Degree Course in Medicine and Surgery 2023/2024
Integrated Teaching: **General Pathology**
SSD Course: **MED/04 e MED/46**
CFU number: **8**
Integrated Teaching Head: Professor **Federica Wolf**
email: **federica.wolf@unicamillus.org**

MODULE: **General Pathology**
SSD Course: **MED/04**
CFU number: **6**
Professors:

- Professor: **Federica Wolf** (4 CFU) e-mail: federica.wolf@unicamillus.org
- Professor: **Gabriella D'Orazi** (1 CFU) e-mail: gabriella.dorazi@unicamillus.org
- Professor **Cristina Capuano** (1 CFU) e-mail: cristina.capuano@unicamillus.org

MODULE: **Laboratory Medicine Technical Sciences**
SSD: **MED/46**
CFU number: **2**
Professor: **Emiliano Fabiani** email : emiliano.fabiani@unicamillus.org

PREREQUISITES

Knowledge and skills in Human Anatomy, Histology and Embryology, Physiology, Biology and Genetics, Biochemistry, and Molecular Biology are required.

LEARNING OBJECTIVES

The integrated teaching of General Pathology aims to provide the student with the fundamentals for understanding the main disease mechanisms: from genetic-molecular modifications to morpho-functional characteristics, that will outline the pathogenesis of the most relevant diseases. The disease mechanisms represent the foundation for medicine aimed at patient's diagnosis, therapies, and cure.
Thus, general pathology represents the transition between the basic and clinical sciences, by using previously acquired notions to delineate the biological-molecular events characterizing diseases. The integrated teaching is structured into two modules:

- The General Pathology module will provide the student with the fundamentals for understanding the pathologic events from the cellular pathology (mechanisms of damage response, adaptation, regression, and cell death and relevant disease examples) to the body's defense mechanisms (innate and adaptive immunity, hemostasis). The student should be able to know the basics of general etiology and interpret the etiopathogenetic classification of diseases. The classification and biology of tumors, the molecular basis of neoplastic transformation, and the principles of therapy. The teaching concludes with a description of the pathophysiologic consequences involving the most important systems: circulatory-blood, and metabolic systems.
- The Laboratory Medicine Technical Sciences will provide the student with the knowledge useful in understanding the main laboratory testing systems, and cellular and molecular biology methods, applied to blood pathophysiology (diagnosis and prognostic evaluation of blood diseases).

LEARNING OUTCOMES

The expected learning outcomes are consistent with the general provisions of the Bologna Process and the specific provisions of Directive 2005/36/EC. They are found within the European Qualifications Framework (Dublin descriptors) as follows:

Knowledge and understanding
At the end of the integrated teaching, the student must be able to :

- Know and independently understand the molecular mechanisms of cell damage as well as the damage responsiveness at both cellular and tissue levels, (cellular stress, adaptation, regression, necrosis, apoptosis); tumor biology and the molecular basis of neoplastic transformation, and the pathogenetic mechanisms of the major human diseases.
- Know the mechanisms and recognize the major pathophysiologic manifestations of the circulatory, hepatobiliary, and metabolic system
- Know the principles used for:
  - flow cytometry in the field of hematology
  - evaluation of the diagnostic and prognostic role of gene mutations in the field of onco-hematology

Applying Knowledge and understanding
At the end of the integrated teaching, the student should demonstrate the capability to apply the acquired knowledge to:

- Analyze and understand the alterations of the cellular, immunological, and genetic mechanisms underlying human pathologies.
- Recognize the main manifestations of the most important pathophysiological events of the major systems: circulatory, hepatobiliary, and metabolic system

Communication skills
At the end of the integrated teaching, the student must be able to:

- Use the scientific terminology as appropriate.
- Communicate information, ideas, problems, and solutions to both specialists, and non-specialists recipients about the mechanisms of cellular damage, neoplastic transformation, and the pathophysiological mechanisms of diseases.

Making judgments
At the end of the integrated teaching, the student must be able to use the acquired knowledge to identify and explain the molecular, immunological, and pathophysiological mechanisms that lead to a disease. The independent judgment will be acquired through the analysis of examples of relevant human pathologies (simple clinical cases).

Learning skills
At the end of the integrated teaching, the student must be able to understand the mechanisms and effects of cellular damage, and the mechanisms underlying the process of carcinogenesis and have memorized the knowledge that will allow understanding of the pathophysiology of diseases. These skills will be developed favoring a critical discussion in specific cases.
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COURSE SYLLABUS
GENERAL PATHOLOGY (MED/04)
ETIOLOGY (Prof. Wolf)

- Health and Diseases: definitions. Concepts of etiology, pathogenesis, and pathophysiology. Etiologically-based classified diseases: intrinsic and extrinsic diseases.
- Genetic disorders: mutations, mendelian disorders, multifactorial disorders (inherited and acquired), normal karyotype, cytogenetic disorders, and malformation diseases.
- Pathogenesis of infectious diseases: general features, viral, bacterial fungal, and parasitic infections.

