MEDTEC SCHOOL

Course: Pathology, Immunology and Microbiology
Year (1st-2nd-3rd-4th-5th-6th): 3rd
Period (1st-2nd semester – annual): Annual
Credits: 19 CFU

Objectives

The course will offer an integrated introduction to the causes of cell, tissue and organ injuries (cellular pathology), the major microbial agents that cause human diseases (microbiology), the principal mechanisms of defense against pathogens and responses to injury (inflammation and immunity), and the general processes of the most relevant causes of human diseases (immunopathology, vascular pathology and oncology).

The module of Pathology aims to bring students closer to clinics by translating the basic knowledge of the first part of the course (1st semester) into its clinical counterpart illustrating the gross, microscopic and molecular features of disease, with particular attention to immunological and degenerative disorders. This part of the course (2nd semester) will give a professionalizing profile, through student exposition to interactively presented and discussed case studies.

Application of knowledge and understanding:
At the end of the course students will gain understanding of:

- how the body reacts to physical and biological agents to recover homeostasis
- general pathological mechanisms leading to cell injury and death
- molecular and cellular basis for inflammatory disease states
- normal and abnormal functions of the innate and adaptive immune system
- body's immune reactions to infections
- molecular basis for neoplastic disease
- pathological mechanisms leading to thrombosis, atherosclerosis, ischemia, infarction
- morphological counterparts and their correlation with clinical features, in Infectious-related diseases, Immune-related disorders and Inflammation-cancer pathways

Making judgements; Communication skills; Learning skills.
By the end of the course students will have

- developed some abilities to communicate and work in team

- acquired some learning skills such as study in a group, organize knowledge, revise and retain information, select information.

Prerequisites

General knowledge of cell biology, cell physiology, histology and anatomy.

Contents

FIRST SEMESTER

I- GENERAL PATHOLOGY I (Prof Raffaella Bonecchi, Prof Sebastien Jaillon, Prof Alberto Mantovani, Prof Seppo Meri)

Module of CELLULAR PATHOLOGY (Prof Raffaella Bonecchi)

Learning objectives
At the end of these lectures and activities, students should be able to

- Discuss the pathogenesis of hyperplasia, hypertrophy, atrophy, and metaplasia, and com-pare and contrast their possible physiologic and pathologic causes.
- Explain causes of cellular injury and describe cellular alterations during injury
- Demonstrate understanding of cellular changes during injury and cell death

Lectures:

1. Mechanisms of cellular adaptation (in co-teaching with Anatomical Pathology – Lecture 1)

- Adaptation of cellular growth and differentiation
- Hypertrophy, hyperplasia, atrophy, metaplasia

2. Cell injury and cell death

- Causes of cell injury
- Hypoxia exposure and ATP depletion
- Oxidative stress and damage from reactive oxygen species
- Nitrosative stress and damage from reactive nitrogen species
- Mitochondrial damage

3. Programmed cell death

- Apoptosis
- Necroptosis, pyroptosis and autophagy

Module of INNATE IMMUNITY AND INFLAMMATION I (Prof Raffaella Bonecchi, Prof Sebastien Jaillon, Prof Alberto Mantovani, Prof Seppo Meri)

Learning objectives

At the end of these lectures and activities, students should be able to

- Describe and discuss each of the following cell type in terms of the associated type of inflammation and their role in the immune response: mast cells/basophils, neutrophils, eosinophils, monocytes/macrophages, NK cells and dendritic cells.
- Describe the classic vascular changes and cellular events of the acute inflammation and discuss the receptors and ligands that are responsible for these events.
- Define and use in proper context: abscess, chemotaxis, cytokine, edema, exudate, granulation tissue, granuloma, inflammation, margination, phagocytosis, purulent, pus, pyogenic, resolution, transudate, ulcer.
- Discuss the following chemical mediators of inflammation, in terms of origin (cells vs. plasma) and in vivo functions: vasoactive amines, complement system, arachidonic acid metabolites, platelet activating factor, cytokines/chemokines nitric oxide, lysosomal granule contents oxygen-derived free radicals
- Describe the steps involved in the isolation and destruction of an infectious agent by cells of the innate immunity. Describe important molecules involved in the process (opsonins, phagocytic receptors)

Lectures:

1. Origin of innate immune cells: hematopoiesis (Prof Jaillon)

- Definition and general concepts
- The normal blood counts
- The hematopoietic stem cell
- The hematopoietic tissues
- Cytokines and growth factors
- The hematopoietic niche
- General principles of hematopoietic stem cell transplantation

2. The acute inflammatory response (Prof Mantovani)

- Cardinal signs of acute inflammation
- Blood flow alterations and vascular permeability
- The endothelium as a reactive biological structure

3. Collaborative lesson on cells mediators of inflammation (Prof Bonecchi- Prof Jaillon)

- Mast cells
- Neutrophils
- Macrophages
- NK cells

4. Pathogen recognition in innate immunity (Prof Mantovani)

- Pathogen-Associated Molecular Patterns
- Structure and signalling properties of Pattern Recognition Receptors
- Structure and signalling properties of opsonic receptors
- Pentraxins

