

1. SYSTEM DISEASE 1

SYSTEM DISEASE

Faculty and Open Faculty: Calatroni, Civilini, Condorelli, Colombo, Cremonesi, Ferrante, Francone, Fesce, Lodigiani, Moroni, Panico, Reggiani, Reimers, Renne, Roncalli, Stefanini, Tritto, Torracca.

Coordinator: Gianluigi Condorelli

Tutors in the Simulation Labs: Rubino, Montagna, Tommasini, Solbiati, Panico, Ulian, Gerometta, Arena, Lanza, Canevari, Briani, Moroni, Reggiani, Calatroni

Credits 17

Overview of the Course

This course introduces the students to clinical medicine through the study of the "Diseases of the Kidney and Urinary System" (Nephrology) and the "Diseases of the Heart and Vessels" (Cardiology).

The course will cover most of the relevant diseases on a comprehensive basis, i.e. including pathology, pharmacology and imaging in relation to the diseases of the organ.

Teaching methods: Lectures, PBL, Case Method, Simulation

The students will learn and increase proficiency in history taking and physical examination through experience in the wards and in the simulation center.

Simulation is a technique to replace or amplify real experiences with guided experiences that evoke or replicate substantial aspects of the real world in a fully interactive manner

The vocational activities consist of 3 different learning environments, 2 weeks each (3 sessions):

*The wards: to collect the medical interview and to perform the physical examination under the supervision of faculty physicians

*The room of clinical case discussion: to collect the medical interview from a nephrological, cardiological patient (mostly through the presence of real patients)

*The skill lab: to learn the specific manoeuvres in a safe and organized environment under tutorship with task trainers and virtual reality

Textbooks



- Pathophysiology of Heart Disease: A Collaborative Project of Medical Students and Faculty-Leonard S. Lilly Wolters Kluver Ed (recommended**).
- Harrison's Principles of Internal Medicine, McGraw Hill (recommended*)
- Goldman's Cecil Medicine L. Goldman, A. I. Schafer, Elsevier
- Bates' Guide to Physical Examination and History Taking, Lynn S. Bickley
- Robbins and Cotran, Pathologic basis of disease, 10th Edition (Pathology)
- Primer of diagnostic imaging Weisselder et al Elsevier
- Squire's fundamentals of radiology Robert Novelline Harvard shorter books (Radiology)
- Learning Radiology William Herring ELSEVIER
- Essentials Radiology Gunderman Thieme
- 1) Written Exam: the written exam is based on a MCQ test divided into 5 blocks of 10 questions for each of the following subjects: Pathology, Pharmacology, Diagnostic Imaging, Nephrology and Cardiology. To pass the written exam, students must answer at least 60% of all questions.
- 2) Oral Exam: the oral exam is optional. The oral exam is a discussion of one or two key topics in nephrology and cardiology related to the Priority Presenting problems Portfolio (PPP Portfolio) as well as the topics explained during the lessons. The student will also be asked to contextualize these topics in a clinical case.

Scores of the written exam will be based converted into marks out of 30.

The optional oral exam will allow students to increase/decrease the mark of max 3 points.

The final score obtained during the exam (calculated from the average written mark of Cardiology and Nephrology) will be modified by the evaluation of the OSCE and the Portfolio with the following criteria: Portfolio (+ 2, -2); OSCE (+ 1, -1).

To obtain "30 e lode" students will need to score >80% of correct questions and have full marks at the evaluation of OSCE and Portfolio.

DISEASES OF THE KIDNEY AND URINARY SYSTEM (NEPHROLOGY)



This module is designed to provide comprehensive teaching of the pathophysiology and clinical aspects of kidney diseases, electrolytes and acid-base disorders.

The most recent diagnostic and therapeutic tools in the management of patients with kidney diseases will be discussed.

Students are invited to refer to the textbooks to deepen the issues covered in the lessons.

Suggested Textbooks

- Harrison's Principles of Internal Medicine, 20th edition, McGraw Hill (recommended)
- National Kidney Foundation Primer on Kidney Diseases, 8th Edition, Elsevier (alternative)
- Comprehensive Clinical Nephrology, 6th Edition, Elsevier (just for the deepening of selected topics)

Suggested Online Resources

- AJKD Core Curriculum in Nephrology (https://www.ajkd.org/content/corecurriculum)
- AJKD Atlas of Renal Pathology II (https://www.ajkd.org/content/atlasofrenalpathologyii)
- KDIGO Guidelines (https://kdigo.org/guidelines/)
- 2018 ESC/ESH Clinical Practice Guidelines for the Management of Arterial Hypertension (https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Arterial-Hypertension-Management-of)

