UNIVERSITÀ DEGLI STUDI DI MILANO

HUMANITAS RESEARCH HOSPITAL

INTERNATIONAL MEDICAL SCHOOL

STUDENT GUIDE

3RD YEAR - 1ST SEMESTER

CONTENTS

1. SYSTEM DISEASE 1

SYSTEM DISEASE

Faculty
Agostoni, Bizzi, Brambilla, Centanni, Chiti, Cornalba, Cusi, Del Sole, Donadon, Fornasari, Furlan, Di Marco, Di Tommaso, Graziani, Lettino, Locati, Montanelli, Monti, Presbitero, Poretti, Roncalli, Sardanelli, Scaglione, Selmi, Voza.

Tutors
Angelini, Arosio, Badalamenti, Brunetta, Ciccarelli, Citterio, D'Errico, Eusebio, Donadon, Gasparini, Grassi, Lodigiani, Lleo, Mirani, Monti, Muselli, Oldani, Ottolini, Pini, Poggio, Rossi, Ulian, Zavalloni Parenti, Zucali.

Credits 17

Teaching methods: Lectures, PBL, Clinical cases, Case Method, Laboratory skills and videorecording

Overview of the block

This block takes the students into clinical medicine with the study of the "Diseases of the Kidney and Urinary System" (Nephrology) and the "Diseases of the Heart and Vessels" (Cardiology), which include the study of the most relevant diseases of the Kidney and Heart. Such studies will be dealt with on a comprehensive basis, i.e. including pathology, pharmacology and imaging in relation to the diseases of the organ.

An **Introduction to clinical practice** will give the basic knowledge required to understand the medical language and some procedures involving in the diagnostic approach. The module include a Clinical Pathophysiology, which introduces the basic and general concepts of the mechanisms involved in the development and course of the disease and an Introduction to Pathology to Imaging which present an overview of the basic diagnostic tools and approach to the diseases.

Laboratory of History taking and physical examination will offer the basic foundations to the clinical investigation: p.e. how to perform a physical examination and how to take a medical history.

During the semester students should also attend the clinical departments in order to practice the medical interviewing skills and the physical examination on real patients, supervised by clinical tutors. Student's level of confidence with clinical and communication skills will be evaluated by tutors at the end of the clinical clerkship.

IMPORTANTE NOTICE

<u>Attendance to all training labs and clinical clerkship is mandatory and shall be registered.</u>

Textbooks

- Harrison's Principles of Internal Medicine, 18th Edition, McGraw Hill, 2011

- Goldman's Cecil Medicine L. Goldman, A. I. Schafer,
24th ed., Elsevier, c2012

Exams

The exam consists in 2 parts: a practical exam OSCE (part 1) and the exam related to the block of System Disease 1.

OSCE includes a series of different "stations", each designed to test a specific clinical skill (i.e. chest auscultation, history taking, testing blood pressure etc.) Students are required to pass through each station and perform the required clinical skills. An examiner will check the student's performance.

Passing the OSCE is a prerequisite for admission to the System Disease 1 exam.

Regarding the **System Diseases Exam Format** information will be provided at the end of October.

INTRODUCTION TO CLINICAL PRACTICE

CLINICAL PATHOPHYSIOLOGY

The four seminars on Clinical Pathophysiology are meant to give the student a general view of the changes of normal mechanical, physiological, and biochemical functions caused by a disease of an organ or a system.
They underline the complex relationships occurring in clinical conditions, between the physiological mechanisms studied during the block "Functions" on one hand, and the basic pathological processes studied during the block "Mechanisms of diseases" on the other.

Renal Pathophysiology

- What are the functions of the kidney?
- How does the kidney conserve salt and water?
- What causes a low urinary output (Oliguria)?
- What is meant by volume depletion?
- How do I differentiate pre-renal syndrome and acute tubular necrosis?
- What do we learn from the serum urea and creatinine?
- What are the pathological mechanisms responsible for renal injuries?

Learning goals
- Describe the principles behind normal renal function.
- Apply physiological knowledge to interpret changes that occur due to renal injuries.
- Explore potential strategies for preserving renal function.
- Discuss the biochemical changes in serum and urine that occur during renal impairment.

Pulmonary Pathophysiology
- What is the function of the lung?
- What is the difference between ventilation, gas exchange, and respiration?
- What is the meaning of lung compliance and airway resistances? The clinical point of view.
- What are the steps of gas exchange?
- How to define obstructive, and restrictive syndromes?

Learning goals
- Discuss the principles behind normal lung function.
- Discuss lung mechanical changes in patients with obstructive, and restrictive diseases.
- Describe changes in terms of gas exchange in patients with obstructive, and restrictive diseases.
- illustrate how to approach a patient with respiratory symptoms (how to explore mechanical properties of the lung, and gas exchanges in clinical practice)

Cardiovascular Pathophysiology

- Which are the main principles of cardiovascular autonomic control?
- Which are the different mechanisms controlling the homeostatic and heterostatic equilibrium?
- What is the "functional meaning" underlying the spontaneous fluctuations of cardiovascular variables?
- What do we learn by analysing the heart rate and blood pressure variability?
- Which are the boundaries between physiological and pathological cardiovascular variability and haemodynamic abnormalities?
- Does the human cardiovascular system completely adapt to changes in circadian rhythms due to shift work and weightlessness?

Learning goals
- Describe basic concepts of cardiovascular autonomic control including baroreceptor mechanisms
- Recognize the importance of homeostasis and heterostasis in the adaptation of human body to the environment
- Be acquainted with cardiovascular variability as a pathophysiological tool to address the continuum between health and cardiovascular diseases
- Recognize the different pathophysiology leading to occasional and chronic orthostatic hypotension
- Recognise the importance of circadian rhythms in cardiovascular function.

Immunopathophysiology

- What are the functions of the immune system?
- How does the immune system recognize self from non self antigens?
- What diseases may ensue if tolerance goes awry?
- What predisposes to an autoimmune disease?
- What immunological mechanisms are shared by different diseases?
- How can we modulate the immune response to self and non-self antigens?

Learning goals
- Describe the key clinical features, biochemical, and imaging correlates of a case of autoimmune disease
- Describe the characteristic of histological alterations observed in paradigmatic conditions
- Identify "known and unknown" factors in the underlying pathogenetic mechanisms
- Discuss the principles of current and potential therapeutic approaches with a focus on cytokine targeting.

Hematological Pathophysiology
- What are the functions of the blood and bone marrow?
- What are the functions of the spleen?

- What are the functions of the lymph nodes?
- What are the mechanisms regulating the hematopoietic system?
- How should we approach haematological patients?
- How should we perform examination of blood and bone marrow?

Learning goals
- Describe the principles behind normal blood and marrow functions
- Describe the principles behind normal splenic and lymph node functions
- Recognize the importance of homeostasis and physiological changes in the hematopoietic system
- Illustrate how to approach a patient with haematological abnormalities or haematological symptoms
- Describe basic concepts of blood and marrow examination

INTRODUCTION TO PATHOLOGY

This module introduces students to what can be historically considered the very core of modern medicine, i.e. the study of the causes of the morphological changes produced by a disease in the normal structure of an organ and its function. As such, knowledge of pathology is a powerful tool to study and understand the diseases of individual organs and systems. Moreover, pathology today has extremely relevant diagnostic applications in clinical practice.
Pathology will also be dealt with in a special block during the 4th Year.