- Genetic defects in pathogen recognition
- Danger-Associated Molecular Patterns and their receptors

5. Soluble mediators of inflammation (Prof Jaillon)
- Molecular mediators active on vessels
- Molecular mediators active on leukocytes
- Primary inflammatory cytokines
- Eicosanoids

6. Chemokines and leukocyte recruitment (Prof Bonecchi- Prof Jaillon)
- Adhesion molecules and cell adhesion
- Migration and chemoattractants

7. The complement system (Prof Meri)
- Activation pathways
- Functions
- Regulatory mechanisms
- Genetic defects in the complement system

8. Pathogen killing (Prof Jaillon)
- Mechanisms of cell-mediated cytotoxicity
- Phagocytosis and degranulation
- Oxygen-dependent mechanisms
- Oxygen-independent mechanisms
- Genetic defects in pathogen killing

Module of TUMOR BIOLOGY (Prof Jaillon)

Learning Objectives

At the end of the lecture course, students should:

- be able to understand and explain the differences between benign and malignant tumors and their relative characteristics.
- be able to understand and explain the hallmarks of cancer.
- be able to understand the molecular and cellular mechanisms that lead to cancer.
- be able to give an overview of the cancer problem, the modern view on what cancer is, from a basic to a clinical perspective (staging and grading systems, cachexia, praneoplastic syndromes)

Lectures:

1. Introduction to tumors
- Definition
- Nomenclature
- Benign and malignant neoplasms
- Epidemiology of cancer

2. Characteristics of benign and malignant tumors adaptation (in co-teaching with Anatomical Pathology – Lecture 2)

- Differentiation and anaplasia. Metaplasia and dysplasia.
- Local invasion
- Metastasis, pathways of spread

3. Molecular basis of cancer 1 (in co-teaching with Anatomical Pathology – Lecture 3)

- Cellular and molecular hallmarks of cancer
- Genetic and epigenetic alterations
- Oncogenes and proto-oncogenes

4. Molecular basis of cancer 2

- Tumor suppressor genes
- Evasion of apoptosis
- Evasion of immune destruction
- Genome instability
- Metabolic alterations

5. Clinical aspect of patients with tumors adaptation (in co-teaching with Anatomical Pathology – Lecture 4)

- Characteristics of neoplastic cachexia
- Paraneoplastic syndromes
- Grading and staging of tumors

II - MICROBIOLOGY I

Module of BASIC CONCEPTS OF MICROBIOLOGY (Prof Sara Carloni, Prof Valeria Cento)

Learning objectives

At the end of these lectures and activities, students should be able to

- Describe the general categories of infective agents including bacteria, viruses, fungi, and parasites.
- Discuss the pathogenesis of infectious diseases by different types of microorganisms and compare and contrast their pathologic causes.

Lessons:

1. Brief history of microbiology (Prof Sara Carloni): from the early years of Microbiology, to the Golden and Modern ages of Microbiology. To describe how the discovery of the existence of microbes impacted on human life and survival.

- To describe **cell structure and function in prokaryotic and eukaryotic cells**: external structures, cell wall and Cytoplasm of bacterial and eukaryotic cells. To describe the relevance in the pathogenesis of infections.
- To describe major techniques to perform **Microscopy and microbial staining**
- To describe Microbe **classification**, Microbial nutrition and growth, metabolism, Growth requirements.

2. To describe how **Culturing microorganisms** and how we can **Control microbial growth** in the environment through physical and chemical methods, and in the body through antimicrobial drugs. (Prof Sara Carloni)

- To describe the mechanisms of action of principal classes of antimicrobial drugs and the resistance to antimicrobial drugs. Challenges and Limitations of Anti-quorum Sensing Therapies. To describe the role of prebiotics, probiotics and postbiotics in microbial homeostasis and disease. (Prof Sara Carloni)

3. **To characterize and classify prokaryotes** (Prof Sara Carloni)

- To describe general characteristics and modern classification of bacteria relevant in medical microbiology.

4. **To characterize and classify eukaryotes** (Prof Valeria Cento)

- To describe general characteristics of protozoa, fungi and parasites relevant in medical mycology.

5. To characterize and classify viruses, viroids and prions (Prof Valeria Cento)

- To describe general characteristics and classification of viruses. To describe viroids and prions.

6. **To describe mechanisms of Infection, characteristics of infectious diseases and the principles of epidemiology**. (Prof Sara Carloni)

- To describe principles of Immunization and immune testing.