Learning outcomes

Introduction to Nephrology

- Describe the physiology and the major functions of the kidneys:
 - o excretion of waste products
 - o control of body fluids and pressure
 - o electrolyte homeostasis and acid-base balance
 - o production of hormones
- Discuss glomerular filtration rate (GFR) regulation under physiological and pathological conditions (e.g. intravascular volume depletion or fluid overload)
- Discuss how GFR is measured or estimated, knowing the pros and cons of estimated GFR formulas
- Collect a detailed clinical history and perform an in-depth physical examination in order to diagnose renal diseases and their causes
- Discuss the causes and the differential diagnosis between acute and chronic kidney dysfunction
- Describe normal and pathological urinalysis and normal and pathological urine sediment
- Recall the main immunological investigations required for the diagnosis of some causes of intrinsic acute renal failure

Potassium disorders

 Describe causes, clinical features, diagnostic approach and principles of therapy of hyperkalemia and hypokalemia

Extracellular Fluid Volume and Sodium Disorders

- Describe causes, clinical features, diagnostic approach and principles of therapy of disorders of sodium and water homeostasis (hypernatremia and hyponatremia)
- Discuss the forces involved in edema formation
- Describe the pathogenesis of edema. Discuss how edema forms in congestive heart failure, cirrhosis and nephrotic syndrome
- Discuss the rationale and the clinical use of diuretics in fluid overload and edema

Calcium and Phosphorus Disorders



- Describe the physiology of calcium and phosphorus metabolism
- Describe causes, clinical features, diagnostic approaches and principles of therapy related to calcium and phosphorus

Acid Base Disorders

- Discuss how acid-base balance is assessed in clinical practice
- Describe the causes, clinical features, diagnostic approach and principles of therapy of:
 - o metabolic acidosis
 - o metabolic alkalosis
 - o respiratory acidosis and alkalosis
 - o mixed acid-base disturbances

The Approach to Glomerular Disease Syndromes and Renal Biopsy

- Define isolated urinary abnormalities and macroscopic hematuria of glomerular origin
- Define nephrotic syndrome and recall the major primary and secondary causes
- Define nephritic syndrome and rapidly progressive renal insufficiency recall the major primary and secondary causes
- Discuss the indications for renal biopsy, the contraindications and the potential harmful consequences
- Describe the histology of the glomerulus, underlining the possible sites of damage (capillaries, endothelial epithelium, basement membrane, visceral epithelium, urinary space and mesangium)
- Discuss the main histologic patterns of glomerular diseases
- Regarding the distribution of glomerular changes, define the terms focal, diffuse, segmental and global
- Describe the definitions: tip lesion, collapsing lesion, endocapillary proliferation, mesangial hypercellularity, extracapillary proliferation and crescents

Major Primitive Glomerulonephritis

- Define primary glomerulonephritis (GN)
- Describe the most frequent subtypes of primary GN, focusing on their clinical presentation, physiopathology, and natural course
- Discuss whether, when and how a patient with a defined primary GN should receive "etiologic" treatment to prevent the disease progression
- Recognize the signs or symptoms that may raise suspicion of the presence of a glomerular disease
- Know the clinical approach for the diagnosis of primitive glomerulonephritis
- Discuss the prognosis of primitive glomerulonephritis
- Describe the histology of:
 - o Minimal change disease
 - o Membranous nephropathy
 - o Focal and segmental glomerulosclerosis
 - o IgA nephropathy
 - o Membranoproliferative glomerulonephritis/ C3 nephropathy
 - o Acute postinfective glomerulonephritis

Secondary Glomerular Diseases

- Describe the most frequent types of secondary glomerular diseases, focusing on their clinical presentation, physiopathology, and natural course
- Define the classification of vasculitides, identifying those of renal significance
- Discuss the epidemiology, causes, clinical features, diagnostic approach and principles of therapy of vasculitides



- Describe the renal involvement in systemic vasculitides, with particular attention to the etiopathogenesis and to the natural history and prognosis of these diseases
- Briefly discuss the epidemiology, etiopathogenesis and clinical features of systemic lupus erythematosus (SLE)
- Describe renal involvement in SLE (lupus nephritis)
- Describe the renal histopathological patterns of vasculitis and SLE
- Describe the main therapies for SLE and its prognosis
- Discuss anti-GBM disease
- Discuss Henoch-Schonlein purpura