- What is pathology? How pathology has changed over the years.
- The pathologist at work: a fascinating mission.
- The pathologists at work: language prognosis and prediction.

INTRODUCTION TO DIAGNOSTIC IMAGING AND NUCLEAR MEDICINE

Medical Imaging is one of the most powerful diagnostic tools used by doctors in their medical practice. Students will be confronted with Imaging from the very first modules (heart and kidney diseases). This is why this module has been designed to give a general overview of the techniques and clinical applications of imaging, to give them the basic information required for understanding diseases.
Imaging will be completed during the 4th year.

- An overview of imaging and its role in medical care
- Traditional approach to imaging Principles of CAT scan
- Principles of PET and nuclear medicine
- Principles of intervention radiology

Diagnostic Imaging
Learning Goals:
- Explain briefly what digital radiology is and the differences from the analogue version.
- Explain briefly the physical principles of the ultrasound scan and the Doppler ultrasound
- Explain briefly the physical principles of computed tomography
- Explain briefly the physical principles of the MRI scan
- Illustrate the basic notions of radiation protection for patients and operators, specifying absolute and relative contraindications to radiographic examinations
- Exemplify the correct terminology relating to the concept of radiographic 'projection' and explain characteristics of the image in relation to the grey-scale (for traditional radiology, ultrasound, CAT and MRI scans)
- Explain what the contrast media are and illustrate precautions, side effects and contraindications, with special reference to iodinated ones; discuss the indications for the use of contrast media by intravenous infusion route in CAT and MRI scans
- Know the general details of Interventional Radiology, explaining indications, method and results in both the vascular field (angioplasty, stenting, placement of endograft and embolisation) and extravascular field (biliary, urinary and muscolo-skeletal)

Introduction to Nuclear Medicine: from radioactivity to diagnostic imaging.
Learning goals:
- Describe the imaging techniques used in Nuclear Medicine.
- Describe the general aspects of the uptake of radiopharmaceuticals in organs and tissues.

HISTORY TAKING AND CLINICAL EXAMINATION LABORATORIES

During the first part of the semester students will attend some theoretical and practical experiences in which they will become familiar with the medical interview, the medical record, the basic manoeuvres for physical examination of the Heart, Thorax, Abdomen, and how to record and interpret an ECG and BGA.

At the end of the semester (see the date scheduled on the planning) the student have to present his/her portfolio. The Portfolio is a collection of materials chosen by the student to demonstrate the quality of their work during the clinical attendance and it will be evaluated by the Commission for the Development of Professional Competencies.
The Portfolio must include the following materials:
- opinion expressed by the tutor responsible for the student
- presence in the department at least 75% attendance (in days)
- 3 clinical traditional medical record (in Italian) 1 translated in English;
- 3 physical examination (Heart, Chest, Abdomen, Blood pressure, circulation lower limbs, peripheral pulses) in Italian and 1 for each regions in English
- 3 rectal exploration (within three semesters of Semiotics)

- 3 ECG reported out and 3 EGA

DISEASES OF THE KIDNEY AND URINARY SYSTEM (NEPHROLOGY)
Prof. Cusi

Overview

New diagnostic and therapeutic tools have emerged in the management of patients with kidney diseases. This course is designed to provide a complete understanding of what is today understand as chronic kidney disease.

The focus of this course will be to discuss the pathophysiologic and clinical advances in the major areas of Nephrology The module will not cover the entire topic of kidney and urological diseases in detail. Students are invited to refer to the textbook to cover the entire examination programme.

At the end of these blocks, the student will be able to:

- Discuss the classification of kidney diseases
- Discuss the main clinical symptoms and signs
- Discuss the pathological basis of kidney diseases
- Discuss the clinical evolution of chronic renal disease, from the initial asymptomatic stage to end stage, requiring artificial substitution of renal function.
- Discuss the use of imaging in kidney diseases
- Discuss the diagnosis and treatment of electrolyte disorders including sodium and potassium derangements.
- Outline diagnosis and envisage potential treatment options for glomerular diseases
- Describe optimal treatment options for hypertension
- Discuss how to appropriately manage acute and chronic kidney disease
- Recognize issues in dialysis (and transplantation)
- Discuss diagnosis and treatment of arterial hypertension (primary and secondary).
- Kidney biopsy: procedure and histopathology of normal kidney and major glomerular diseases (immunofluorescence)
- Acute renal insufficiency
- Nephrotic and nephritic syndromes
- Nephrolithiasis
- Hereditary nephropathies
- Essential Hypertension; Hypertension and the kidney

DIAGNOSTIC IMAGING AND NUCLEAR MEDICINE
(modules integrated to Nephrology) Dr. Brambilla, Dr. Poretti, Prof., Del Sole
Learning goals:
- Illustrate the indications and the methods of performance of the main methods of investigation through images of the urinary apparatus (chest X-ray, urography, urethrocystography, ultra sound, CT and MRI).
- Consider these methods of imaging in particular for the recognition of: renal masses, calcolosi renal-ureteral-bladder calculi, inflammatory diseases, and prostate disease.
- Recognise the main imaging of renal pathology using radiological semeiotics, also on the basis of normal contrastographic anatomy, (*on easy to interpret images*) (*consider* calculi, hydronephrosis, renal and bladder neoplasms and prostatic pathology).
- Know the main techniques of interventional radiology in the urological sphere - nephrostomy, arteriography and renal stenting, embolisation of renal bleeding and embolisation of varicocele.
  Nuclear medicine
- Describe the radiopharmaceuticals available to assess renal function.
- Describe the role of Nuclear Medicine in the diagnosis of renal diseases.

PATHOLOGY (modules integrated to Nephrology)   Prof. Roncalli, Dr. Di Tommaso
Learning goals
- Indications at the biopsy renal and criteria di adequacy;
- Illustrate the elementary lesions of the glomerulus;
- Illustrate the contribution of immunofluorescence and electronic microscopy in the diagnostics of the main glomerular pathologies
- Illustrate the epidemiology and natural history of prostatic neoplasms;
- Correlate the anatomopathological features of hyperplasia and carcinoma to clinical signs;
- Indicate what information is expected from the clinician on the biopsy and surgical specimen of a prostatic carcinoma;
- Interpret the meaning of degree and stage of a prostatic carcinoma;
- Illustrate the morphological features and natural history of benign and malignant renal neoplasms with special reference to renal carcinoma;
- Indicate the epidemiology, risk factors and the morphological pictures of urothelial neoplasms;
- Describe the natural history of the papillary and non-papillary carcinoma of the bladder with particular attention to the concept of multifocality of the carcinoma in situ and that of degree and stage;
- Indicate the potential and limits of the different cytological and histological tests in the diagnostics of urogenital tract tumours;
- Indicate what information there must be in an anatomopathological diagnosis of urothelial and prostatic neoplasms;
- Illustrate the morphological features and natural history of the main renal neoplasms
- Illustrate the morphological features and natural history of urothelial neoplasms

BASIC CONCEPTS IN PHARMACOLOGY

The module Get Started: Basic Concepts in Pharmacology (3rd year, 1st Semester) is devoted to introduce the students to the basics of Pharmacology in order to prepare them to deal with Pharmacology of System 1, 2 and 3. In particular, students will learn the basis of pharmacodynamics and pharmacokinetics and the organization of the autonomic nervous system.
Advanced Pharmacology, will be completed during the 4th year and introduces students to state-of-the-art pharmacology in selected topics.