ENVIRONMENTAL PATHOLOGY (Prof. Wolf)

- Occupational and environmental diseases: Occupational exposure, air pollution, natural toxins. Mechanisms of toxicity. Phase I reactions.
- Lifestyle diseases: tobacco, alcohol, and obesity.
- The pathogenic effect of physical agents: radiation, radiation classification (exciting and ionizing), ultraviolet radiation.
- Mechanical agents, temperature, electricity and pressure

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CELLULAR PATHOLOGY (Prof. Wolf)

- Adaptation, damage and cell death: cellular responses to stress and radical-based pathologies. Reversible and irreversible cell injury. Mechanisms of cell damage and associated pathology (examples). Cellular adaptations of growth and differentiation: hyperplasia, hypertrophy, atrophy, metaplasia, dysplasia.
- Irreversible cell damage. Necrosis, ischemic and hypoxic injury, ischemia-reperfusion injury.
- Apoptosis: causes of apoptosis, morphology, biochemical characteristics of apoptosis, mechanisms of apoptosis, examples of apoptosis.

INFLAMMATION (Prof. Wolf, Prof. Capuano)

- Acute inflammation: historical evidence, stimuli for acute inflammation, vascular changes (changes in vascular caliber and flow and vascular leakage); cellular events: leukocyte diapedesis (leukocyte adhesion and transmigration) and phagocytosis. Adhesion molecules, chemotaxis.
- Chemical mediators of inflammation: vasoactive amines, plasma proteins, arachidonic acid metabolites: prostaglandins, leukotrienes, and lipoxins, platelet-activating factor (PAF), cytokines and chemokines, nitric oxide (NO), lysosomal constituents of leukocytes, oxygen-derived free radicals, neuropeptides. Activation of the complement system.
- Outcomes of acute inflammation. Examples of acute inflammation. Chronicization (abscess, ulcers)
- Chronic inflammation: causes of chronic inflammation, morphologic features, mononuclear cell infiltration, cells involved in chronic inflammation. Granulomatous inflammation, lymphatics in inflammation.
- Systemic effects of inflammation: leukocytosis, acute phase proteins, ESR, and fever. Thermoregulation: neurophysiology of thermoregulation. Thermoregulation center of the body. Pyrogens. Fever. Types of fever.
- Outcomes of the inflammatory process: Regeneration, repair and fibrosis. Control of normal cell proliferation and tissue growth. Pathogenesis of healing and fibrosis. Wound Healing.

NEOPLASIA: (Prof.ssa Wolf, Prof.ssa D'Orazi, Prof.ssa Capuano)

- Tumor definitions and nomenclature. Tumors' classification and staging. Tumor growth biology: benign and malignant neoplasms. Differentiation and anaplasia, the growth rate of cancer cells.
- Epidemiology: cancer incidence, geographical and environmental factors, genetic predisposition to cancer, chronic inflammation and cancer, precancerous lesions.
- Molecular basis of neoplastic transformation: alterations essential for malignant transformation, normal cell cycle, self-sufficiency in growth signals: oncogenes. Insensitivity to growth inhibitory signals. Oncosuppressor genes. Retinoblastoma as a paradigm for the two-hit hypothesis of oncosuppressor genes involved in neoplastic transformation. Oncosuppressor genes involved in human neoplasms. p53: guardian of the genome. Evasion of apoptosis. DNA repair defects and genomic instability in cancer cells. Unlimited replicative potential: telomerase. Development of angiogenesis. Invasion and metastasis. Stromal microenvironment and tumor growth. Dysregulation of genes associated with neoplastic transformation.

- Molecular basis of neoplastic transformation: gatekeeper and caretaker genes. Tumor progression and heterogeneity. Carcinogens and their cellular interactions: chemical carcinogenesis, metabolic activation of carcinogens. Molecular targets of chemical carcinogens. Classification of chemical carcinogens. Radiation carcinogenesis: ultraviolet radiation, ionizing radiation. Microbial carcinogenesis: oncogenic DNA and RNA viruses. Effects of tumors on host and organism response. Tumor biomarkers and principles of anti-tumor therapy.

PATHOPHYSIOLOGY (Prof. Wolf).