Module of MEDICAL MICROBIOLOGY (Prof Sara Carloni)

Learning objectives

At the end of these lectures and activities, students should be able to

- Describe Gram positive bacteria and associated diseases; describe pathogenic mechanisms and the resulting pathology at the cellular, tissue, and organism levels; and the clinical manifestations
- Compare mechanisms characteristic of infection with particular categories of bacteria.
- Describe Gram negative bacteria and associated diseases; describe pathogenic mechanisms and the resulting pathology at the cellular, tissue, and organism levels; and the clinical manifestations

1. Pathogenic Gram-positive bacteria (Prof Sara Carloni)

- Staphylococcus
- Streptococcus

2. Pathogenic Gram-positive bacteria (Prof Sara Carloni)
- Enterococcus
- Bacillus
- Clostridium
- Listeria
- Micoplasma

3. Pathogenic Gram-positive bacteria (Prof Sara Carloni)
- Corynebacterium
- Propionibacterium
- Mycobacterium
- Nocardia and Actinomyces

4. Pathogenic Gram-negative cocci (Prof Sara Carloni)
- Neisseria

5. Pathogenic Gram-negative bacilli (Prof Sara Carloni)
- Anaerobic bacilli: Opportunistic Enterobacteriaceae, Pathogenic Enterobacteriaceae, Pasteurellaceae

6. Pathogenic Gram-negative bacilli (Prof Sara Carloni)
- Aerobic bacilli: Bartonella, Brucella, Bordetella, Burkholderia, Pseudomonads
- Francisella, Legionella, Coxiella
- Anaerobic bacilli: Bacteroides, Prevotella

III Module of ANATOMICAL PATHOLOGY (Prof Terracciano L, Prof Roncalli M, Prof Di Tommaso L, Prof Renne S, Prof Colombo P)

Learning objectives
At the end of these lectures and activities, students should be able to
- Describe what is pathology; what are the main areas of application of pathology in the modern medicine; how does pathology integrate in the management of a patient.

In particular, students should know:
the type and differences of materials examined in pathology (fresh, fixed, frozen);
the type and differences of fields in pathology (cytological, histological, molecular);
the principles of gross and microscopic evaluation;

1. Morphological features of cellular adaptation and their clinical impact: aortic stenosis and cardiac hypertrophy (in co-teaching with CELLULAR PATHOLOGY – Lecture 1)

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- Describe the macroscopic and microscopic features of cardiac hypertrophy and correlate them with its clinical features.

2. Morphological features of metaplasia and dysplasia and their clinical significance: gastric reflux, intestinal metaplasia (Barrett Esophagus) and esophageal cancer (in co-teaching with Tumor Biology – Lecture 2).

- Describe the endoscopic and microscopic features of Barret Esophagus and correlate them with its clinical features and outcome.

3. The evaluation of the molecular profile in the clinical practice: HER2/neu in breast cancer and its role in patient management (in co-teaching with Tumor Biology – Lecture 3).

- Describe what is immunohistochemistry and what is HER2; correlate the evaluation of HER2 expression with breast cancer treatment (definition of tissue biomarkers: diagnostic, prognostic and predictive).

4. Grading and staging of tumors. Breast cancer grading: morphological criteria and clinical impact. Colorectal cancer staging: morphological criteria and clinical impact (in co-teaching with Tumor Biology – Lecture 5).

- Illustrate the significance of grading and staging; describe their impact on prognosis and management of patients, using the example of colorectal cancer

5. From basic concept of microbiology to clinical presentation of infective diseases: the example of lympho-adenitis.

SECOND SEMESTER

I - GENERAL PATHOLOGY II Prof Raffaella Bonecchi, Prof Sebastien Jaillon, Prof Alberto Mantovani, Prof Seppo Meri)

Module of INNATE IMMUNITY AND INFLAMMATION II (Prof Raffaella Bonecchi, Prof Sebastien Jaillon, Prof Alberto Mantovani, Prof Seppo Meri)

Learning objectives

- Compare and contrast acute, chronic, and granulomatous inflammation in terms of: etiology, pathogenesis, histologic appearance, laboratory findings, characteristic cells involved, outcome, systemic effects.
- Describe the phases of tissue repair and cutaneous wound healing, the mechanisms of healing by first intention (primary union) and second intention (secondary union) and possible clinical consequences of abnormal wound healing.

Lectures:

1-2. Chronic inflammation, fibrosis and tissue renewal (Prof. Bonecchi)
- Cellular and molecular effectors of chronic inflammation
- The chronic inflammatory response and immune polarization
- Stem cells and tissue renewal
- Growth factors and tissue regeneration
- Fibrosis

3-4. Small groups activity on WHIM syndrome (Prof. Bonecchi, Prof. Kallikourdis)

5-6. Small groups activity on chronic granulomatous disease (Prof. Bonecchi, Prof Jaillon, Prof. Kallikourdis, TBD)

7. Dendritic cells/antigen presenting cells (Prof Bonecchi)
- Origin and heterogeneity of dendritic cells
- Maturation and function
- Clinical use.