Learning goals
- Describe how charge determines the distribution of drugs across biological compartments and how this is influenced by pH.
- Describe how transporters influence drugs absorption, distribution and excretion
- Define bioavailability and first-pass metabolism.
- Describe the consequences of drug binding to plasma proteins
- Distinguish drug metabolism by Phase 1 and Phase 2 reactions and identify the major enzymes involved.
- Describe the major molecular targets of drugs, with major emphasis on receptors.
- Discuss the concept of receptor occupancy and distinguish the difference between drug potency and efficacy.
- Illustrate the effects of full and partial agonists, competitive and non-competitive antagonists, inverse agonists and drugs that exhibit state- and use-dependence.
- Discuss the mechanisms of drug tolerance
- Describe the organization of central and peripheral synapses
- Describe structure and function of neuromuscular junction
- Discuss synthesis, storage and release of acetylcholine and monoamines
- Describe Degradation of acetylcholine and monoamines
- Illustrate pharmacology of the neuromuscular junction and use of botulinum toxins
- Illustrate the functional organization of the autonomic nervous system and discuss the influence of autonomic reflexes.
- Describe the molecules, the major receptor subtypes and mechanisms that mediate and regulate transmission at cholinergic neuro-effector junctions.
- Distinguish major classes of drugs that act on cholinergic neuro-effector junctions and major indications and contraindications for their use.
- Describe the molecules, the major receptor subtypes and mechanisms that mediate and regulate transmission at noradrenergic neuro-effector junctions.
- Distinguish major classes of drugs that act on adrenergic neuro-effector junctions and major indications and contraindications for their use.
- Describe the mechanisms and the functions of NANC (non-adrenergic non-cholinergic) fibres.

Renal pharmacology and diuretics (module integrated to Nephrology
 Learning goals
- Recapitulate regulation system of drug renal elimination
- Illustrate diuretic drugs
- Illustrate nephrotoxic drugs

DISEASES OF THE HEART AND VESSELS (Cardiology)
Prof. Agostoni, Prof. Condorelli

This module will focus on some relevant aspects of cardiology, which shall be discussed with a predominantly pathophysiological approach.

Lesson 1 Presentation of the course. A journey through cardiovascular diseases.
Learning goals:
- Discuss the risk factors and epidemiology of cardiac disease in developed and developing countries.
- Discuss cardiovascular disease markers.
- Discuss the importance of lifestyle (smoking, diet and exercise) and prevention for cardiovascular disease.
- Assess and manage patients with risk factors for cardiovascular disease.
- Discuss the mode of action of different prevention methods.
- Manage risk factors appropriately, including pharmacological and non-pharmacological therapies.

Lesson 2 Grading the severity of cardiovascular diseases through interview and objective evaluation.
Learning goals:
- Perform a medical interview and a general examination of the cardiac patient.
- Recognize cardiac sounds and the severity of the cardiovascular disease.

Lesson 3 Cardiopulmonary interaction and the cardiovascular response to exercise as tools to study the cardiac patient.
Learning goals:
- Discuss of the pathophysiology of lung–heart interactions.
- Discuss of the clinical and physiological modifications that occur during exercise.
- Discuss of Wasserman plots, CPET parameters and their correlation with prognosis.
- Evaluate exercise tolerance and differentiate between cardiovascular and pulmonary aetiology of exercise intolerance.

Lesson 4 Assessment of congenital cardiac abnormalities in adults.
Learning goals:

- Discuss the anatomy of the heart, veins and great vessels, their major congenital malformations and the principles of nomenclature.
- Discuss the physiology of the foetal and transitional circulations; aetiology of congenital heart disease, including the developmental anatomy of the heart and vasculature.
- Discuss the pathophysiology, natural history and complications of: valve and outflow tract lesions; septal defects; patent ductus arteriosus; Eisenmenger syndrome; coarctation of the aorta; Ebsteins's anomaly; aortic and pulmonary artery malformations; venous anomalies; transposition of the great arteries (complete and congenitally corrected); tetralogy of Fallot; congenital malformations of coronary arteries; cyanotic congenital heart disease and secondary erythrocytosis; and pulmonary hypertension in congenital heart disease.
- Evaluate adolescent and adult patients with simple congenital heart defects (grown-up congenital heart disease (GUCH), including those who have undergone cardiac surgery.
- Describe and recognize physical signs of congenital heart disease and its complications

Lesson 5 ECG and conduction disorders and arrhythmias.
Learning goals:

- Understand the epidemiology, pathophysiology, diagnosis and clinical features of arrhythmias and conduction disturbances.
- Understanding of the cellular and molecular mechanisms involved in the electrical activity of the heart; the anatomy and physiology of the conduction system; and the electrical vectors throughout the cardiac cycle.
- Understanding of the normal ECG and to recognize the characteristic appearances of, and explanation for, the ECG in the main pathological conditions.
- Understanding of the classification and definition of bradycardias, tachycardias, supraventricular arrhythmias (including atrial fibrillation and flutter) and ventricular arrhythmias.

Lesson 6 Heart failure.
Learning goals:

- Understanding of the epidemiology and prognosis of heart failure with reduced and preserved ejection fraction.
- Understand the definition of heart failure and recognize the different underlying causes and the precipitating factors of heart failure.
- Understanding of the pathophysiology of heart failure and systolic and diastolic dysfunction.
- To be able to evaluate the prognosis of the heart failure patient.
- To be able to manage acute and chronic HF.
- Understanding of the role of exercise training programmes in HF patients.
- Understand the complications of HF.

Lesson 7 Pulmonary hypertension and comorbidity affecting the heart.
Learning goals:
- Understanding of the pathophysiological classification of pulmonary hypertension and the type of investigations used for diagnosing pulmonary hypertension and recognizing the etiology.
- Understanding of the medical, surgical and interventional management of pulmonary hypertension.

Lesson 8 Inflammatory pathologies and endocarditis.
Learning goals:
- Myocarditis and pericarditis: understanding of the mechanisms underlying the disease, the pathophysiology of the disease and diagnostic and therapeutic approaches.
- Endocarditis: understanding of the epidemiology, aetiopathogenesis, pathophysiology, diagnosis and therapeutic approaches.
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Lesson 9 Genetic of cardiovascular diseases.
Learning goals:
- Understand the approaches used to identify the genetic predisposition to cardiovascular diseases.
- To be able to define monogenic vs. multifactorial cardiovascular diseases: description of examples.
- Understand the clinical impact of risk stratification using genetic tools.

Lesson 10 Coronary artery disease and atherosclerosis.
Learning goals:
- Understand myocardial ischemia: from pathophysiology to the clinical spectrum (angina, myocardial infarction).
- Comprehend the diagnostic tools for assessing myocardial ischemia.
- Define the basis of the therapeutic approaches.

Lesson 11 Arterial hypertension and vascular diseases.
Learning goals:
- Understand the pathophysiology and the clinical impact of arterial hypertension and of the vascular consequences of systemic diseases.
- Comprehend the therapeutic approaches for treating hypertension and vascular diseases.