Acute Kidney Injury (AKI): overview and Pre-renal AKI

- Define AKI considering its current classification (KDIGO Clinical Practice Guideline for Acute Kidney Injury)
- Discuss the current epidemiology of AKI, considering the differences between community- and hospital-acquired AKI
- Describe symptoms and signs of AKI and those of the conditions that can precipitate it
- List the most threatening consequences of AKI that may require an urgent dialytic treatment
- Describe the etiopathogenetic classification of AKI (pre-renal, intra-renal, post-renal), bearing in mind the principal causes of AKI in each category
- Describe the diagnostic approach to a patient with AKI
- Describe the pathophysiological bases of kidney damage in pre-renal AKI
- Describe the main causes, the diagnostic approach and the principles of therapy of pre-renal AKI
- Discuss what options are available for volume resuscitation and the guiding principles behind intravenous fluid replacement
- List the main causes of intrinsic AKI and discuss the etiopathogenetic mechanisms of kidney damage (glomerulonephritis, vasculitis, rhabdomyolysis, hemolysis, radiocontrast agents, hematological and oncological diseases, thrombotic microangiopathy, malignant hypertension, atheroembolic disease and toxins/drugs)
- Discuss the etiopathogenesis of acute tubular necrosis (ATN) and describe the histopathological picture
- Describe clinical picture, diagnostic approach and principles of therapy of ATN
- Describe the main causes of acute and chronic tubulo-interstitial nephritis
- Discuss the mechanisms of drug-induced nephritis
- Describe the different mechanism through which NSAIDs may affect kidney function
- Describe the main clinical features of thrombotic microangiopathy
- Describe the main causes of post-renal AKI
- Discuss the pathophysiology of AKI caused by an obstructive-disease
- Discuss the most useful tests for the diagnosis of urinary tract obstruction
- Discuss the epidemiology, causes, clinical features, diagnostic approach and principles of therapy of retroperitoneal fibrosis

Pregnancy related kidney changes and diseases

- Describe the main kidney physiological changes that occur in pregnancy
- Describe urinary abnormalities during pregnancy, knowing how to differentiate physiological from pathological ones
- Describe the pathophysiology, clinical presentation, clinical course and principles of therapy of the main kidney diseases in pregnancy



• Describe pathophysiology, clinical course and principles of therapy of hypertensive disorders of pregnancy (preeclampsia-eclampsia, chronic hypertension, gestational hypertension)

Dysproteinemias and Amyloidosis

- Define pathogenesis of MGRS, focusing on the different types of renal involvement in B-cell or plasma-cell clonal disorders
- Discuss how to evaluate patients with suspected MGRS
- Discuss the management of MGRS

Hypertension

- Describe the pathophysiology of nephroangiosclerosis and its implications of kidney function Define hypertension and discuss the major classifications
- Describe how BP must be correctly measured
- Discuss the etiopathogenetic classification of hypertension, with particular emphasis on the renal causes of hypertension
- Discuss the pathophysiological mechanisms through which parenchymal renal disease may lead to the development of hypertension
- Define the clinical features and diagnostic approach of renovascular disease, recalling differential diagnosis with other forms of hyperaldosteronism
- Discuss the therapy and clinical outcomes of hypertension in patients with renal disease
- Describe the epidemiology, clinical presentation and clinical course of hypertensive nephropathy
- Describe the histopathological patterns of hypertensive nephropathy
- Discuss the management of hypertensive nephropathy and the strategies that may be adopted to slow its progression

Diabetic Nephropathy

- Briefly describe the main types of diabetes mellitus (causes, symptoms, diagnostic approach and principles of therapy)
- Describe the epidemiology, clinical presentation and clinical course of diabetic nephropathy
- Discuss the strategies that may be adopted to slow diabetic nephropathy progression
- Describe the histopathological patterns of diabetic nephropathy

Cystic Diseases and Other Hereditary Kidney Disorders

- Define the clinical criteria for diagnosis of autosomal dominant polycystic kidney disease (ADPKD) and describe the pathogenesis and clinical history of ADPKD, autosomal recessive polycystic disease, cystic disease of the renal medulla, and acquired cystic kidney disease
- Describe inherited disorders associated with generalized dysfunction of the proximal tubule (renal tubular acidosis [RTA] type 2 and Fanconi syndrome)
- Describe inherited disorders associated with specific distal tubule transport defects (RTA Type 1 and 4, Bartter syndrome, Gitelman syndrome, Liddle syndrome)
- Describe the epidemiology, clinical presentation and clinical course of Alport syndrome and Fabry disease

Hepatorenal and Cardiorenal Syndrome

- Define hepatorenal syndrome
- Discuss the pathophysiological mechanisms of hepatorenal syndrome
- Describe the clinical features, diagnostic approach and principles of therapy of hepatorenal syndrome
- Define cardiorenal syndrome and its classification



- Discuss the pathophysiological mechanisms of cardiorenal syndrome
- Describe the management of cardiorenal syndrome