8. Acute phase reaction and systemic inflammation (Prof. Mantovani)
- Fever
- Leukocytosis
- Acute phase proteins

9. Recap lesson on inflammation (Prof. Bonecchi)

Module of VASCULAR PATHOLOGY (Prof Bonecchi)

Learning objectives

1. Angiogenesis and tumor angiogenesis
- Multipotent endothelial cells
- Angiogenesis and vasculogenesis
- Angiogenetic cytokines and their receptors
- Role of angiogenesis to tumor survival and growth
- Soluble angiogenic factors and chemokines
- Endothelial progenitor cells and other relevant bone marrow-derived cells

2. Hemostasis and coagulation
- Platelets
- Primary and secondary emostasis
- Coagulation cascade
- Fibrinolitic system

3. Thrombotic diseases and Atherosclerosis
- Thrombus formation and evolution
- Clinical manifestations
- Mechanisms of plaque generation
- Risk factors
- Clinical manifestations and complications

II – IMMUNOLOGY AND IMMUNOPATHOLOGY (Prof. Rescigno, Prof Kallikourdis, Prof Mantovani, Prof Jaillon)

Module of MUCOSAL IMMUNE SYSTEM AND MICROBIOTA (Prof. Rescigno)

At the end of the lecture course, students should be able to:
- Understand the structure of the mucosal immune system (the sites where the response is initiated)
- Understand how immune responses are initiated or repressed at mucosal sites
- Understand how immune homeostasis is carried out at mucosal sites.
- Understand the bases of several disorders initiated at mucosal surfaces (allergies, asthma, metabolic disorder, etc.)
- Understand what is the microbiota, its activities on our well-being and how we tolerate

Lectures:

1. Development and structure of Mucosal tissue
- Description of the mucosal associated lymphoid tissues
- Nasal associated lymphoid tissue (NALT), Waldeyer's ring
- Broncho-alveolar associated lymphoid tissue (BALT),
- Gut associated lymphoid tissue (GALT), Peyer's Patches, Isolated lymphoid follicles

2. Cellular constituents of the mucosal immune system I: Epithelial cells and antigen uptake

- Epithelial cells,
- Bile acids and enterohepatic circulation,
- Antigen uptake
- Initiation of oral tolerance to food

3. Cellular constituents of the mucosal immune system II

- Intraepithelial lymphocytes, dendritic cells, macrophages, Mast cells and neutrophils
- Atypical CD8 T cells
- □□□T cells
- iNK T cells
- Innate lymphoid cells
- ILC and chronic disorders

4. Lymphocyte trafficking and oral tolerance

- Lamina propria lymphocytes
- T regulatory cells (thymus derived and peripherally derived)
- T regulatory cells and IBD

5. Asthma

- Pathogenesis
- Allergic and non-allergic airway inflammation
- Atopic dermatitis and atopic marsh

6. The Microbiota and its impact on immune responses

- What it is
- How to analyse the microbiota
- Microbiota and Th17 and Tregs
- Th17 and brain disorders

7. The microbiota and cancer

- How the microbiota impact on cancer
- Protumorigenic and anti-tumorigenic bacteria
- Microbiota and cancer treatment

Module of ADAPTIVE IMMUNITY (Prof. Kallikourdis)

Learning Objectives

At the end of the lecture course, students should be able to:

- Understand and explain to others the function of adaptive immunity, *with all its associated features and physiopathological facets* (see below).
- Understand the key biological problems that drove the evolutionary selection of adaptive immunity as an answer to these problems.

- Be able to identify mechanisms driven by adaptive immunity when faced with a complex clinical problem.

Lectures:

1. Introduction to adaptive immunity:
- key concepts

2. MHC, antigen processing and presentation:
- Intro and link to other lectures
- Initiation of adaptive responses
- Antigen presentation; lymph nodes
- Nomenclature and historic overview of MHC studies
- Haplotypes
- Dominant epitopes; superantigens
- Topology issues
- MHC processing for Class I and Class II
- Cross-presentation.

3. T cell development and functions - Lecture 1
- T cell development
- Generation of T cell receptor diversity
- Assembly of the mature TCR
- Thymic selection (an introduction)
- T cell signalling (T cell activation).

4. T cell development and functions - Lecture 2
- T cell functions
- Immune synapses
- Costimulation - checkpoint blockade
- Cytotoxic function.

5. B cell development and functions - Lecture 1
- BCR diversification
- B cell development

6. B cell development and functions - Lecture 2
- Th-B cell interactions; germinal centers
- affinity maturation/somatic hypermutation, class-switch recombination, AID and Neuberger.
- class switching and polarization of responses
- Memory B cells
- Antibody structure and function; integration with innate immunity
- Monoclonal antibodies and Cesar Milstein; uses in diagnostics and therapy; patent of the technology

- Humanized monoclonal antibodies; Neuberger and Winter
- Future directions of monoclonal antibody technologies, bispecific antibodies, fully humanized antibodies.