Important notice:
The lectures do not cover all diseases of Heart and Vessels. In particular, the following topics need to be studied independently: Rheumatic Fever and Heart Diseases; Congenital Heart Diseases; Hypertrophic Cardiomyopathy; Degenerative Cardiac Diseases; Hypertension; Atherosclerosis and Diseases of the Vessels (Aneurisms, Inflammatory Vessel Diseases)

DIAGNOSTIC IMAGING AND NUCLEAR MEDICINE
(modules integrated to Cardiology) Dr. Brambilla, Dr. Poretti, Prof., Del Sole
Learning goals

- Illustrate the main non-invasive vascular imaging methods (CT angiography and MRA), also with reference to coronary CT, and discuss the indications and limits for the diagnosis of aneurism and aortic dissection, steno-occlusive peripheral arterial disease and arterio-venous malformations.
- Explain the principles of cardiological diagnostics based on chest X-ray and the use of echocardiography and cardiac MRI in valvular and myocardial (ischaemic, inflammatory and neoplastic) and pericardial disease.
- Illustrate the technique and indications of the various types of arteriography (with particular reference to coronary catheterisation and the arteriography of the carotid, renal and celiac-mesenteric arteries and those of the lower limbs) and venography (lower limbs, upper limbs, superior and inferior vena cava and portal venous system).
- Using the semeiotic arteriography of the arterial lesions, recognise the images of aneurism, stenosis and occlusion of the main arterial trunks (*on easy to interpret radiograms*).
- Illustrate the indications and methods of performance of the main techniques of vascular interventional radiology (angioplasty, stenting, embolisation and positioning aortic endograft).

Nuclear Medicine
- Describe the radiopharmaceuticals available to imaging myocardial perfusion and measure ventricular function.
- Describe strength and limits of Nuclear Medicine in the diagnosis of CAD, in comparison with other imaging modalities.

PATHOLOGY (modules integrated to Cardiology)   Prof. Roncalli, Dr. Di Tommaso
Learning goals
- List the clinical syndromes associated with ischemic heart disease
- Illustrate the alteration of vessels coronary during coronary artery disease correlate it with any clinical symptoms;
- Describe the macroscopic and microscopic alterations detectable in myocardial infarction;
- Illustrate the complications of the myocardial infarction describing its pathogenetic mechanisms
- Illustrate the features of bacterial endocarditis (acute and sub-acute) with particular reference to the aetiology, pathogenetic mechanism and anatomopathological aspects, comparing them with those of rheumatic endocarditis;
- Briefly illustrate the acute and chronic complications of endocarditis;
- Illustrate the cardiac and extra-cardiac repercussions of stenosis and valvular insufficiency;
- Describe the gross and microscopic appearance of an atherosclerotic plaque
- Understand how atherosclerotic lesions cause clinical events

- Describe the macroscopic alterations detectable in myocardial infarction;
- Describe the morphological aspects of the heart in heart failure;

PHARMACOLOGY (modules integrated to Cardiology)
Learning goals

- Recapitulate the determinants of intravascular volume, volume regulators and renal control of sodium excretion
- Describe the different transporters acting along the nephron
- Recapitulate pathophysiologic mechanism of edema formation, with emphasis on heart failure, nephrotic syndrome and cirrhosis
- Illustrate diuretic drugs and their action mechanisms
- Illustrate the therapeutic use of diuretics in cardiovascular medicine
- Recapitulate vascular smooth muscle contraction and relaxation
- Illustrate drugs modifying the vascular tone on the basis of their action mechanisms
- Illustrate the therapeutic use of drugs affecting vascular tone in cardiovascular medicine
- Recapitulate myocyte contraction and regulation of contractility
- Illustrate drugs acting on cardiac contractility
- Illustrate the therapeutic use of drugs modifying cardiac contractility in cardiovascular medicine
- Describe the pharmacologic classes of antiarrhythmic agents and their therapeutic use in cardiovascular medicine

2. COMMUNICATION

COMMUNICATION

Faculty
Moja, Lamiani, Montagna

Credits 8

Texbook:
M. Lloyd, R. Bor, Communication skills for Medicine, Churchill Livingstone Elsevier, 2009
Journal articles will be provided during lessons.

Overview of the block
This block is designed to give the student the basic concepts of communication and train him/her to apply them in daily practice. Building trust is one of the most relevant 'musts' in medical practice. In order to reach this goal, a doctor must be able to understand the complexity of the patient and his/her experience of illness, taking into account all the components of his/her culture, education, personality, values, and understand his/her ideas, feelings, fears, expectations, anxieties, as well as the family and social environment in which he/she lives.
Since learning communication skills requires a great deal of personal engagement and reflection, students are strongly invited to refer to the textbook and the articles provided at the end of all lectures.

EXAM
The evaluation of the student's knowledge of the basic principles of communication will be performed by a MCQ test at the end of the 2nd Semester.

Lecture 1: The Disease centred model in medicine
- Discuss the evolution of the clinical method (Disease centred)
- Define the Disease Centred medical approach
- Discuss the strengths and weaknesses of the Disease centred model with regard to doctor-patient relationships
- Illustrate the reason why we need a new clinical method

Lecture 2: Overview of the patient-centred clinical method in medicine
- Discuss the patient centred model in medicine

- Describe the concept of "agenda" and the difference with the concept of "illness"
- Discuss the four components of the patient's agenda: concerns, beliefs, expectations and context
- Discuss the strengths and weaknesses of the patient centred model

Lecture 3: Communication in a patient centred consultation I
- Describe the logic structure and the phases of the medical interview
- Discuss the following goals of communication in a clinical consultation:
- Gathering information
- Building the relationship
- Apply the basic communication techniques in a simulation

Lecture 4: Communication in a patient centred consultation II
- Describe the techniques to gather information
- Describe the techniques to give information
- Discuss the problem of empathy in the clinical consultation

Lecture 5 Values in communication
- Discuss the concept of values in medicine
- Describe the following values applied to clinical practice: Be beneficial, Do not harm, Autonomy, Confidentiality, Tell the truth, Distributive justice
- Describe and comment the following types of doctor-patient relationships: Paternalistic, Informative, Interpretative, Deliberative

Lecture 6: The role of communication in patient education and adherence
- Discuss the goals of patient education according to a patient centred model
- Describe the Prochaska Di Clemente's model for behavioral change

Lecture 7: Learning the patient centred method: the role playing strategies
- Describe the role playing method and its use in research and medical communication skills training
- Engage in a role-play to apply some of communication skills taught during the course

Exam program
- To discuss the goals of a disease-centred approach in a clinical consultation
- To discuss the goals of a patient-centred approach in a clinical consultation
- To discuss weak and strength points of the disease-centred model in medicine
- To discuss weak and strength points of the patient-centred model in medicine
- To discuss the concept of 'agenda' of the patients
- To discuss the areas of the 'agenda' of the patients (ideas, feelings, expectations, and context)
- To discuss the goals of communication in a clinical consultation
- To discuss the main techniques to gather information in a clinical consultation
- To discuss the main techniques to give information in a clinical consultation
- To briefly discuss the area of building a relationship in a clinical consultation
- To discuss the structure of a clinical consultation
- To discuss the concept of 'cues' and 'prompts'

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- To discuss the role of values in the relationship between doctor and patient
- To illustrate examples of ethical dilemmas in a clinical consultation
- To discuss the paternalistic model in a clinical consultation
- To discuss the informative model in a clinical consultation
- To discuss the concept of adherence
- To discuss the concept of patient education and the role of the patient centred approach in chronic disease

3. LABORATORY MEDICINE

LABORATORY MEDICINE

Faculty
Corsi Romanelli, Borghi, Ferrante, Montanelli, Gelfi.