Chronic Kidney Disease

- Know the definition and the staging of chronic kidney disease (CKD), according to KDIGO guidelines
- Describe the clinical features of CKD, including those of terminal uremia
- Discuss how to distinguish CKD from AKI through the patient's history, laboratory tests and imaging
- Discuss the two most common causes of CKD in Western countries: diabetic nephropathy and vascular nephroangiosclerosis
- Describe the consequences of CKD on water and electrolyte homeostasis (volume expansion, hyperkalemia, acidosis, hypocalcemia and hyperphosphatemia)
- Discuss the rationale of nutritional therapy in CKD
- Briefly describe what treatments slow the progression of CKD and improve symptoms
- Discuss the most relevant aspects in the preparation of CKD patients for renal replacement therapies
- Describe the effects of CKD on mineral metabolism, including secondary and tertiary hyperparathyroidism and renal osteodystrophy
- Discuss the major therapeutic approaches to bone disorders in CKD
- Discuss the clinical features of anemia in CKD patients
- Discuss the therapeutic approaches to anemia in CKD, including erythropoiesis-stimulating agents (ESAs)
- Discuss the pathophysiological basis of cardiovascular disease in CKD

Dialysis

- Briefly describe the features of hemodialysis and peritoneal dialysis, recalling the underlying physical principles
- Describe briefly the continuous renal replacement therapy types, recalling the underlying physical principles
- Describe the types of vascular access for hemodialysis
- Discuss the indications for dialysis in the setting of AKI and CKD

Lesson 18 – Kidney Transplantation

- Briefly describe kidney transplantation, knowing the steps and the procedures that precede the transplantation
- Describe the pathophysiology of the different types of rejection (hyperacute, acute and chronic; cellular and antibody-mediated) in kidney allotransplantation
- Describe the main pathologic events other than acute rejection that can occur in the early and in the late post-transplant period
- Describe the immunosuppressive drugs used to protect transplanted kidney from rejection, outlining pros and cons of these drugs

DISEASES OF THE HEART AND VESSELS (Cardiology)

This module will focus on some relevant aspects of cardiology, including pathophysiology, functional and structural semeiotics, clinics and therapeutic pharmacology of cardiovascular diseases, including broad concepts of cardiovascular surgery and cardiovascular diseases of the young.



Basic semeiotics for patient evaluation in cardiovascular medicine

Learning goals:

- Students should acquire knowledge on how to perform a comprehensive history taking and a general
 examination of the patient with cardiovascular disease.
- Students should be able recognize cardiac sounds and correlate them to the underlying pathology.

The Electrocardiogram

Learning goals:

- Describe how to perform an ECG. Theory of bipolar peripheral leads and unipolar pre-cordial leads of the baseline human ECG. Description of the theory of dominant vector orientation and its influence on the surface ECG amplitude and duration waveform
- Describe how to interpret an ECG. At the end of the course, the student will be able to
 - o distinguish the P wave, the QRS complex and the ST-T wave segments of the baseline ECG
 - recognize the fundamental findings associated with bradycardia and with tachycardia syndrome in real life ECG recording
 - recognize the fundamental findings associated with ST segment depression/elevation syndrome in real life ECG recording
 - correlate the fundamental findings of pathological real life ECG variations with the underlying clinical condition
 - identify and describe the fundamental therapies and the expected outcomes in response to the pathological real life ECG variations

Risk factors and epidemiology of cardiac diseases

Learning goals:

- Illustrate the global epidemiology of cardiac disease.
- Discuss the definition of risk factors and the impact of lifestyle on CV diseases and their prevention.
- Define some strategies for the prevention of risk factors.

Lesson 4. Tools for assessing cardiovascular diseases

Learning goals:

 Illustrate the main radiological techniques for the evaluation of cardiac function and for the assessment of cardiovascular diseases.



- Recognize normal cardiac anatomy on chest X-ray (assessment of heart size and normal contours of the heart) and echocardiography. Foundamentals of cardivascular anatomy on cardiac CT and cardiac MR.
- Imaging findings in common cardiovascular diseases.
- Describe the basic principles of imaging stress tests.

Coronary artery diseases 1: pathophysiology and medical management

Learning goals:

- Discuss myocardial ischemia: from pathophysiology to clinical presentation.
- Clarify the diagnostic tools for assessing myocardial ischemia.
- Define the basis of therapeutic approaches.

Acute coronary syndromes and cardiogenic shock

Learning goals:

- the basic mechanisms of acute coronary syndromes.
- the different presentations of acute coronary syndromes.
- Discuss risk stratification in patients with acute coronary syndromes.
- Define the management of patients with non-ST-segment elevation and ST-segment elevation.
- Describe the pathophysiology and define the management of cardiogenic shock.