7. Polarization and memory:
- Th1 Th2 Th17, innate/adaptive immunity coordination
- Nomenclature issues on M2-like vs Th2 and Treg
- Development and function of polarized responses
- Clinical examples
- Autoimmunity
- Allergy (Atopy)
- Memory responses
- Vaccines

8. Tolerance and negative regulation of immune responses:
- Central tolerance; Peripheral tolerance
- Intracellular mechanisms of immunoregulation: via signaling; via degradation; via inhibition of costimulation
- Mechanisms of peripheral tolerance at the level of cell-cell interactions
- Treg cells
- Other suppressive populations

9A. Small Team Work – Flipped Classroom: Immunological issues in reproduction (optional – depending on availability of time slots))

9B. Immunology of pregnancy:
- Immune evasion mechanisms
- Medawar
- Treg
- Consequences of maternal-fetal tolerance for the evolution of immune system control

Module of IMMUNOPATHOLOGY (Prof Jaillon, Prof Mantovani)

Learning Objectives

At the end of the lecture course, students should:

- be able to understand and explain the general mechanisms and effector functions of the immune system.
- be able to understand and explain the causes and the pathogenesis of the main alterations of the immune response.
- be able to understand and explain the mechanisms involved in the rejection of tissue transplants.
- be able to understand and explain the mechanisms involved in the alterations of the immune system in tumors and the principles of immunotherapy.
- be able to understand and explain the importance of biomedical research in immunopathology and cancer.

1. Hypersensitivity reactions (1) (Prof Jaillon)

- Overview of the normal immune response
- Classification of hypersensitivity diseases
- Immediate (type I) hypersensitivity

2. Hypersensitivity reactions (2) and autoimmune diseases (Prof Jaillon)

- Antibody-mediated (type II) hypersensitivity
- Immune complex-mediated (type III) hypersensitivity
- T cell-mediated (type IV) hypersensitivity
- Autoimmune diseases: The central and peripheral tolerance
- Mechanisms of autoimmunity
- General features of the most common autoimmune diseases (Systemic Lupus Erythematosus)

3. Rejection of tissue transplants and immunodeficiency syndromes (Prof Jaillon)

- Rejection of tissue transplants: Generalities and definition, Type of rejection reactions
- Graft-versus-host disease
- Immunodeficiency syndromes: Primary immunodeficiencies
- Primary immunodeficiencies: Defect in innate immunity
- Primary immunodeficiencies: Defect in adaptive immunity
- Secondary immunodeficencies: Acquired immune deficiency syndrome (AIDS)

4. Vaccines (Prof Mantovani)

5-6. Immune responses to tumors and principles of cancer immunotherapy (Prof Jaillon)

- Introduction
- The immunosurveillance hypothesis
- Defensive mechanisms against tumors
- Mechanisms of cancer immune evasion
- Cancer immunoediting
- Principles of cancer immunotherapy (antibodies, inhibitors of immune checkpoints, CAR-T cells)

7.Inflammation and cancer (Prof Mantovani)

- Epidemiologic evidence
- Myeloid-derived suppressor cells
- Tumor-associated macrophages: origin and function
- Tumor-associated neutrophils

8. Innate immunity in translational medicine (Prof Jaillon)

- Recognition and elimination of pathogens
- Role of neutrophils in tumors and response to therapy

III - MICROBIOLOGY II (Prof Valeria Cento, Prof Sara Carloni)

Learning objectives

At the end of these lectures and activities, students should be able to

- Describe Rickettsias, Chlamydias, Spirochetes, Vibrios and associated diseases; describe pathogenic mechanisms and the resulting pathology at the cellular, tissue, and organism levels; and the clinical manifestations.
- Describe fungi and associated diseases; describe pathogenic mechanisms and the resulting pathology at the cellular, tissue, and organism levels; and the clinical manifestations.
- Describe RNA and DNA viruses and associated diseases; describe pathogenic mechanisms and the resulting pathology at the cellular, tissue, and organism levels; and the clinical manifestations.
- Describe parasites (protozoan, helminths, Arthropod vectors) and associated diseases; describe pathogenic mechanisms and the resulting pathology at the cellular, tissue, and organism levels; and the clinical manifestations.
- Compare mechanisms characteristic of infection with particular categories of pathogens.

1, 2. **To describe Pathogenic** (Prof Sara Carloni)

- Rickettsias
- Chlamydias
- Spirochetes (Treponema, Borrelia, Leptospira)
- Vibrios (Vibrio, Campylobacter, Helicobacter)

(Prof Sara Carloni)

3, 4 - **To describe Pathogenic fungi (**Prof Valeria Cento)

- Classification of mycoses
- Dermatophytes
- Endemic mycoses
- *Pneumocystis jirovecii*
- Fungal agents of opportunistic invasive infections (*Candida* spp; *Aspergillus* spp.; *Cryptococcus* spp.)

5,6,7 - To describe pathogenic parasites (Prof Seppo Meri)

To describe the epidemiology of the more important protozoan and helminthic parasites, life cycles, mechanisms of disease.