Year / Semester
3rd year, 1st semester

Credits: 4

Overview
This block is aimed to give the students a general overview of the role that Laboratory Medicine plays in modern Medicine at the beginning of the clinical years. The block consists of three modules:

Clinical Pathology will provide the student with a general overview of the conceptual evolution of Laboratory medicine and its relationships to translational medicine and genomic medicine.
Clinical Microbiology will give the students the information regarding the main technical aspects of microbiology as applied to diagnosis in clinical practice.
Chemical Chemistry will bridge the gap between the clinical laboratory and medical management by relating pathophysiology to analytical results in health and disease. Will deal with defining analytical criteria for the medical usefulness of laboratory procedures, describe variables that affect tests and results, introduce new approaches and modern analytical tools and their impact on lab management and costs.
Students will apply the procedures required by international rules in daily practice in a chemical chemistry laboratory and learn how to use them during the clinical training.

Textbook
Clinical Chemistry
Tietz Textbook of Clinical Chemistry and Molecular Diagnostics

Exams
The exam will consist of a series of MCQs on the three modules at the end of the semester

CLINICAL PATHOLOGY

Lecture New tools in laboratory medicine

Clinical laboratories are an area of healthcare that has always undergone major changes because of technological advances and external economic pressures. In the recent past, many new diagnostic techniques and laboratory tests were introduced as a result of both research on the fundamental pathogenesis of diseases and the development of new methods in themselves. The two Nobel prizes awarded respectively to the inventors of monoclonal antibodies (G. Koehler and C. Milstein, 1984) and the polymerase chain reaction (K. B. Mullis, 1993) are only the most visible tips of a huge iceberg of innovation in the field. Without these techniques, many immunoassays and methods of molecular genetic testing currently taken for granted would simply not have been possible. On the other hand, in recent years, significant changes have been made to health care systems and care policies, largely because governments have had to address extremely complex economic issues.

Laboratory Medicine, supported by computerized information and expert systems, will promote the use of this new knowledge in a timely and responsible manner, contributing to the provision of better, more economic care by integrating pathophysiologic rationale and preferences of the clinicians responsible for the care of the patient with valid and up-to-date clinical research evidence. It is impossible to predict the future but that does not mean that it is impossible to prepare for it, keeping the best interest of the patient in mind. As laboratory professionals, we will remain viable only if we build our own future and educate others about the contribution that Laboratory Medicine can and does make to health care.

Lecture From bedside to bench and return: a translational relationship

Translational Medicine (TM) is the emerging field which focuses on using what is learned in pre-clinical studies to do better things in the clinic. Translational Medicine helps in the blocks of predicting, preventing, diagnosing and treating diseases. It also uses what can be gleaned in clinical studies to sharpen and improve what is done in pre-clinical efforts to discover new medicines. Translational medicine represents a paradigm shift in the biomedical research enterprise. Translational Medicine is a relatively young area of biomedicine in which pharmaceutical companies use a patient driven approach to drug development. Translational medicine involves the transformation of laboratory findings into new ways of diagnosing and treating patients. Many biotech companies are introducing Translational Medicine departments entrusted with the task of facilitating the transition of basic research into practical treatments and clinical trials.

Lecture The Omics world

The complete sequencing of the human genome has ushered in a new era of systems biology referred to as omics. This has transformed cell biology in academia and industry from a cottage industry in which genes or proteins are studied one at a time to a world where whole organelles and pathways are studied simultaneously. The term omics refers to the comprehensive analysis of biological systems. A variety of omics sub-disciplines have begun to emerge, each with their own set of instruments, techniques, reagents and software. The omics technology driving these new areas of research

consists of DNA and protein microarrays, mass spectrometry and a number of other instruments that enable high-throughput analyses. SImilarly, the field of bioinformatics has grown in parallel and, with the help of internet, rapid data analysis and information exchange is now possible. Omics will not only have an impact on our understanding of biological processes but the prospect of more accurately diagnosing and treating disease will soon become a reality. However, new technology is developing constantly and quickly so it is important that researchers keep up to date with the latest protocols, commercial products and other sources.

CLINICAL MICROBIOLOGY

Lecture The infectious disease laboratory
Learning goals
- Discuss the basis of Infectious Disease Laboratory Diagnosis (IDLD)and their relation with pathogenesis: when, where, what.
- Define when an Infectious Disease Laboratory need to be involved in the process of making a diagnosis
- Describe the special areas and structures that need to be present inside an Infectious Disease Laboratory
- Illustrate the viruses and bacteria infecting humans of common investigations in a Infectious Disease Laboratory

Lecture Cultivating microbial agents for IDLD.
Learning goals
- Define the classical methods employed in order to isolate and cultivating microbial agents
- Describe the classical methods employed in order to purify the cultivated microbial agents

Lecture Serological tests and direct search of microbial agents for IDLD: from staining to antigens to genes.
Learning goals
- Describe the methods used to search in the patient's serum the antigens of microbial agents and their antibodies
- Describe the principles and applications of the following different methods: ELISA, IFA, Western Blot
- Describe the methods employed to search, amplify and detect the nucleic acids of the microbial agents
- Define the different molecular methods as applied in a microbiological laboratory: Polymerase Chain Reaction (PCR), Reverse-Transcriptase PCR, Real Time PCR
- Describe the methods employed to characterize the amplified viral/bacterial genes: automatic sequencing, RFLP

Lecture Direct search of microbial agents for IDLD: from proteomic to future technology
Learning goals

- Describe the most innovative technologies employed in order to search microbial agents
- Illustrate the principles and applications of Isoelectrofocusing and bi-dimensional gel,
- Discuss the meaning and relevance of proteomics
- Discuss the principles and applications of mass spectrometer analysis,
- Discuss the next generation sequencing technique,
- Describe the principles and applications of the laser-based meth

CLINICAL CHEMISTRY

Lecture 1: Clinical Investigation Laboratory: from assay to data clinical management
Learning goals
- Illustrate the main use of the laboratory tests.
- Understand the place of clinical chemistry in medicine: the Lundberg loop.
- Describe the laboratory role for screening, diagnosis and monitoring of treatment.
- Define the emergency laboratory.
- Illustrate how the reference values are used in clinical practice.
- Discuss the limitations of population-based reference intervals.
- Elucidate the difference between reference interval and decisional limits.

Lecture 2: Specimen collection and storage. Point of care testing and automation
Learning goals
- Recognize the importance of correct blood collection in managing total patient care.
- Describe what is the correct specimen for the requested test.
- Differentiate between whole blood, plasma and serum.
- Describe the collection of the urine sample.
- Describe the collection of CSF.
- Illustrate the different stability of the biological samples.
- Understand and illustrate core lab and point of care testing.

Lecture 3: High throughput technologies. Contribution to patient stratification and monitoring
Learning goals
- Define the biological variation and its influence on laboratory results
- Define a high throughput technology.
- Define DNA microarray for SNPs profiling.
- Discuss the significance of high throughput DNA sequencing in clinical laboratory.
- Define pharmacogenetics and its role in patients monitoring.

