FOUNDATIONS FOR SYSTEM DISEASES

Course: Foundations for System Diseases

Year 3rd

Period (1st semester)

Credits: 7

Faculty: Michela Matteoli, Maurizio D'Incalci, Arturo Chiti, Armando Tripodi, Luca Di Tommaso, Martina Sollini, Ciro Franzese, Luigi Terracciano, Massimo Roncalli, Lorenzo Renne, Davide Pozzi.

Guest Lecturer: Riccardo Fesce, Guido Cavaletti, Diego Fornasari,

Coordinator: Davide Pozzi

Objectives

The purpose of this course is to lay solid foundations of this specific topics, which represent the main pillars of the subsequent course of System Disease I and II. The knowledge provides by this course, together with some in-deeper lecture on specific topic held by expert in the field, will be instrumental for the students to reach a proper introduction of these modules.

Prerequisites

Solid basis of anatomy, cellular/system physiology and principles of pathology are needed in order to tackle the course of Foundations for System Disease.

Contents:

Foundations for system diseases is an integrated course composed by four different modules, Pharmacology, Biochemistry, Imaging and Pathology. The course will cover fundamental aspects of each single module providing the main principles required for the study and understanding of system disease.

Teaching Methods:

The course will be based on in-person lectures through ppt-slides which will be provided at the beginning of each lectures.

Assessment

The evaluation of the content of Foundations for system disease is organized to ensure a proper and well-balanced assessment of the students' knowledge in all the modules of the course. The exam will be based on multiple choice-like test in which the number of questions of each module is proportional to the number of credits. The details of the exam will be better explained at the end of the course.

PHARMACOLOGY

Faculty: Davide Pozzi, Michela Matteoli, Maurizio D'Incalci, Riccardo Fesce.

Year/Semester
3st year/1nd semester

Credits
3 CFU

Textbooks
- Title: "Basic & Clinical Pharmacology"
Author: Bertram G. Katzung Anthony J. Trevor

- Title: "Goodman and Gilman's The Pharmacological Basis of Therapeutics"
Author: Laurence Brunton, Bjorn Knollmann (13° Edition)

- Title: "Pharmacology"
Author: Rang and Dale

- Title: "General and Molecular Pharmacology: Principles of Drug Action"
Author: Clementi and Fumagalli

Overview
The course of Pharmacology is focused on general concepts of Pharmacology which represent the fundamental background for facing system diseases. In particular, the course will be a comprehensive course dealing with concepts of pharmacokinetics, pharmacodynamics chemotherapy, providing an essential understanding about interactions between pharmaceutical drugs and human body.

Learning/teaching methods
The synchronous sessions will be organized as lectures (on campus and TEAMS), interactive discussions and collaborative activities for medium sized groups. Guest lecturers will enrich the course through the inclusion of relevant, specialized knowledge on specific issues.
The asynchronous sessions (off campus) will be characterized by in-depth articles and investigations related to specific topics.

General learning goals:

1. Understanding and Learning of the main principles of pharmacokinetics

2. Understanding and Learning of the main principles of pharmacodynamics

3. Understanding and Learning of the principles of chemotherapy

Topic 1: PRINCIPLE OF PHARMACOKINETICS
Learning goals:
- Topics covered by clinical pharmacology.
- General aspects of pharmacokinetics. Description of the main pharmacokinetic parameters. Mathematical representation of drug absorption, distribution and excretion. Clinical application of pharmacokinetics.
- ADME processes: Absorption - routes of drug administration and main physical/chemical factors regulating drug absorption; Distribution - main physical/chemical factors regulating drug distribution; Metabolism - phase I and phase II reactions of drug metabolism; Elimination - different ways of drug elimination.
- Personalisation of the therapeutic regimen, drug-drug interactions, pharmacokinetics of biologicals. Pharmacogenetics.

Topic 2: PRINCIPLES OF PHARMACODYNAMICS
Learning goals:
- General concepts of pharmacodynamics: history, principles of drug discovery, the concept of receptor.
- Class of receptors fundamental in pharmacology: nuclear receptors, G-coupled receptors, ion channels (including ligand- voltage-gated channels), membrane transporters, enzymes, receptor tyrosine receptors and cytokine receptors.
- Dose-response relationship: occupancy theory, quantifying agonists (including full and partial agonist) and antagonists (including competitive, non-competitive antagonist and inverse agonist). Concepts of tolerance, dependence and sensitization.
- Flipped lesson: Quantitative aspects of drug-receptor relationship (examples of dose-response relationships)

Topic 3: DRUGS ACTING ON THE AUTONOMIC NERVOUS SYSTEM
Learning goals:
- Structure and function of central and peripheral synapses.
- The sympathetic and parasympathetic systems
- The cholinergic synapse and the drugs affecting cholinergic neurotransmission
- The catecholaminergic synapses and the drugs affecting adrenergic neurotransmission

Topic 4: DRUG DEVELOPMENT
Learning goals:
- Processes of drug development: target discovery and validation, hit discovery, lead identification and optimization, preclinical development, clinical studies.
- Adverse effects of drugs, focusing on the problem of neurotoxicity.