- Parasites protozoa (Apicomplexans: malaria)
- Parasites protozoa (Ciliates, Amoebae, Flagellates)
- Parasites (Helminths and Arthropod vectors)

8, 9. To describe Pathogenic DNA viruses (Prof Valeria Cento)

- Poxviridae (Smallpox, Molluscum contagiosum)
- Herpesviridae (Herpes simplex, Varicella-Zoster, Epstain-Barr, Cytomegalovirus)
- Papillomaviridae (Papillomavirus)
- Polyomaviridae (Polyomavirus)
- Adenoviridae

- Parvoviridae

10, 11, 12, 13 - To describe Pathogenic RNA viruses (Prof Valeria Cento)
- Picornaviridae (Enteroviruses, Rhinoviruses), Caliciviridae (Noroviruses)
- Reoviridae (Rotavirus)
- Togaviridae: Rubella virus
- Paramixoviridae (Measles, Mumps, Respiratory syncytial virus)
- Orthomyxoviridae (Influenza)
- Arboviruses: Togaviridae, Flaviviridae
- Bunyaviridae, Arenaviridae
- Rhabdoviridae
- Hepatitis viruses: HAV, HBV, HCV, HDV, HEV
- Retroviridae (Lentiviruses-HIV)
- Coronaviridae

14. Small group - sepsis (Bonecchi, Jaillon, Kallikourdis, Cento, Carloni**)**
15. Small group - HIV (Bonecchi, Jaillon, Kallikourdis, Cento, Carloni**)**
16. **Small group - Infections and cancer**: Helicobacter, HPV, HBV, HCV (Bonecchi, Jaillon, Kallikourdis, Cento, Carloni)
17. **Small group – emerging infections** (Bonecchi, Jaillon, Kallikourdis, Cento, Carloni)
18. Oral Presentation of different **research projects** developed by the students with the following goals:
1- Interaction between microbiota and immunity in health and disease
2-correlation between diseases / dysbiosis (caused by real / opportunistic pathogens or by molecules produced by them) and the development of pathologies.
3-identification of new biomarkers
4-development and extension of technologies for the diagnosis and monitoring of pathologies

IV - ANATOMICAL PATHOLOGY (Prof Terracciano L, Prof Roncalli M, Prof Di Tommaso L, Prof Renne S, Prof Colombo P)

Learning objectives
At the end of these lectures and activities, students should be able to
- Describe what is pathology; what are the main areas of application of pathology in the modern medicine; how does pathology integrate in the management of a patient.

In particular, students should know:
the type and differences of materials examined in pathology (fresh, fixed, frozen);
the type and differences of fields in pathology (cytological, histological, molecular);
the principles of gross and microscopic evaluation;

Lessons 6 and 7. What is pathology? Prof Di Tommaso
- What pathology is;
- The basic instruments: macroscopic and microscopic evaluation;
- How pathology has evolved over the years;
- The fields of pathology today;

- The role of pathology in the predictive/precision medicine;
- Digital Pathology, augmented microscopy and Artificial Intelligence

Lessons 8 and 9. The pathologist at work: a fascinating mission. Prof Di Tommaso
- Cells, tissues and organs: principles of sampling, fixation and processing;
- Gross evaluation and microscopic pattern recognition
- The diagnostic workflow;
- Beyond morphology: the phenotype aiding to prove the histopathological diagnosis;
- The role of pathology in the predictive/precision medicine

Lessons 10. The pathologist's report. Prof Colombo
- The language of pathologist;
- The report of pathology and the check list;
- The pathology archive as a bank of tissue samples for treatment and research;
- The intra-operatory examination

Lessons 11 and 12. The clinical pathological correlations Prof Renne
- The role of autopsy over the years;
- Gross evaluation of surgical specimen and correlation with clinical feature;
- Gross evaluation of autoptic organs and correlation with clinical features
- Practical activity: Clinical-pathological discussion of selected examples Prof Terracciano L, Prof Roncalli M, Prof Di Tommaso L, Prof Renne S, Prof Colombo P

Lessons 13 and 14. The myth of Prometheus: tissue response in the damaged liver. Prof Terracciano
- Illustrate the pathogenesis of liver cirrhosis;
- Illustrate the role of the liver biopsy in the characterization of inflammatory diseases of the liver;
- Discuss the concept of liver biopsy adequacy in these settings;
- Illustrate the main features and significance of a few histopathological elementary lesions (spotty necrosis, piecemeal necrosis, confluent necrosis, cholestasis, pericentral and periportal fibrosis, septal fibrosis, nodular fibrosis, steatosis) occurring in different etiological settings (viral, metabolic, autoimmune, drug-induced) of chronic hepatitis;
- Illustrate the concepts of grading and staging in chronic inflammatory conditions of the liver in the biopsy and their quantification in a scoring system

Lesson 15. From TBC to Covid19: inflammatory and interstitial lung diseases. Prof Renne
- Illustrate the pathological basis of the main inflammatory and interstitial lung diseases with particular emphasis to chronic obstructive pulmonary diseases, chronic diffuse interstitial diseases and pulmonary infection (lobar pneumonia and bronchopneumonia and interstitial pneumonia) and related local, cardiac and systemic complications.
- Illustrate the pathological basis of lung abscess and its main complication.
- Illustrate the pathological basis of pulmonary embolism.
- Illustrate the pathological basis of diffuse alveolar damage.