Lecture 4: Biological fluids profiling: a new challenge in clinical laboratory
Learning goals

- Define why biological fluids should be profiled.
- Describe the most innovative technologies for profiling biological fluids.
- Discuss the meaning and relevance of profiling results.
- Define the relationship between biological fluid profiling and biomarkers identification.

Lecture 5: AMI management: present and future
Learning goals
- Discuss the historical development of the ECG and its limitations as a diagnostic tool for AMI.
- Define biochemical markers for AMI.
- Discuss their kinetic of release, sensitivity and specificity.
- Describe an ideal marker.
- Discuss the use of troponin in AMI management and define its limitations.
- Define future markers.

Lecture 6: The clinical laboratory in neuromuscular disorders management. Present and future perspectives
Learning goals
- Diagnosis of neuromuscular disorders.
- Define CK levels in neuromuscular disorders.
- Define methods for CK assessment.
- Discuss the significance of new biomarkers for patients follow up.
- Discuss if new technologies can be translated to clinical laboratory to improve diagnosis and follow up of neuromuscular disorders.

4. STATISTICS

STATISTICS

Faculty
Ambrogi, Bruzzi, Boracchi

Guest Lectures
Carlo Lavecchia (University of Milan)
Elia Biganzoli (University of Milan)

Year/semester:
1st Semester

Credits: 7

Textbook

J. Mark Elwood, Critical Appraisal of Epidemiological Studies and Clinical Trials
Third Edition, Oxford University Press

Additional sources

R. Bonita, R. Beaglehole, T. Kjellström, Basic epidemiology. 2nd edition.
World Health Organization.
<u>**Available free**</u> at: whqlibdoc.who.int/publications/2006/9241547073_eng.pdf
Marcello Pagano, Kimberlee Gauvreau Principles of Biostatistics, 2000, Duxbury
Press

Exam

Multiple choice at the end of the course covering each of the arguments developed
during the course.

Overview

Since the mid-nineteenth century, the idea that for treating a disease it was enough
to understand the patho-physiological processes and to prescribe medications or
other treatments that may interrupt or interfere with such processes became
predominant among physicians. This optimistic view, summarized by the Claude
Bernard's statement "Medicine is moving towards the final scientific resolution", is
countered, however, by a complex reality, in which the mechanisms of the disease
are often known only partially and sometimes unknown at all. Beneficial or adverse

effects of therapy are not always predictable nor can be deduced from the current knowledge of biological processes. As a typical example, the widespread practice of prescribing anti-arrhythmic drugs to patients with previous myocardial infarction who had ventricular arrhythmias can be mentioned. This practice had its rationale in the observation that subjects with post-myocardial infarction arrhythmias were at high risk of sudden death. Controlled clinical trials conducted later to assess the actual impact of such a therapy on the survival of these patients, rather than on patho-physiological processes, surprisingly showed that many of these drugs increased rather than decreased the risk of sudden death.

The purpose of this course is to develop student's critical ability to evaluate, on the basis of data reported in scientific literature, the diagnostic utility of medical history, physical examination and laboratory tests, the practical efficacy of prevention programs and therapeutic or rehabilitation protocols, and the validity of prognostic indices. The acquisition of these abilities, during the process of medical training, contributes to the formation of a methodological habitus suitable to integrate, in daily practice, the clinical knowledge coming from personal experience with the evidence provided by biosciences and good clinical research. A habitus which is today required for all physicians, general practitioners included, increasingly involved, even directly, in the evaluation of their own professional practice.

PART 1 (Risk and prognostic factors)

Most diseases are not the product of a single cause, but a complex concatenation multiple causes. In vitro and in animals experiments are not always adequate to identify all the factors that may be responsible for a disease or accelerate its adverse outcome. On the other hand, the identification of determinants of diseases cannot, for obvious ethical reasons, be based on studies involving the experimental exposure of humans to suspected risk factors. Hence the need for planned observational studies that do not require the intervention on the subject, but due to their nature, make it complex to interpret associations between exposure to risk factors and disease occurrence in terms of cause effect relationship.
The purpose of this module is to develop the student ability to carefully evaluate the role and importance of risk and prognostic factors, by learning the principles of planning observational studies. With this aim the students will develop skills to evaluate the measures of disease occurrence and association between risk factors and occurrence of the disease, or between prognostic factors and outcome of the disease, with particular attention to the problem of confounding.

1. *Introductory Lecture* Types of epidemiologic studies and measures of association between risk factors and disease.
   - Observational studies and their role in evidence based medicine
   - cross-sectional studies
   - retrospective or case-control studies
   - longitudinal or cohort studies
   - Measures of disease occurrence in epidemiology and clinical epidemiology: prevalence, incidence rate, cumulative incidence (risk).

- Measures of exposure-disease association: attributable risk, relative risk, odds ratio.

2. *Seminar* An Introduction to Epidemiology: Lifestyle and Disease Risk
(La Vecchia)

3. *group work* Cohort and case-control studies: cigarette smoking and lung cancer.

4. *Lecture* Why different studies have different results (systematic and random effects)?
- measures and parameters, sampling variability and estimates distribution.
- uncertainty of the estimates: standard error.
- the standard error of estimates of prevalence, incidence, relative risk and odds ratio.
- meta-analysis of observational studies

PART 2 (Evaluation of the efficiency of a diagnostic procedure)

Instrumental tests (blood count, determination of levels of analytes in serum and urine, determination of enzyme activities, spirometry, ECG, EEG, imaging) have an increasing role in medical diagnostic activity and tend to marginalize, rather than integrate, the traditional collection of anamnestic data and the recognition of signs and symptoms directly on the patient. However, the actual utility of a diagnostic test is not necessarily proportional to the quantity and quality of technology on which it is based.
The purpose of this module is to develop the student critical attitude to the use of diagnostic tests, by learning the concepts of normality and probability in medicine, and the acquisition of the ability to interpret the measurements of reliability and the indexes of the importance of a diagnostic test. In this module, finally, the links among pre- and post-test probability of disease and decision thresholds will be explored, highlighting the process that brings the physician from the diagnostic suspicion to the decision to prescribe a specific therapy.

1. *Lecture* How to measure the accuracy of a diagnostic test procedure
The clinical decision: quantifying uncertainty through probability
- Screening and diagnostic tests
- Test sensitivity and specificity
- I was found positive to a test: how much should I worry?
- I was found negative to a test: how can I feel comfortable?
- How much the outcome of a test can affect a clinical decision
- The rules SnNout and SpPin
- How to estimate sensitivity, specificity and predictive values

2. *Seminar* Health technology assessment
(Biganzoli)

3. *Group work* Evaluation of a screening test: HIV infection

4. *Lecture* Meaning and use of reference limits (ranges) in medicine. ROC curves and multiple diagnostic tests.
- Centiles of the distributions of quantitative indicators in medicine
- Definition of reference individual
- Factors that determine the reference values (normal values)
- Meaning and use of reference limits in medicine
- The choice of a threshold: ROC curves

PART 3 (Evaluation of efficacy and safety of therapy)

It seems that the first example of a clinical trial date back to 1836, when the French clinician Louis published the results of a study to determine whether the practice of bleeding, in those days still in common use, would benefit patients with pneumonia. By comparing the percentage of survivors in groups of patients undergoing or not undergoing phlebotomy he concluded that this practice was totally useless (possibly harmful). However it was not until the late forties that the use of clinical trials conducted in accordance with the principles of randomization and replication (already used by a dozen years in agricultural, industrial and biological experiments) began to spread.
The purpose of this module is to develop student's ability to critically evaluate the results of clinical trials, through learning the principles that underpin the planning and analysis of clinical trials as well as the concept of statistical inference, and the acquisition of the ability to interpret the measurements of efficacy and safety of a therapy.