Heart failure 1: basic mechanisms and pathophysiology

Learning goals:

- Discuss the epidemiology and prognosis of heart failure with reduced and preserved ejection fraction.
- Describe the definition of heart failure and recognize the different underlying causes and precipitating factors.
- Discuss the pathophysiology of heart failure and systolic and diastolic dysfunction.

Cardiac arrhythmias 1: basic mechanisms and pathophysiology

Learning goals:

 Distinguish the epidemiology, pathophysiology, diagnosis and clinical features of arrhythmias and conduction disturbances.



- Illustrate 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.
- Indicate how to recognize the characteristic appearances of, and explanation for, the ECG in the main pathological conditions.
- Discuss the classification and definition of bradycardia, tachycardia, supraventricular arrhythmia (including atrial fibrillation and flutter) and ventricular arrhythmia.

Essential hypertension

Learning goals:

- Discuss the pathophysiology and clinical impact of arterial hypertension and of the vascular consequences of systemic diseases.
- Discuss the therapeutic approaches for treating hypertension and vascular diseases.

Coronary artery disease 2: invasive diagnostics and treatment

Learning goals:

- Illustrate the invasive diagnostic tools for assessing coronary artery disease and myocardial ischemia.
- Define the basis of therapeutic approaches, with a focus on the clinical indications for myocardial revascularization.
- Discuss the treatment options for myocardial revascularization.
- Discuss the indications for percutaneous and surgical myocardial revascularization.
- Discuss optimal medical management after myocardial revascularization.

Heart Failure 2: clinics and therapeutics

Learning goals:

- to be able to distinguish acute from chronic HF.
- to be able to understand the bases of acute heart failure treatment
- understanding the bases of therapeutic options for chronic heart failure treatment
- understanding the major prognostic components in heart failure.

Cardiac arrhythmias 2: clinics and therapeutics

Learning goals:

- Present the mechanism of action of the various classes of anti-arrhythmic drugs and their use in the clinic, as related to the classification of arrhythmias.
- Discuss the basic functioning of the pacemaker and its indications.



- Describe the basic functioning of the implantable cardioverter–defibrillator (ICD) and its indications for arrhythmia prevention.
- Discuss the flow-chart of therapeutic options in arrhythmias, with clinical examples

Clinical and surgical approaches for great vessel disease

Learning goals:

- Discuss the epidemiology, pathophysiology, diagnosis and clinical features of aneurysms and occlusive artery diseases in different anatomical settings.
- Define the basis of open or endovascular therapeutic approaches.
- Introduce planning and sizing for vascular diseases.

Cardiac valve diseases

Learning goals:

- Define the pathophysiology and clinical presentation of cardiac valve diseases.
- Discuss the clinical evaluation of cardiac valve diseases.
- Discuss the diagnostic tools for assessing cardiac valve diseases.
- Discuss the treatment options and indications for intervention for cardiac valve diseases.
- Discuss the optimal medical management after interventions for cardiac valve diseases.
- Multidisciplinary integration
 - Radiology: describe the role of non-invasive cardiac imaging in the diagnosis of cardiac valve diseases.

Endocarditis

Learning goals

- Illustrate the epidemiology and the etiopathogenesis of infective endocarditis.
- Discuss the clinical presentation and complications of infective endocarditis.
- Discuss diagnostic tools for assessing infective endocarditis.
- Discuss antimicrobial therapy for infective endocarditis.
- Discuss the recommendations for prophylaxis of infective endocarditis.
- Discuss the indications for and timing of surgery for infective endocarditis.

Assessment of congenital cardiac abnormalities in adults

Learning goals:

- Discuss the anatomy and the development 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.

- Describe 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.

Myocarditis and diseases of the pericardium

Learning goals

- Discuss the mechanisms underlying the disease and the pathophysiology of myocarditis.
- Discuss the diagnostic and therapeutic approaches of myocarditis.
- Discuss the mechanisms underlying the disease and the pathophysiology of pericarditis.
- Discuss the diagnostic and therapeutic approaches of pericarditis.

Primary cardiomyopathies

Learning goals:

- Review the genetics and basic mechanisms of primary cardiomyopathies
- Discuss the etiology classification and pathophysiology of the diseases
- Discuss the possible therapeutic strategies
- Multidisciplinary integration
 - Radiology: describe the role of non-invasive cardiac imaging in the diagnosis of cardiomyopathies.