Lesson 16. Chronic inflammation and fibrosis: the example of thyroiditis and pancreatitis. Prof Di Tommaso

- Illustrate the main etiology and morphological features and complications of thyroiditis, multi-nodular goiter, hyperthyroidism and hypothyroidism.
- Illustrate the main etiology and morphological features and complications of acute and chronic pancreatitis
- Describe epidemiology, clinical features, macroscopic and microscopic features of acute and chronic pyelonephritis

Lesson 17. Morphological features of atherosclerosis at gross and microscopic level. Prof Renne

- Define atherosclerosis
- Describe the epidemiology of atherosclerosis
- Discuss the pathogenesis of atherosclerosis
- Discuss the evolution of an atherosclerotic plaque
- Discuss the complication of atherosclerosis
- Discuss the clinical implication of an atherosclerotic complication.
- Describe the macroscopic and microscopic features of atherosclerosis in the different stages of diseases

Lesson 18. Ischemic heart disease: from morphology to clinical features. Prof Renne

- Define ischemic heart disease
- Describe the epidemiology of ischemic heart disease
- Discuss the pathogenesis of ischemic heart disease
- Compare and discuss the pathological bases of stable and unstable angina
- Define acute myocardial infarction
- Describe the epidemiology if acute myocardial infarction
- Describe the risk factors of acute myocardial infarction
- Discuss the pathogenesis of acute myocardial infarction
- Describe the microscopic and macroscopic features of acute myocardial infarction in relationship with time from ischemia
- Describe and discuss the consequences and complications of acute myocardial infarction
- Define and discuss the chronic ischemic heart disease
- Define and discuss the sudden cardiac death

Lesson 19: endocarditis and heart failure. Prof Colombo

- Define endocarditis
- Discuss the pathological classification of endocarditis
- Define and discuss rheumatic heart disease
- Describe morphological features of acute rheumatic fever
- Describe morphological features of chronic rheumatic fever
- Define and discuss infectious endocarditis
- Describe the causes of infectious endocarditis
- Describe the morphology of infectious endocarditis
- Define and discuss non-bacterial thrombotic endocarditis

- Describe the causes of non-bacterial thrombotic endocarditis
- Define and discuss Liebman-Sacks endocarditis
- Describe the causes of Liebman-Sacks endocarditis
- Define heart failure
- Discuss epidemiology of heart failure
- Discuss the pathophysiology of heart failure
- Discuss the classification of heart failure
- Describe the clinical and pathological features of left-sided heart failure
- Describe the clinical and pathological features of right-sided heart failure

Lessons 20 and 21. Inflammatory Bowel Disease: from morphology to clinical features. Prof Roncalli, Prof Terracciano

- Illustrate the main morphological findings of self-limiting, infectious, antibiotic-associated, ischemic and radiation-induced colitis
- Illustrate the main morphological features of idiopathic inflammatory bowel diseases (IBD) with emphasis on the distinction between Ulcerative colitis and Crohn diseases with emphasis on epidemiology, etiology, pathogenesis, clinical, macroscopical and microscopical features
- Discuss the main complication of IBD
- Discuss the link between colorectal cancer and IBD and illustrate the role of colorectal biopsy and the concept and classification of mucosal dysplasia

Lesson 22 and 23. Helicobacter Pylori, Gastritis and gastric cancers, including MALT. Prof Terracciano, Prof Colombo

- Illustrate the main etiology and morphological features of acute and chronic gastritis (atrophic/autoimmune) with emphasis on the role of HP infection
- Illustrate the main complications of autoimmune gastritis
- Discuss the concept of intestinal metaplasia as a common as a common step to adenocarcinoma from GERD and from HP-related gastritis.
- Illustrate the sequence of morphological events linking HP infection to gastric cancer and malignant lymphoma
- Illustrate the histologic features of gastric dysplasia with emphasis on dysplasia grading and on the concept of "indefinite for dysplasia"
- Illustrate the natural history of gastric dysplasia in chronic gastritis

Lesson 24. HPV infection and cervical cancer. From Papanicolaou to molecular characterization: 100 years that changed the history of human cancer. Prof Di Tommaso

- Illustrate the epidemiology of cervical carcinoma.
- Define the cervical transformation zone.
- List risk factors for the development of cervical carcinoma.
- Illustrate the correlation between HPV genotype and the risk of cervical carcinoma.
- Explain the role of human papillomaviruses (HPV) in the pathology of benign and malignant cervical tumors.
- Illustrate the morphologic and biologic spectrum of squamous intraepithelial lesion (SIL) in PAP smear.

