

SUBJECT	PATHOLOGICAL ANATOMY					
CREDITS	Total	9	Theory	6	Practical	3

GENERAL OBJECTIVES

- To acquire the basic knowledge, morphopathological concepts and pathoanatomical vocabulary needed to understand physiopathology, clinical signs, and the evolution and treatment of disease.
- To be able to understand and use a pathoanatomical diagnostic report.
- To understand the importance of pathological anatomy in the process of reaching an opinion and medical diagnosis.

SPECIFIC OBJECTIVES

Knowledge objectives

Topic 1

- To explain the etymological definition of *pathological anatomy* and how it differs from the current concept.
- To explain how the first autopsies were carried out in Alexandria in 3 BC.
- To explain the evolution of disease concepts from Hippocrates' theory of humours to the organic pathology of Morgagni, Bichat's ideas on tissue pathology, the cell pathology of Virchow and Pauling's molecular pathology.

Topic 2

- To understand how cells respond to insult. To distinguish between reversible and irreversible cell damage, adaptation and lethal acute lesion.
- To define the concepts of *adaptation*, *hypertrophy* and *cell atrophy*, distinguishing them from hyperplasia and understanding the pathogenic mechanisms and main aetiological factors.
- To identify certain special kinds of cell adaptation, such as induction of the endoplasmic reticulum and autophagocytosis.
- To identify certain endogenous pigments, such as melanin, lipofuscin, haemosiderin and ochronosis.

Topic 3

- To identify the main causes of cell lesion.
- To understand the main pathological mechanisms of cell lesion.
- To identify the main ultrastructural alterations that may appear in cell lesions.

Topic 4

- To identify the main alterations in cell water content and the pathogenic mechanism.
- To define hyaline degeneration and identify the main examples.
- To identify the pathogenic mechanism of fat degeneration or steatosis in general, the functional implications and the macroscopic and microscopic characteristics of hepatic and myocardial steatosis.
- To define the concept of *fat infiltration* and identify the main examples.
- To identify the mechanisms of cholesterol ester accumulation and the main examples.
- To identify the main examples of accumulation of mucins from epithelial and connective tissue.

Topic 5

- Concept of *cell death*.
- Concept of *necrosis* and *apoptosis*.
- To understand the relationship between the manifestation time of cell death and morphological alterations according to the techniques used.

- To identify the main varieties of tissue necrosis, the morphological alterations and the most common causes.
- To identify the main forms of evolution of necrotic foci according to the localization and aetiology.
- To identify the most common consequences of necrotic foci according to the functional importance of the affected area and its extension.
- To define heterotopic calcification.
- To identify the process of histological calcification and how it translates into pathology.
- To identify the main forms of dystrophic calcification.
- To define the concept of *psammoma body* and the main examples.

Topic 6

- To define the terms *hypoxia* and *anoxia*.
- To explain that hypoxia can cause tissue lesions that may lead to necrosis.
- To define the terms *passive congestion* or *stasis*, *active congestion* and define the types of related blood vessels.
- To explain that passive congestion may be localized, regional or systemic. To be able to give examples.

Topic 7

- To explain that a stasis oedema is the direct local consequence of venous hypertension.
- To define the terms *exudation* and *transudation*.
- To explain that prolonged venous stasis may cause tissue lesions due to anoxia.
- To describe the macroscopic and microscopic aspects of acute and chronic liver stasis.
- To describe the macroscopic and microscopic aspects of chronic and acute pulmonary stasis.
- To define the term *ischemia*.
- To name the local causes of ischemia.
- To explain that ischemia does not necessarily cause tissue necrosis.
- To name the factors that determine ischemia in an organ.

Topic 8

- To define the terms *thrombus* and *thrombosis*.
- To describe the macroscopic and microscopic aspects of the different kinds of thrombus at the different stages of development. To determine the topographical varieties.
- To describe how the organization of a thrombus represents normal development and that its mobilization represents a greater developmental accident.
- To name the developmental possibilities of a thrombus.
- To name the aetiological factors in thrombosis and give examples of diseases in which it forms a part.
- To name the most common and most serious tissue consequences of an arterial thrombosis.

