAJON (isabella.barajon@unimi.it) MD. Professor of Human Anatomy of the Faculty of Medicine and Surgery, University of Milan, since 1998. She teaches medical students in specialist Schools and medical biotechnology students. Her main research interests are related to the field of Neuroscience and Embryology and her current research topics deal with the expression of immunological molecules and cancer testis antigens during embryonic development. She has spent research periods in neurophysiology, medical physiology and anatomy laboratories of the Panum Institute of the Faculty of Health Sciences at the University of Copenhagen and collaborates with the Division of Haematology and Oncology, Texas Tech University Health Sciences Center.

RAFFAELLA BONECCHI (raffaella.bonecchi@unimi.it) Doctor in Biological Sciences, PhD in Immunology. Assistant Professor of General Pathology and Immunology since 2000. She teaches medical biotechnology students and she is senior scientist in the laboratory of Leukocyte Biology in the Department of Traslational Medicine of the University of Milan hosted by Istituto Clinico Humanitas Research Center. Her main research interests are: innate immunity, inflammation and cancer, monocytes and macrophages, chemokine and chemokine receptors. She is author of 45 original articles in peer-reviewed international journals indexed in PubMed that have been cited 3.307 times giving an h-index of 19 (ISI Web of Science Thomson Reuters).

ELISA BORGHI (elisa.borghi@unimi.it) , Assistant Professor in Microbiology at the University of Milan. She received her degree in Biological Sciences from the University of Pavia, and her PhD in Molecular Medicine from the University of Milan. During PhD study, she has been research assistant for few months at the Center for Neurovirology and Cancer Biology of the Temple University of Philadelphia. Her scientific activity has involved several fields of interest. At first she concentrated on the involvement of neurotropic viruses in the aetiology of neurodegenerative disorders, especially studying Polyomaviruses infection in HIV positive patients. Moreover, recently, she collaborated with Prof. Morace in the study of molecular aspects of bacterial and fungal infections, focused on rapid diagnosis and molecular typing of clinical isolates. In the last two years she focused her studies on microbial biofilm, especially in terms of antimicrobial drug resistance. To better understand microbial pathogenesis and to learn invertebrate models for in vivo studies, she has been hosted as visitor scientist at the Harvard Medical School, Massachusetts General Hospital, Division of Infectious Diseases.

ROBERTO CERBINO (roberto.cerbino@unimi.it) received a PhD in Physics, Astrophysics and Applied Physics from Milan University in 2004. He has later been Marie Curie fellow at the University of Fribourg (Switzerland) and since 2007 he is assistant professor of Medical and Applied Physics at the Milan University, Department of Medical Biotechnologies and Translational Medicine. His research activity ranges from soft and biological matter to non-equilibrium statistics and fluid dynamics. His experimental activity is also focused on the development of

innovative optical techniques mostly for quantitative microscopy, scattering and metrology with light and X-rays. He acted as a reviewer for 20 journals and authored 3 book chapters and 30 articles indexed on ISI-Web of Science.

GABRIELLA CERRI, (gabriella.cerri@unimi.it) MD, PhD. Assistant Professor of Human Physiology. Ten-year experience teaching in medical school both to medical students and interns. Dr Cerri's main research interest is the cortical control of hand movements in humans. The experience matured in the Department of Human Physiology of UniMi on human motor control and in the Institute of Neurology, UCL London, on non-human primates (the best animal model for the human sensori-motor system controlling the hand) resulted in dr Cerri's present research effort, aimed at understanding the crucial role exerted by the corticospinal tract in controlling skilled hand movements. The main present activity in her laboratory, which includes different experimental approaches such as recordings of spinal reflexes, Transcranial Magnetic Stimulation, neuroimaging, high resolution recording systems in pre-surgical and intra-operatory monitoring during neurosurgery, is devoted to describing the functional properties of the neural circuits linking the different cortical areas involved in human motor control and to improve the knowledge of the cortical control exerted by the corticospinal tract on the spinal machinery necessary to perform highly skilled movements.

SILVIA DELLA BELLA, (silvia.dellabella@unimi.it) MD, PhD in Internal Medicine, Specialization in Allergology and Clinical Immunology, Specialization in Internal Medicine. Assistant Professor of General Pathology and Immunology at the University of Milan. Her constant teaching of Immunology and General Pathology are mainly dedicated to Degree programs (Medicine), Bachelor programs (Nursing), Specialisation Schools (Allergology and Clinical Immunology; Rheumatology) and PhD courses. Main research topics: pathogenesis of autoimmune diseases and virus-related tumors, mainly focused on the involvement of dendritic cells, cytokines, vascular endothelium and endothelial progenitor cells. She is author of 48 original articles published in peer-reviewed international journals.

SERENA DELBUE (serena.delbue@unimi.it) Doctor in Medical Biotechnology, PhD in Molecular Medicine. Fixed-term assistant professor of Microbiology and Clinical Microbiology since 2012 at University of Milano and Adjunct Assistant Professor at Temple University, Philadelphia. She teaches medical biotechnology students and is senior scientist in the laboratory of Translational Research in the Department of Biomedical, Surgical and Dental Sciences of the University of Milan. Her main research interests are the molecular characterization and the molecular pathogenesis of the human polyomaviruses, with a particular focus on JC Virus. She has spent a research period at the Center of Neurovirology and Cancer Biology, Temple University, Philadelphia. She is author of 48 original articles in peer-reviewed international journals indexed that have been cited 522 times giving an h-index of 15 (Scopus).