Topic 5: CHEMIOTHERAPY OF MICROBIAL AND PARASITE DISEASES
Learning goals:

- Introduction to antibacterial agents: classification and mechanisms of action of antibacterials. Therapeutic choice. Pharmacokinetic aspects. Antibiotic toxicity, antibiotic resistance.
- Classes of antibacterial agents: drugs targeting folic acid metabolism, inhibitors of cell wall synthesis, inhibitors of nucleic acid synthesis, inhibitors of protein synthesis.
- Antibiotics against tuberculosis.
- Antiprotozoal agents, with a particular focus on antimalarial agents.
- Antiviral agents: drugs against Herpes viruses, Influenza viruses, HIV, Hepatitis viruses, SARS-CoV-2.
- Introduction to antifungal agents: classification, resistance.
- Introduction to antihelmintic agents.

Topic 6: DRUG THERAPY OF INFLAMMATION
Learning goals:

- Introduction to the main classes of anti-inflammatory agents.
- Pharmacology of the eicosanoid systems. Nonsteroidal anti-inflammatory drugs (NSAIDs).
- Cytokine inhibitors.
- Glucocorticoids.

Topic 7: CHOLESTEROL AND TRYGLICERIDES LOWERING DRUGS
Learning goals:

- Rationale for preventing and managing high cholesterol levels.
- Drugs targeting cholesterol synthesis, with a particular focus on statins.
- Drugs targeting other pathways involved in cholesterol absorption and metabolism.

CLINICAL BIOCHEMISTRY

Faculty

Armando Tripodi

Year/Semester

3rd year/ 1st Semester

Credits
2 CFU

Overview

The module of Clinical Biochemistry is focused on general concepts of Laboratory Medicine, which represent the fundamental background to assist clinicians to substantiate diagnoses, help preventing diseases and monitoring treatments. In particular, the module will be a comprehensive course dealing with the general concepts on prescribing clinical analyses, obtaining results and their interpretation.

General learning goals

To understand on how the laboratory can help clinicians to

4. Making diagnoses

5. Preventing diseases

6. Making decision on appropriate treatment

7. Monitoring treatment

Teaching Methods

Lectures, clinical case presentation and interactive discussion

Text book & Consultation materials

1. Widman's Clinical Interpretation of Laboratory Tests. RA Sacher, RA McPherson. Ed. FA Davis Company, Philadelphia.

2. The PowerPoint presentations used across lectures will be made available

Topic 1. Aims and fields of the clinical laboratory

Learning goals

Understanding the aims and the fields of the clinical laboratory

Topic 2. Laboratory organization

Learning goals

Core laboratory, specialized laboratory, emergency laboratory, point-of-care laboratory

Topic 3. Laboratory test prescription

Learning goals

Understanding the indications to prescribe laboratory tests, their limitation and appropriateness of prescription.

Topic 4. General characteristics of laboratory tests

Learning goals

Understanding the concept of precision, accuracy, analytical sensitivity, diagnostic sensitivity & specificity and their estimation

Topic 5. Types of errors in laboratory medicine

Learning goals

Understanding the concept, causes and consequences of casual, systematic and gross errors and their estimation

Topic 6. Reference intervals

Learning goals

Understanding the concept of reference interval and the parameters for its estimation (e.g., frequency distribution, mean, standard deviation, percentiles)

Topic 7. Decision levels

Understand the concept of "decision levels" in special clinical situations (e.g., risk levels of cardiovascular disease owing to hypercholesterolemia, diagnosis of acute venous thromboembolism, etc.).

Topic 8. Risk estimation

Learning goals

Understanding the concept of Odds Ratios and their significance in the risk estimation of diseases associated with the presence/absence of genetic polymorphisms.

Topic 9. Preparation of patients to blood sampling

Learning goals

Understanding on how to prepare patients to blood sampling and the impact that some variables (e.g., timing of blood drawing, circadian variation, fasting, physical & emotional status) may have on results interpretation.

Topic 9. Biological specimens

Learning goals

Types of biological specimens (e.g., blood, urine, etc.) and the modality of blood drawing (e.g., syringe-plastic tube, vacuum devices, etc.). How to collect urine specimens.

Topic 10. Pre-analytical variability of blood tests

Learning goals

Understanding on how to centrifuge blood, prepare and store plasma until the analysis and their impact on laboratory results.

Topic 11. Expression of results in laboratory medicine

Learning goals

Understanding the concept of concentration & activity measurements and their differences.

Topic 12. Types of methods in laboratory medicine

Learning goals

Understand the principles of the polymerase chain reaction and search for genetic polymorphisms and their diagnostic significance; main immunochemistry methods and their characteristics (e.g., radial immune-diffusion, immune-electrophoresis, latex agglutination, nephelometry, ELISA, etc.).