Topic 9

- To define the term *embolism* and *embolus*.
- To name the various possible consequences, both general and local, of an embolism.
- To name the different types of embolus that may be found.
- To explain that the veins of the lower extremities are the most common origin of pulmonary embolisms.
- To explain that an arterial embolus of the large circulation may come from the left side of the heart, the aorta or the aortic branches.

Topic 10

- To define the terms *infarct* and *gangrene*.
- To describe the vascular conditions which cause white and red infarcts.
- To describe the macroscopic and microscopic aspects and the lesional development of white and red infarcts.
- To define the terms *haemorrhagic infarct* and *apoplexia*. To give examples.

Topic 11

- To name the possible local developments of an interstitial haemorrhagic focus and of a haemorrhage inside a serous cavity.
- To name the visceral lesions that follow a prolonged state of shock.

- To define the term *disseminated intravascular coagulation*. To learn the practical requirements for using pathoanatomical diagnostic techniques.

Topic 12

- To define the concept of *inflammatory reaction*.
- To name the most frequent causes of inflammation.
- To distinguish between the concepts of *inflammation* and *infection*.
- To describe the stages of an inflammatory reaction and the main morphological events associated with each one.

Topic 13

- To name the cells involved in the inflammatory reaction and determine their respective role.
- To define the term *chemical mediator* of inflammation.
- To identify the main chemical mediators of inflammation and their most important effects.
- To identify the different ways in which inflammation develops and name the conditions which affect the process.

Topic 14

- To define the concepts of *organization* and *granulation tissue*.
- To define the concepts of *abscess*, *phlegmon*, *fistula*, *serous inflammation*, *fibrinous*, *suppurating* or *purulent*, *haemorrhagic* and *eosinophilic*.

Topic 15

- To define the concepts of *chronic inflammation* and *specific and non-specific chronic inflammation*.
- To define the terms *granuloma*, *epithelioid cell* and *foreign body*.
- To identify the most frequent causes of granulomatous inflammation and their corresponding morphology.
- To explain the difference between tuberculous and tuberculoid granuloma and be able to give examples of the latter.

Topic 16

- To identify the diagnostic requirements for a tuberculous granuloma.
- To identify the morphological characteristics of tuberculous lesions in the different stages of disease development and in different organs.
- To explain the relationship between mycobacteria, immune response and the different types of morphological lesion.
- To identify the typical lesions associated with the different anatomical and clinical forms of leprosy.

Topic 17

- To define the concepts of *regeneration* and *repair*.
- To learn to classify cells according to their regenerative capacity.

Topic 18

- To identify the healing mechanisms of cutaneous wounds and be able to distinguish between first and second intention wound healing.
- To identify the basic characteristics in the healing of bone fractures, nervous system lesions and lesions of parenchymal organs.

Topic 19

- To identify the general and local factors that influence the healing of tissue lesions.

Topic 20

- To define the concepts of *agenesia*, *aplasia*, *atrophy*, *hypoplasia*, *hypotrophy*, *hyperplasia*, *hypertrophy*, *metaplasia* and *dysplasia*.
- To identify the causes, morphological translation and clinical importance of atrophy, hypertrophy and hyperplasia.
- To define the different types of metaplasia. To identify its causes and biological significance.

Topic 21

- To identify the defence mechanisms found in the animal kingdom and the progressive complexity as one moves up the evolutionary scale.
- To establish the differences between the natural or innate immune system and the adaptive or acquired immune system (AIDS).
- To identify the basic defining characteristics of AIDS.