- Illustrate the morphologic and biologic spectrum of cervical intraepithelial neoplasia (CIN).
- Correlation between cytological information (SIL) and pathological findings (CIN).
- Describe the impact of PAP test in the screening and prevention of cervical carcinoma.
- Role of vaccination in cervical carcinoma.
- Illustrate the main morphological features of cervical carcinoma with regard to histotype, invasive properties, staging and grading and way of metastatization

Teaching Methods

Disciplines: General Pathology and immunology (10 CFU), Microbiology (5 CFU), Pathological Anatomy (4 CFU)
Faculty: Sebastien Jaillon (Coordinator), Rescigno Maria, Alberto Mantovani, Bonecchi Raffaella, Kallikourdis Marinos, Cento Valeria, Carloni Sara, Terracciano Luigi, Roncalli Massimo, Di Tommaso Luca, Salvatore Lorenzo Renne, Colombo Piergiuseppe.
Visiting professors: Seppo Meri (FIN)

Lectures: Attendance is mandatory and students are expected to follow the rules of the Ateneo.
The main purpose of lectures is to transfer knowledge to students by guiding them through the most relevant subjects of the disciplines. Students are encouraged to actively participate to the lectures with questions and comments.
Collaborative lessons with teachers of the course will be done in order to increase the integration of the different modules.

Group work activities/activation of knowledge: the purpose of these activities is to activate and solidify knowledge acquired during lectures and independent study, in a collaborative learning setting.

Research project (led by Prof. Carloni and Prof. Cento): The aim of the research activity is focused on the acquisition of critical skills derived from the extrapolation and integration of notions and concepts given by the various disciplines during the course

Students will be divided into working groups and will be given a topic related to the course to develop as interdisciplinary research project.

This work will be done in collaboration with the professors of the course and should have the objective of proposing a research project concerning one of these points:

1- interaction between microbiota and immunity in health and disease
2-correlation between diseases / dysbiosis (caused by real / opportunistic pathogens or by molecules produced by them) and the development of pathologies.
3-identification of new biomarkers.
4-development and extension of technologies for the diagnosis and monitoring of the pathologies discussed during the course.

This project will be carried out in the second part of the second semester (April, May), and should correspond to a workload of 20-30 hours of study.

Meetings (2 or 3 meetings) with professors will be requested by the students. The presentations will be scheduled at the end of the second semester.

Assessment

Students' evaluation will be assessed through multiple choice examinations at the end of the year.
The faculty reserves the possibility to have also an oral exam.

Exam content and evaluation

During the first session of the exam, the student will have the option to attempt the whole exam (PIMtotal) or to attempt half of the questions (PIM1).

Depending on his/her choice and the result of the exam (PIM1, see below), the student will be allowed to attempt only PIM2 or the whole exam in the following sessions.

PIM 1 (9,5 CFU) 33 questions (each question 0.5 points):

- General pathology (5CFU) 17questions:
Cellular pathology 2q
Tumor biology 4q
Innate immunity and inflammation 9q
Vascular pathology 2q

-Microbiology I (2,5 CFU) 9 questions
Basic concepts of microbiology 2q
Medical microbiology 7q

- Anatomical pathology I (2CFU) 7questions.

To pass the test PIM1 the student will have to answer to at least 18 questions correctly with a minimum of correct answers in each module:
general pathology (9 correct answers)
microbiology (5 correct answers)
anatomical pathology (4 correct answers).

PIM 2 (9,5 CFU) 33 questions (each question 0.5 points).

- Microbiology II (2,5CFU) 8questions

- Immunology and immunopathology (5CFU) 17questions:
Mucosal immune system and microbiota 3q

Adaptive immunity 7q
Immunopathology 7q

- Anatomical pathology II (2CFU) 8questions.

To pass the test PIM2, the student will have to answer to at least 18 questions correctly with a minimum of correct answers in each module:

microbiology II (4 correct answers)
immunology and immunopathology (9 correct answers)
anatomical pathology II (5 correct answers).

Full exam (PIMtotal)

Content of Exam (66 questions each question 0.5 points):

- General pathology (17q):

cellular pathology 2q.
innate immunity and inflammation 9q.
vascular pathology 2q.
tumor biology 4q.

- Microbiology (17 q).

Basic concepts of microbiology 2q
Medical microbiology 15q

Research Project:

As mentioned above, students will develop and present different research projects with the following goals:

1- Interaction between microbiota and immunity in health and disease
2-correlation between diseases / dysbiosis (caused by real / opportunistic pathogens or by molecules produced by them) and the development of pathologies.
3-identification of new biomarkers.
4-development and extension of technologies for the diagnosis and monitoring of the pathologies discussed during the course.

One day will be devoted to the presentations in the presence of the Professors of the different disciplines. Based on these presentations, 1 point of bonus will be given to students who have reached the learning objectives.

- Immunology and immunopathology (17q):

Adaptive Immunity 7q.
Mucosal immunology 3q.
Immunopathology 7q.

- Anatomical pathology (15q).

To pass the test, the student will have to answer to at least 36 questions correctly with a minimum of correct answers in each module:

general pathology (9 correct answers),
microbiology (9 correct answers),
Immunology and immunopathology (9 correct answers)
anatomical pathology (8 correct answers).

More than 60 correct answers (Full exam or PIM1+PIM2) = 30 lode

Texts

Robbins and Cotran
Pathologic Basis of Diseases
10th edition; 2020 Elsevier

Cellular and molecular immunology
10th edition, 2021; Elsevier

Microbiology with Diseases by Taxonomy, Bauman RW
4th edition, Pearson

Medical Microbiology,
9th Edition, 2020; Elsevier