- Pathophysiology of the circulatory system: edema, hemorrhage, hemostasis, thrombosis, embolism, infarction, shock.
- Pathophysiology of the vessels: atherosclerosis and hypertension.
- Pathophysiology of the hepatobiliary system: liver function and related diseases, jaundice, hepatitis, cholestasis, cirrhosis, portal hypertension, liver failure.
- Pathophysiology of metabolism: diabetes.

LABORATORY MEDICINE TECHNICAL SCIENCES (MED/46) (Prof. E. Fabiani)

- Blood sampling and bone marrow aspirate
- CBC analysis, Principles of Flow Cytometry
- Blood smear on slide, fixation, and staining
- Isolation of mono- and polymorphonuclear cells from blood venous samples
- Isolation of stem cells: culture, amplification and cryopreservation
- Classification of blood diseases: anemias, leukocytosis, leukopenias, thrombocytosis/thrombocytopenias hematologic diseases, Minimal Residual Disease.
- Alterations in karyotype: cytogenetics and FISH
- Diagnostic and prognostic role of molecular biology in the field of onco-hematology
- Basic molecular biology techniques: nucleic acid amplification, qualitative (PCR and RT-PCR) and quantitative (Q-PCR and Q-RT-PCR) analyses
- Sanger sequencing, next-generation sequencing, and personalized medicine: applications, advances, costs, and benefits

COURSE STRUCTURE

The integrated teaching comprises 80 hours of lectures with mandatory attendance (67%). According to the academic calendar, lessons (2 or 3 hours) will be structured as follows:

- 60 hours of lectures for the General Pathology
- 20 hours of lectures for the Laboratory Medicine Technical Sciences

The integrated teaching includes lectures and additional support by the teacher through e-mail or explanations during office hours. During lectures, slides containing topics from the program will be shown to guide students in their study and learning. To achieve the learning objectives, practical examples (in the form of clinical cases) will be used to stimulate and encourage critical discussion of the topic. At the beginning of each lecture, the learning objectives and learning outcomes will be stated; at the end of the lecture, the lecturer will summarize the key points of the discussed topics to meet the learning outcomes.

COURSE GRADE DETERMINATION

The exam for integrated teaching is structured in a written and oral exam.
Written exam: 60 multiple-choice questions with one correct answer (SBA, Single Best Answer). For each correct answer 0.5 points will be assigned. No penalty will be assigned to unanswered questions or incorrect answers. To sit the oral exam, the student must have obtained at least a score of 18/30 (36 correct answers).
Oral exam: the student will be asked to discuss program topics, demonstrating knowledge and skills described in the learning outcomes. Specifically, reasoning, independent judgment, and communication skills will be evaluated following the indications of Dublin descriptors.
The exam includes the entire integrated teaching and it is not allowed to sit the exam for an individual modules. Students who pass the written and oral exam of general pathology are admitted to sit the lab medicine module. If they do not pass the lab med module they have to repeat the whole exam (written and oral). The grade will be expressed in a mark out of thirty, obtained from the weighted average (according to the CFU) between the marks of the oral individual modules.

The exam will be assessed according to the following criteria:

Not suitable: Poor or lacking knowledge and understanding of the topics; limited capacity for analysis and synthesis, frequent generalizations of the requested contents; inability to use technical language.
18-20: Just enough knowledge and understanding of the topics, with obvious imperfections; just sufficient capacity for analysis, synthesis, and autonomy of judgment; poor ability to use technical language.
21-23: Sufficient knowledge and understanding of the topics; sufficient ability to analyze and synthesize with the ability to reason with logic and coherence the required contents; sufficient ability to use technical language.
24-26: Fair knowledge and understanding of the topics; discrete ability to analyze and synthesize with the ability to rigorously argue the required contents; good ability to use technical language.
27-29: Good knowledge and understanding of the required contents; good ability to analyze and synthesize with the ability to rigorously argue the required contents; good ability to use technical language.
30-30L: Excellent level of knowledge and understanding of the required content with excellent ability to analyze and synthesize with the ability to argue the required content in a rigorous, innovative and original way; excellent ability to use technical language.

OPTIONAL ACTIVITIES

Teachers can suggest websites for learning or exercising. Scientific seminars will be organized to introduce and train students on up to date topics or on the scientific research methodology. Optional credits will be awarded to participants.

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READING MATERIALS

The teachers will provide handouts. Students are strongly encouraged to study in one of the following textbook:

-Robbins & Cotran, Pathologic Basis of Diseases, X edition, 2017. Elsevier
-Rubin's Pathology: Clinicopathologic Foundations of Medicine, VII edition, Woulter's

COORDINATOR AVAILABILITY

Office hours by appointment, by e-mail

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