Topic 13. Serum proteins

Learning goals

Understanding the general characteristics of serum proteins. Protein separation and quantitation by zone electrophoresis (e.g., albumin and globulins). The equipment used for separation (e.g., electrophoresis chambers, buffers, electrodes, power supplier, etc.). The significance of protein results in different clinical settings.

Topic 14. Testing for Hemostasis

Learning goals

Revision of the concepts of blood coagulation. Understanding the translational relevance that the laboratory diagnosis of hemorrhagic coagulopathies may have across different medical specialties or organs, including their method of investigation (e.g., bleeding time, prothrombin and activated partial thromboplastin time, factor XIII, fibrinolysis, von Willebrand factor, dysfibrinogenemia).

Topic 15. Testing for thrombosis

Learning goals

The translational relevance that the laboratory diagnosis of thrombotic coagulopathies may have across medical specialties or organs, including their methods of investigation (e.g., prothrombotic parameters, the presence of genetic polymorphisms, etc.).

Topic 16. Monitoring drugs

Learning goals

The role of the clinical laboratory in monitoring drugs with special interest in the laboratory methods used for dose adjustment of heparin, warfarin, direct oral anticoagulants and antiplatelet drugs.

DIAGNOSTIC IMAGING AND RADIOTHERAPY

Faculty: Arturo Chiti, Martina Sollini, Ciro Franzese

Credits
1 CFU

Teaching Methods

Lectures, recorded lectures, flipped classrooms, clinical case presentation and interactive discussion.

At the end of the course there will be a general wrap-up, with small groups discussions.

Learning goals:

- Understand the physical principles that form the basis of diagnostic imaging techniques (radiology, computed tomography, magnetic resonance, ultrasound, single photon emission tomography, positron emission tomography), interventional radiology, radionuclide therapy and radiotherapy
- Know the general aspects of technologies used to generate medical images
- Know the general aspects of technologies used in radiation therapy
- Be able to recognize the characteristics of the different disciplines: Radiology, Nuclear Medicine and Radiotherapy, what they have in common and what are their peculiarities
- Understand the general principles related to the appropriate use of diagnostic imaging
- Understand the main indications of radiotherapy in the multidisciplinary approach to patient's treatment
- Know the basic information for the safe use of ionising radiation in medicine

Textbooks

- Brant and Helms's Fundamentals of Diagnostic Radiology, 5th Edition. Jeffrey Klein, Emily N. Vinson, William E. Brant

- Radiation Oncology Primer and Review Essential Concepts and Protocols. George Rodrigues MD FRCPC MSc Vikram Velker MD Lara Best MD

INTRODUCTION TO PATHOLOGY

Faculty: Luigi Terracciano, Massimo Roncalli, Luca Di Tommaso, Lorenzo Renne

Textbooks
Robbins and Cotran, Pathologic Basis of disease, 10th Edition

Overview
This module introduces students to Pathology: a topic that can be considered the central core of modern medicine, i.e. the study of the morphological changes produced by a disease in the normal structure of an organ and its function. As such, pathology is a powerful tool to understand the clinical features of the diseases of individual organs and systems.

Prerequisites
Knowledge of:
- normal anatomy and histology;
- physiology;
- biochemistry

Learning/teaching methods
The Module will be organized as follows:
Synchronous sessions
Asynchronous sessions

The Synchronous sessions will be organized as formal lessons (TEAMS or on campus) and
as collaborative activities for medium sized groups to clarify the doubts related to what is
proposed in the asynchronous sessions.
The Asynchronous sessions (Off Campus) will be characterized by recorded lessons and/or
in-depth articles related to specific topics.

Examination

The knowledge and abilities developed during this course of Foundation in pathology, will be verified during an oral exam at the end of the course of Pathology.

Learning goals

At the end of the Course, students should have **knowledge and understanding skills** to 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:
1. the type and differences of materials routinely examined in pathology (fresh, fixed, frozen);
2. the type and differences of fields in pathology (cytological, histological, molecular and frozen exam);
3. the principles of gross and microscopic evaluation;
4. Use of cytology and/or histology in the management of oncological patients
5. Basic principles and clinical significance of immunohistochemistry and molecular pathology

At the end of the course, students must be **able to apply their knowledge** to interpret a pathological report.

In particular, students should be able to describe and interpret:
1. the terminology used in the report
2. the differences between diagnosis, prognosis and prediction
3. the differences between histotype, grade and stage of an oncological disease.

TOPIC 1: What is pathology?

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

TOPIC 2: The pathologist at work: a fascinating mission.

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

TOPIC 3: The pathologist's report

The language of pathologist

Histotype, grading and staging

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

TOPIC 4: The clinical pathological correlations

the role of autopsy over the years

gross evaluation of surgical specimen and correlation with clinical feature

gross evaluation of autoptic organ s and correlation with clinical features