Vascular diseases 2: venous thromboembolisms (VTE), deep vein thrombosis (DVT), and pulmonary embolism (PE)

Learning goals:

- Discuss the mechanisms of blood clot formation at the basis of VTE.
- Discuss the pathophysiology, symptoms and diagnosis of VTE and DVT.
- Discuss the complications, its prevention (risk assessment) and the therapeutic options of DVT.
- Discuss the pathophysiology, clinics and therapy of PE.
- Multidisciplinary integration
 - o Radiology: describe the role of non-invasive cardiac imaging in the diagnosis of PE.

Cor Pulmonale - Pulmonary hypertension

Learning goals:

- Discuss the pathophysiological classification of pulmonary hypertension and the type of investigations used for diagnosis and recognizing the etiology.
- Discuss the medical, surgical and interventional management



Principles of Cardiovascular Surgery

Learning goals:

- Describe the surgical approaches to cardiac diseases.
- Describe the basic techniques for cardiac surgery (coronary artery bypass surgery, valvular replacement/repair, correction of congenital diseases)
- Describe the principles of extracorporeal circulation

DIAGNOSTIC IMAGING (nephrology)

- Illustrate indications and technique of the main methods of investigation through images of the urinary apparatus (chest X-ray, urography, cystography, ultra sound, CT and MRI).
- Consider these methods of imaging for the recognition of: renal masses, renal-ureteral-bladder stones, inflammatory diseases, prostate diseases.
- Recognize 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 prostate pathology).
- Discuss the main techniques of interventional radiology in urology nephrostomy, arteriography and renal stenting, embolization of renal bleeding and embolization of varicocele.
- Describe the radiopharmaceuticals available to assess renal function.
- Describe the role of scintigraphy in the diagnosis of renal diseases.

DIAGNOSTIC IMAGING

Suggested textbooks:

- William Herring. Learning Radiology (Third Edition). Elsevier.
- Gunderman et al. Essential Radiology. Thieme

Imaging of the kidney and urinary system

- Illustrate indications and technique of the main methods of investigation through images of the urinary apparatus (chest X-ray, urography, cystography, ultra sound, CT and MRI).
- Consider these methods of imaging for the recognition of: renal masses, renal-ureteral-bladder stones, inflammatory diseases, prostate diseases.
- Recognize 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 prostate pathology).
- Discuss the main techniques of interventional radiology in urology nephrostomy, arteriography and renal stenting, embolization of renal bleeding and embolization of varicocele.
- Describe the radiopharmaceuticals available to assess renal function.
- Describe the role of scintigraphy in the diagnosis of renal diseases.



Cardiovascular imaging

- Illustrate the main non-invasive vascular imaging techniques (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 artero-venous malformations.
- Explain the principles of cardiologic imaging 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, recognize 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, embolization and positioning aortic endograft).
- Describe the radiopharmaceuticals available to image myocardial perfusion and measure ventricular function.
- Describe strength and limits of myocardial scinitgraphy in the diagnosis of CAD, in comparison with other imaging modalities.

PATHOLOGY

Suggested textbooks:

• Aster, J. C., Abbas, A. K. (2020). Robbins & Cotran Pathologic Basis of Disease. Elsevier.

Pathologic basis of heart diseases

Lesson 1. Atherosclerosis

Learning objectives:

- Describe impact of atherosclerosis to the global burden of deaths.
- Illustrate acquired and inherited risk factor of atherosclerosis.
- Define atherosclerosis and list its acute and chronic clinical manifestation.
- Illustrate the pathogenesis of atherosclerosis, describing the *response to injury* hypothesis.
- Define the term xanthoma, intimal thickening, fibroatheroma.
- Discuss how the different cap type might clinically manifest.
- Correlate the site and severity of atherosclerosis to its clinical manifestations.
- Illustrate the complications of atherosclerosis.

Lesson 2. Ischemic Heart Disease Learning Objectives:

- Define ischemic heart disease.
- List the clinical presentations of ischemic heart disease.
- Define acute, subacute and healed myocardial infarction.



- Correlate the clinical presentation with the type and the extent of vessel involvement.
- Illustrate the evolution of gross and microscopic changes in myocardial infarction.
- Illustrate the complications of myocardial infarction.

Lesson 3. Endocarditis

Learning Objectives:

- Define rheumatic fever and rheumatic heart disease.
- Describe the pathogenesis of rheumatic fever.
- Illustrate the morphologic element and the clinical outcomes of rheumatic fever.
- Illustrate complications of rheumatic heart disease.
- Define and illustrate the characteristics of acute and subacute infective endocarditis
- Describe the types of noninfected vegetations.
- Compare and contrast the major forms of vegetative endocarditis.
- Describe the complication of endocarditis.