Seminars The Ethics and methodology of clinical trials" (Boracchi, Bruzzi)
- Phases of clinical trials from Phase I to Phase IV
- Single-blind and double-blind studies
- Single-arm studies or controlled studies
- Randomization: why?

Lectures Deciding from study results: the logic of statistical inference
- The logic of statistical inference in controlled clinical trials: testing hypotheses
- Primary endpoint and effect size
- The variability of results in clinical trials
- Statistical significance and clinical importance
- Power and study size
- A random variable of great success: the Gaussian
- All roads (or almost) lead to the Gaussian
- Uncertainty of estimates: confidence interval of the parameter
- Meta-analysis of controlled clinical trials

Group works

1.   How to express the results of a clinical study regarding biologic markers. Comparing means: efficacy expressed by a biologic marker.

2.   How to express the results of a clinical study regarding a percentage of successes. Comparing proportions: efficacy expressed by the percentage of therapeutic successes.

3.   How to express the results of a clinical study regarding survival times.
Comparing survival curves: efficacy expressed through survival time.

Practical activity (computer lab):
The use of Excel for basic data collection, summarization, graphs and statistical analysis.
- Good practice for data collection
- Pivot tables
- Graphs
- Basic data analysis

PART 4 (Assessment of health system quality)

As outlined by David Spiegelhalter and colleagues: "Current demand for accountability and efficiency of healthcare organizations, combined with the greater availability of routine data on clinical care and outcomes, has led to an increased focus on statistical methods in healthcare regulation".
The purpose of this module is to develop student's ability to critically evaluate the results of studies aimed at the assessment of the performance of health systems, hospitals and wards.

5. FACULTY

PIERGIUSEPPE AGOSTONI (piergiuseppe.agostoni@cardiologicomonzino.it) MD, PhD. Associate professor of Cardiology at the University of Milan and adjunct associate professor of Critical Care and Respiratory Medicine at University of Washington, Seattle, WA. Teacher at several international Universities. President of CPX International. He runs the Heart failure Unit at the University of Milan. His research is dedicated to cardiopulmonary interaction and cardiopulmonary exercise testing. He is also an expert in cardiorespiratory adaptation to high altitude.

FEDERICO AMBROGI (federico.ambrogi@unimi.it) Ph.D. Researcher of Biostatistics, Faculty of Medicine, University of Milan. He teaches Bio-Medical Statistics to Biotechnologits, Logopedists and Developmental Neuropsychomotor Therapist and Survival Analysis at the Master in Medical Statistics and Statistical Methods for Epidemiology. His main research interests concern computational statistics and learning methodology for the analysis of complex biomedical data. He collaborates with the Functional Genomics and Proteomics group of Fondazione IRCCS National Cancer Institute, Milan, for the study design, data normalization and Computational processing.

GIORGIO BRAMBILLA MD, Head, Radiology and Diagnostic Imaging Department, Istituto Clinico Humanitas

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.

STEFANO CENTANNI (stefano.centanni@unimi.it) Md.Phd. is Full Professor of Pneumology at The University Of Milan. He attended the Pulmonary Division of the Mcmaster University, Hamilton, Canada and the Pulmonary Division Of The Mount Sinai Medical Center At The University Of Miami, Florida, USA. He is presently Head Of The Division of Pneumology at San Paolo Hospital, Milan. Professor Centanni is Director of The Post-Graduate Medical School in Respiratory Medicine at the University of Milan and has been the Italian National Delegate 2007/2009 at the ERS and the Italian National Delegate 2007/2012 at Fers. He has also served as President of Simer. Professor Centanni is author of more than 150 Scientific Publications In International and Italian Journals and several book Chapters and Books in the Field of Respiratory Medicine.

GIANLUIGI CONDORELLI (Gianluigi.condorelli@humanitasresearch.it) graduated in Medicine at the University "Federico II", Naples, Italy; he is board-certified in cardiology. He trained in molecular cardiology at Harvard University, Boston and molecular oncology at Thomas Jefferson University working with Carlo Maria Croce; he was faculty at Thomas Jefferson University and he is currently full professor of cardiology at the University of Milan, attending physician at the Humanitas Clinical and Research Center, where he directs the area of cardiovascular research and Adjunct professor of medicine at the University of California San Diego. He was previously professor of medicine at the University "La Sapienza", Rome, and Milano-Bicocca and Director of the Department of Medicine of the National Research Council of Italy. He received many highly competitive grants from agencies such as the National Institute of Health (RO1), USA, the European Research Council (Advanced grant), the American Heart Association, the Fundation LeDucq etc. He has published more than 140 manuscripts on peer-review journals (current H factor of 55) and received international prizes such as the Outstanding Achievement Award of the European Society of Cardiology.His work focuses on the molecular mechanisms of myocardial contraction and in particular on signaling and regulation of gene expression in the normal and failing heart. His studies led to the identification of the role of microRNAs in regulating myocardial function and their possible therapeutic use in cardiovascular diseases. Other ongoing studies focus on the epigenetic control of gene expression in myocardial diseases.

GIANPAOLO CORNALBA (Gianpaolo.cornalba@unimi.it) MD PhD, Full Professor of Radiology, University of Milan

MASSIMILIANO M. CORSI ROMANELLI,(mmcorsi@unimi.it) MD,PhD and Specialized in Experimental Endocrinology. He is Full Professor of Clinical Pathology and Director of the Laboratory Medicine Service 1- Clinical Pathology, Policlinico San Donato ,I.R.C.C.S, Milan. He was trained in basic immunology in the Microbiology and Tumor Biology Center by Prof. Rolf Kiessling (Karolinska Institutet, Sweden, 1995-96) and then in immunogenetic in the Christian De Duve Center (Universitè Catholique de Louvain, Brussels, Belgium, 1997). His main research interests are the pathogenesis, natural history and detection of new biomarkers in laboratory medicine. Over the past 20 years, he focused on the development of new diagnostic approaches, of reliable biomarkers for assessing the prognosis and response to therapy. He is the author of over 130 papers in refereed journals. He has served on a number of national and international committees and scientific societies and he is now Member of the Education Board of WASPaLM (World Association of Societies of Pathology and Laboratory Medicine) He is the secretary of the EUSPM (European Society of Predictive Medicine), and Scientific President of The AIPacMeM (Italian Association of Clinical Pathology and Molecular Medicine).

ANGELO SILVESTRO DEL SOLE (angelo.delsole@unimi.it) MD. Assistant Professor of Nuclear Medicine of the Faculty of Medicine and Surgery, Department of Health Sciences hosted by San Paolo Hospital, University of Milan, since 2003. He teaches medical students, specialist Schools students and imaging technology students. His main research interests are related to the field of PET and SPET imaging applications in Neurology and Psychiatry. The main research filed at the

moment is on the role of dopamine reuptake imaging in dementias. He is authors of more than 40 peer reviewed articles.