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Chief Medical Officer and Scientific Director, Istituto Clinico Città Studi, Milan
The research activity of prof. Pasquale Ferrante is devoted to the study of the molecular basis of various human diseases, including: Acute and Subacute Viral Infection of Central Nervous System, Multiple Sclerosis, NeuroAIDS, and cardiovascular disease.
He is author and coauthor of more than 200 indexed publications

MARINOS KALLIKOURDIS (marinos.kallikourdis@unimi.it) MA Cantab in Natural Sciences, PhD in Immunology (Cambridge, UK). Assistant Professor of General Pathology and Immunology in the Department of Medical Biotechnology and Translational Medicine, University of Milan, as of 2012. He teaches Adaptive Immunology and is currently a Junior Principal Investigator in the Laboratory of Adaptive Immunity, Department of Medical Biotechnology and Translational Medicine, hosted within Istituto Clinico Humanitas. His principal scientific contributions include the discovery of the requirement for regulatory T cells for the sustenance of maternal-fetal tolerance and the deciphering of the mechanism of pregnancy-associated amelioration of Rheumatoid Arthritis. Current research interests of his group also include the study of immunodeficiency via 2-photon imaging as well as Adoptive Cell Therapy applied to metastatic tumours and neurodegenerative disease.

MASSIMO LOCATI, (massmo.locati@unimi.it) PhD in the Department of Immunology and Cell Biology at the Mario Negri Institute of Milan (1992-1995) Research fellow in the Laboratory of Host Defenses, National Institutes of Health in Bethesda, Washington (1995-1996). During these years he was mainly involved in the definition of chemokine receptors signalling properties and in particular he defined the role of chemokine receptors' signalling in HIV-1 infection. In 1998 he was enrolled as Research Assistant at the University of Brescia and in 2001 he moved to the University of Milan were he is now Associate Professor of

Immunology and General Pathology at the Department of Translational Medicine. His major scientific contributions include the characterization of the biological role of chemokines and chemokine receptors inflammatory diseases, the identification of the first chemokine decoy receptor, the first description of macrophage polarized activation through transcriptional profiling approaches and the identification of new microRNA involved in innate immunity and immunomediated pathologies. On these topics he is author of over 100 peer-reviewed publications, with a total Impact Factor above 600 and more than 5000 citations. His present H index is 38.
A complete list of scientific publications is available at
http://www.researcherid.com/rid/A-3146-2009

ALBERTO MANTOVANI (alberto.mantovani@unimi.it) MD, Ph.D. After specializing in oncology, he has worked in England at the Chester Beatty Research Institute, London (1975-1976) and the United States, National Institutes of Health (1978-1979 and 1985-1986) and as Head of the Department of Immunology and Cell Biology of the Mario Negri Institute for Pharmacological Research in Milan (1996-2005).
Professor of Pathology at the Faculty of Medicine, and Vice Rector for Research, University of Milan. Scientific Director of Istituto Clinico Humanitas since October 2005 and President of the Humanitas Foundation for Research, which supports basic and clinical research in the field of immunology and its applications in the treatment of chronic inflammatory and autoimmune diseases, oncology, gastroenterology, cardiovascular and neurological diseases.
From 2007 to 2010 he served in The Board of Global Alliance for Vaccine Immunization.
He was awarded national and international prizes for his scientific contributions.He is one of, or the, most quoted and /or productive Italian scientist(s). The Institute for Scientific Information (ISI) ranked him as one of 100 most quoted immunologists in the world over the last 20 years of the 20th century. As of Spring 2011 he has had over 46,000 citations and an H index of 109 (WOS).

DOMENICO MAVILIO (domenico.mavilio@unimi.it), M.D.-Ph.D. Assistant Professor of Translational Medicine at University of Milan and Head of the Unit of Clinical and Experimental Immunology at Humanitas Research Hospital, Rozzano, Milan, Italy. He teaches university classes within the schools of medicine, biotechnology and laboratory technicians. He is also within the board of the professors of the Ph.D. program of “Experimental Medicine and Biomedical Technologies” of University of Milan serving as a mentor of students involved in projects of translational and experimental immunology. His main research interests are related to human physiology and physiopathology of immune responses. In particular, his projects are focused on innate immune compartments and on their contributions on the pathogenesis and therapy of several models of human disorders such as HIV-1 infection, autoimmune diseases and cancer. Dr. Mavilio spent 8 years at the National Institute of Allergy and Infectious Diseases of the National Institute of Health (Bethesda, Maryland, USA), where under the mentorship of Dr. Anthony S. Fauci he first won a post-doctoral fellowship and was then appointed as Research Fellow heading the “Innate Immunity Section” of the Laboratory of Immunoregulation.
(Website:http://www.humanitas.it/hur/cms/english/activities/lab/index.html)

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LAURA RIBONI (laura.riboni@unimi.it) PhD in Biochemistry, MD and degree in Biological Sciences. Post-doctoral specialisation in Biochemistry. Present position: Professor of Biochemistry, Faculty of Medicine at the University of Milan, Italy. Member of various national and international scientific associations. Member of the Editorial Board and reviewer for various international scientific journals. Invited speaker at several national and international scientific congresses. Author of 80 papers on internationally refereed journals, 12 chapters in books and more than 150 communications to national and international scientific congresses. Scientific collaboration with international scientific groups in Spain, USA and Japan. Her main research topics are the biochemistry and functional properties of biological membranes, the biochemistry of cancer, the structure, enzymology, metabolism, transport and functional roles of sphingolipids in the nervous system, and molecular mechanisms of sphingolipid-mediated signal transduction in health and disease.