Pathologic basis of kidney, lower urinary tract and male genital system

Lesson 4. Introduction to renal pathology

Learning objectives:

- Illustrate the pathologic response of the glomerulus to injury.
- List the pathogenetic mechanisms of glomerular injury.
- Describe the main pathologic features of glomerular diseases comparing and contrasting primary glomerulopathies and systemic diseases with vascular involvement.
- Illustrate the elementary lesions of the glomerulus.
- Illustrate the contribution of immunofluorescence and electronic microscopy in the diagnostics of the main glomerulopaties.
- Describe the main tubulo-interstitial diseases focusing on the patterns of tubular damage.
- Correlate the onset and distribution of pyelonephritis with the main etiologies.
- Describe the pathogenesis and morphologic features of nephrosclerosis.

Lesson 5. Kidney tumors

Learning objectives:

- Describe the main symptoms and signs of renal tumors.
- Illustrate and describe the gross and microscopic features of the clear cell renal cell carcinoma.
- Describe the impact of grade and sarcomatoid change in renal cell carcinoma.
- Illustrate the features used in renal cell carcinoma staging.
- Describe the microscopic features of the papillary renal cell carcinoma.
- Describe and compare gross and microscopic features of chromophobe renal cell carcinoma and oncocytoma
- Illustrate the role of immunohistochemistry in differential diagnosis of renal cell tumors

Lesson 6. Urinary tract tumors Learning objectives:

- Describe the microscopic anatomy of the muscular layers of the urinary bladder.
- Define a (bladder) diverticulum.



- Indicate the epidemiology, risk factors and the morphological features of the neoplasms of the urothelium.
- Describe the natural history of papillary and non-papillary neoplasms of the bladder with emphasis on in situ carcinoma, muscle invasiveness, multifocality, grading and staging;
- Indicate the potential and limits of the different cytological and histological procedures in the diagnostics of urogenital tract tumours;
- Indicate what information are needed for a pathological report of a urinary tract tumor to be complete.

Lesson 7. Prostate pathology

Learning objectives:

- Describe the zonal anatomy of the prostate, considering the different diseases and symptoms related to it
- Illustrate the morphological characteristics of benign prostatic hyperplasia.
- Illustrate the epidemiology, risk factor and natural history of prostatic neoplasms.
- Illustrate the diagnostic strategy of prostate cancer.
- List the prognostic parameters of prostate cancer.
- Define and compare the Gleason pattern, the Gleason score and the Grade group.
- Indicate what information are needed for a pathological report of prostate carcinoma to be complete.

Lesson 8. Testicular tumors

Learning objectives:

- Describe the epidemiology of testicular tumor.
- Describe the age distribution of different histotypes.
- Illustrate the rationale for classification in testicular tumor.
- Define germ cell neoplasia in situ and describe its pathogenetic role in germ cell neoplasia.
- Define the terms prepubertal-type, postpubertal-type, pure, mixed and regressed germ cell tumor.
- Illustrate the clinical, serological, gross, microscopic and immuhistochemical features of seminoma, embryonal carcinoma, yolk sac tumor, choriocarcinoma, teratoma.
- Describe the staging system of testicular tumor.

PHARMACOLOGY

Overview

The course focuses on the pathologies of the cardiovascular and renal systems, and on the possible therapeutic approaches to such pathologies.

The pharmacological approach to the cardiovascular and renal systems is discussed by taking two distinct perspectives and subsequently integrating them: initially, the various molecular targets of pharmacological intervention are considered (ion channels, transporters, enzymes, transmitter receptors), the clinical effects of stimulating or inhibiting each of such targets are discussed, and the drugs that are available to these scopes are examined in detail; afterwards, all these drugs will be reexamined in terms of their use in facing major clinically relevant conditions — such as cardiac ischemia, heart failure, hypertension and arrhythmias.

THE TARGETS OF CARDIOVASCULAR AND RENAL DRUGS



Lecture_Drugs that target ion channels.

- Recall the roles of ion channels in cell excitability and briefly mention the pathologies related to ion channel dysfunctions (so-called channelopathies).
- Recall the relevance of sodium channels with respect to cell excitability and examine the consequences of their blockade, especially with reference to fast conduction cells and common myocytes in the heart. Mention voltage-independent sodium channels expressed by epithelia.
- Recall the relevance of potassium channels with respect to resting potential and repolarization
 and examine the consequences of their activation or blockade, with particular reference to the
 function of smooth muscles and the action potential of heart cells.
- Recall the relevance of the various subtypes of calcium channels with respect to cell bioelectric
 and contractile properties and examine the consequences of their blockade, with respect to the
 electrical and contractile activity of the heart and to the tone of vascular muscles.