FABIANO DI MARCO (fabiano.dimarco@unimi.it) MD, PhD. Assistant Professor of Respiratory Medicine University of Milan, since 2006. He teaches medical and physiotherapy students, and is assistant in the Respiratory Unit of San Paolo Hospital,Milan.. His main research interests are related to the field of COPD, asthma, and ARDS. He has spent a research period in the Intensive Care Unit of Mondor Hospital (Creteil, France). He is author of 50 original articles in peer-reviewed international journals indexed in PubMed.

LUCA DI TOMMASO (luca.di_tommaso@humanitas.it) MD. Adjunct Professor of Pathology, University of Milan, in charge of cytology and breast, thyroid and thymic pathology at the Istituto Clinico Humanitas since 2003. His main field of interest is liver pathology with emphasis on the detection of early cancerous conditions using tissue biomarkers. He collaborates with several international peer-review journals. He is author of 51 original articles in national and international journals indexed in PubMed with an h-index of 11 (ISI Web of Science Thomson Reuters).

PASQUALE FERRANTE, (pasquale.ferrante@unimi.it) Md, Ph.D in Public health and Preventive Medicine, University of Milan, Ph.D. Infectious Diseases, University of Milan. Full Professor, Virology and Microbiology, Department of Public Health-Microbiology-Virology, University of Milan. Adjunct professor, Dept. of Neuroscience, School of Medicine, Temple University, Philadelphia, USA. Visiting Research Professor School of Biomedical Engineering, Drexel University, Philadelphia, USA.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 co-author of more than 200 indexed publications.

DIEGO FORNASARI (diego.fornasari@unimi.it) MD, PhD in Pharmacology & Toxicology; Post-doctoral fellow at Yale University, New Haven CT, Department of Internal Medicine (1990-1992); Researcher at the National Research Council (CNR), Centre of Molecular and Cellular Pharmacology (1993-1999); Assistant Professor of Pharmacology at University of Milan (1999-2005). Associate Professor of Pharmacology at University of Milan and associate member of the Institute of Neuroscience, CNR. Main scientific interests: I) Pharmacology and neurobiology of the Autonomic Nervous System with emphasis on the transcription factors that control its development and regulate the expression of receptors, ion channels and transporters. II) Pharmacological approaches to genetic diseases of the autonomic nervous system due to mutations of transcription factors (CCHS Congenital Central Hypoventilation Syndrome, Hirshsprung disease, neuroblastoma) III) Pharmacogenetics applied to cancer, Parkinson's disease and pain therapies IV) Pharmacology and pharmacogenetics of CYP450 with emphasis on CYP2D6.

RAFFAELLO FURLAN (raffaello.furlan@humanitas.it) Associate Professor of Medicine, University of Milan, and Director of the General Medicine – Clinica Medica ward at the Humanitas Clinical Institute (Rozzano, Milan). Since 1982 he has been co-author or principal authors of several clinical studies aimed at

assessing the changes in the neural mechanisms controlling the cardiovascular system in different physiological and pathophysiological conditions including the gravitational stimulus, physical exercise, athletic training, shift-work, syncope, dysautonomia, active ulcerative colitis, fibromyalgia and others. More recently he focused on the syncope short- and long-term prognosis and was the organizer and senior author of the multicenter study "STePS".
He is the author of 110 peer reviewed full papers on the major cardiovascular journals including Circulation, Hypertension, Journal of the American College of Cardiology, American Journal of Physiology and of several book chapters on the human neural control of the cardiovascular system.

CECILIA GELFI (cecilia.gelfi@unimi.it) Associate professor of Clinical chemistry and molecular biology. She teaches in specialist school of immunology, clinical biochemistry, medical biotechnology students and she is head of the Laboratory of Clinical Proteomics and Separation Sciences at LITA, (Segrate) in the Department of Biomedical Sciences for Health of the University of Milan. Her main research interests are: development of new methodologies for clinical applications, search for new biomarkers in neuromuscular disorders, cancer, inflammatory diseases, muscle ageing. She is author of 213 scientific publications in peer-reviewed international journals indexed in PubMed giving an h-index of 35 (ISI Web of Science Thomson Reuters).

MADDALENA LETTINO, MD (maddalena.lettino@unimi.it) Specialist in Cardiology and Chief of Clinical Cardiology Unit – IRCCS Istituto Clinico Humanitas. She has been Assistant Professor of Cardiology both at the State University of Milano and at the State University of Pavia. Past-Chairman of the Italian Working Group on Atherosclerosis, Thrombosis and Vascular Biology (ATVB), she is now Chairperson of the Italian Working Group on Acute Cardiac Care (ANMCO) and Board member of the ESC Acute Cardiovascular Care Association. Her main research interests are: acute coronary syndromes and antithrombotic treatments and anticoagulation in atrial fibrillation for the prevention of cardioembolic complications. In the past she has spent research periods studying atherothrombosis in animal models in the in Cardiovascular Biology - Cardiovascular Laboratory, Cardiovascular Institute (Chairman: V.Fuster MD), Mount Sinai Medical Center, New York, NY, USA.

MICHELA MATTEOLI (michela.matteoli@unimi.it) Full Professor in Pharmacology, University of Milano; degree in Biological Sciences and PhD in Neuroscience, University of Pisa; EMBO postdoctoral fellow, Yale School of Medicine; Visiting Scientist, University of Virginia School of Medicine, Department of Neuroscience; Head of Pharmacology and Brain Pathology *Lab* at the Humanitas Clinical and Research Center; member of the Boards of Directors of the Center of Excellence for Neurodegenerative Diseases and of the PhD School in Pharmacology, University of Milano. Member of the Editorial Boards of neuroscience journals. Main research interests: pharmacology of the synapse, synaptic defects in psychiatric diseases, cell-to-cell communication in neuroinflammatory and neurodegenerative diseases. Author of more than 100 research papers and scientific reviews and of Pharmacology book chapters. H-Index: 40. Member of national and international Societies in the field of Pharmacology and Neuroscience.

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ALESSANDRO MONTANELLI (alessandro.montanelli@humanitas.it) MD., Postgraduate in Haematology, in Clinical Biochemistry and in Clinical Nutrition. Director of Clinical Investigation Laboratory of Humanitas Clinical and Research Center, Rozzano, Milano. Seven years experience as Director of Clinical Pathology Department in the Hospital Crema. From 1997 to 2010 teaches Clinical Pathology, Molecular Methodology in Clinical Pathology and Clinical Chemistry in Postgraduate Medical School at University of Brescia and from 2010 teaches Clinical Biochemistry in Postgraduate School, University of Milan. His main research interests are: laboratory's clinical investigations on inflammation, autoimmunity and kidney disease.

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MASSIMO RONCALLI (massimo.roncalli@unimi.it) MD PhD. Full Professor of Pathology of the Faculty of Medicine and Surgery, University of Milan, since 2003. He got his PhD at the University of London in 1995 working on human and animal models of neuroendocrine tumors. He is the Director of Pathology since the beginning at the Istituto Clinico Humanitas (1996), with previous experiences in university hospitals. He teaches in postgraduate medical schools and he is a member of the Faculty of the Doctorate in Molecular Medicine and of the MD-PhD course of study of the Milan University. His main field of interest is liver pathology with emphasis on tumors and precancerous conditions where he has gained an international reputation. The development of diagnostic and predictive molecular markers for early diagnosis and prognosis is the current focus of interest. He is author of 150 original articles in peer-reviewed international journals indexed in PubMed with an h-index of 31 (ISI Web of Science Thomson Reuters).

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