Lecture Drugs that target the adrenergic system

- Acquire a critical general perspective on the various subtypes of adrenergic receptors (α and β), and their roles in regulating sympathetic effectors, with particular reference to their effects on the heart, vascular muscles and renin secretion.
- Describe the vasoconstricting action of α 1 receptors and the consequences of their stimulation or blockade.
- Describe the peripheral and central modulatory role of $\alpha 2$ receptors on sympathetic activity.
- Describe the action of β1 receptors on the heart (and the iuxtraglomerular apparatus) and the clinical consequences of their activation or blockade. Examine in detail the differential properties (specificity, intrinsic sympathomimetic activity, hydro-lipophilicity, additional actions) of the various classes of beta-blockers.
- Describe the action of β2 receptors on smooth muscles and other targets and the clinical consequences of their stimulation or (generally unwanted) blockade.

Lecture ACE inhibitors and vasodilators

- Recall the physiopathology of the renin-angiotensin-aldosterone system (RAAS), with particular reference to the short- and long-term actions of angiotensin II on the cardiovascular system and on diuresis.
- Discuss the relevance and clinical advantages of blocking the angiotensin converting enzyme (ACE).
- Review the mechanisms involved in the regulation of smooth muscle tone and contraction, and examine the possible molecular targets to produce vasodilation.
- Classify vasodilator drugs and discuss the possibility of using drugs that possess vasodilator properties in addition to their main activity (such as beta-blockers).

Lecture Diuretics

- Review the transport systems in the kidney and examine how the interference with each of them, or with carbonic anhydrase, can induce diuresis.
- Classify diuretics in terms of their mechanism of action, clinical efficacy and interference with "free water" production and/or elimination.

<u>Lecture Anti-coagulant, anti-platelet, antithrombotic and thrombolytic drugs</u>

• Review the mechanisms of coagulation and platelet aggregation



- Identify the pharmacological targets in the system
- Discuss the drugs available to interfere with coagulation, platelet aggregation and thrombus formation and lysis

THE CLINICAL APPLICATIONS OF CARDIOVASCULAR AND RENAL DRUGS

Lecture Cardiac insufficiency and ischemia

- Examine the pathophysiological factors that influence cardiac contractility, cardiac work and oxygen demand
- Recall the haemodynamic changes and the compensatory mechanisms that occur in the presence
 of inadequate heart contractility.
- Examine the mechanisms by which each of these factors can be pharmacologically modified and the possible pharmacological targets
- Review the drugs that act on cardiac contractility, preload, afterload and cardiac trophism.
- Consider the pharmacological approaches to attenuate / slow down the atherosclerotic process.

Lecture Hypertension

- Recall the complex interaction of heart and kidney functions in regulating blood pressure.
- Examine the possible pharmacological targets in the regulation of blood pressure and in circumventing physiological compensatory mechanisms
- Discuss the mechanisms of action of the various classes of antihypertensive drugs

Lecture Antiarrhythmic drugs

- Recall the complex interaction of ion currents in generating heart automaticity and in shaping the various types of cardiac action potentials.
- Recall the main mechanisms of onset and maintenance of cardiac arrhythmias: alterations in automaticity, excitability and conduction in the different heart tissues.
- Discuss the role of sodium channel blockade in reducing excitability and after-depolarizations, prolonging the refractory period, inhibiting reentry; classify sodium blocking drugs into the three subclasses, I-A, I-B and I-C, depending on the intensity of channel blockade and possible concomitant effects on potassium conductances.
- Discuss the relevance of sympathetic control on heart automaticity, excitability and conduction velocity and the possible antiarrhythmic action of beta blockers (class II), also considering possible local anaesthetic actions.
- Recall the relevance of potassium currents in regulating repolarization and the duration of the
 action potential, and examine the use of potassium current blockers (class III) to prolong and
 homogenize AP duration, thus exerting an antifibrillatory actions.
- Recall the multiple roles of calcium currents in the various heart cell types and examine the antiarrhythmic action of calcium channel blockers (class IV).
- Briefly discuss other pharmacological tools to treat arrhythmias (class V): adenosine and cardioactive glycosides.
- Mention the role of electronic devices as an alternative approach to cardiac arrhythmias.

Notes:



VASCULAR DISEASES: INDEPENDENT LECTURE ON 28/11 (8.30-10.30) OR INTEGRATION TO PROF. CIVILINI'S LECTURE ON 03/11/2017

Describe the main radiological techniques for the evaluation of aneurysms, acute aortic syndromes, peripheral arterial diseases.

Describe the main indications of interventional radiology for vascular diseases.

MULTIDISCIPLINARY INTEGRATION:

Pulmonary embolism (22/11)
Valvular heart disease (09/11 – I will not be available due to previous commitments)
Cardiomyopathies (20/11)
Pericardial diseases (15/11)