- To analyse the different stages of the immune response.
- To identify the cellular elements which form the morphological substrate of AIDS and analyse the role of each one in the immune response.
- To locate the cellular elements related to AIDS in the different myelolymphoid organs.
- To study the mobility within the organism of the cellular component related to AIDS.
- To use immunohistochemical techniques to recognise the populations and subpopulations involved in the specific immune response.

Topic 22

- To associate the different types of pathological response in AIDS with specific clinicopathological processes.
- To correlate functional deficits in AIDS with specific morphological substrates.

Topic 23

- To analyse the failure of immune tolerance as a determining factor in autoimmune diseases.

Topic 24

- To explain why organ transplants pose a challenge as regards the protection offered by AGS.

Topic 25

- To define amyloid substance, the different types and correlate them with the various anatomical and clinical forms of amyloidosis.

Topic 26

- To define the term *tumour* or *neoplasia*.
- To distinguish tumours from pseudotumours by applying strict criteria that characterize a neoplasm.
- To define the concepts of *infiltration*, *relapse* and *metastasis*.
- To consider the geographical variations in cancer and list those forms which are most common in our part of the world.

Topic 27

- To explain why all tumour names end with the suffix *-oma*.
- To describe the characteristics of papilloma, adenoma, fibroma and other benign mesenchymal tumours.
- To describe the characteristics of carcinoma, adenocarcinoma, sarcoma and their corresponding varieties.
- To discuss the reactive nature of the stroma in epithelial tumours.
- To define mixed tumours, embryonic tumours, hamartomas and teratomas.

Topic 28

- To explain why in neoplastic cells all stages of the cell cycle are shorter except for the stage of mitosis.
- To explain why neoplastic cells show reduced intracellular cohesion, a loss of contact inhibition, increased contact orientation and increased motility.
- To describe the main antigenic changes in neoplastic cells.
- To explain how the hybridation of neoplastic takes place and to describe its usefulness.
- To explain anaplasia, karyotype alterations and aneuploidy.
- To explain biochemical dedifferentiation and the formation of unprogrammed substances in neoplastic cells.

Topic 29

- To describe the exogenous aetiological factors involved in cancer: radiation, viruses, chemical carcinogens.
- To explain the main pathogenic mechanisms of neoplastic transformation.
 - cell level: monoclonality, multiclonality.
 - molecular level: mutagenesis, epigenetic theory, substances that operate as initiators or promoters.
- To describe the general concept of *protooncogene*, *oncogene* and *gene suppressor* or *antioncogene*.
- To explain how predisposing factors (inheritance, chronic irritations, embryonic remains, fall in immunity) affect the pathogenesis of neoplastic transformation.

Topic 30

- To describe the risk of producing cancer in humans associated with the following: aromatic hydrocarbons, nitrosamines, aromatic amines, aflatoxins, heterocyclic amines, estrogens, androgens, prescribed drugs, industrial products.

- To explain which of the above are found in tobacco or in food and the types of cancer they cause.

Topic 31

- To explain the relationship between the different types of human papilloma virus and cutaneous warts, laryngotracheal papillomas, genital condyloma acuminatum, premalignant and malignant lesions of the cervix and penis.
- To explain the relationship between the Epstein-Barr virus and Burkitt's lymphoma, other lymphomas and nasopharyngeal carcinoma.
- To explain the relationship between HTLV-11 and a certain type of T lymphoma.

Topic 32

- To explain the relationship between ultraviolet rays and skin cancers: squamous carcinoma, basocellular carcinoma and melanoma.
- To explain the relationship between a reduced ozone layer and increased amounts of ultraviolet radiation in the atmosphere.
- To explain the carcinogenic effect in humans of X-rays, alpha rays, beta rays, gamma rays and neutrons.
- To explain the effects of atomic explosions.
- To explain the presence of polonium 210 in cigarette smoke and its relationship to lung cancer.
- To explain the protein products of oncogenes: growth factors, growth factor receptors, signal transduction proteins, cell cycle regulatory proteins.

Topic 33

- To explain the mechanisms of protooncogene activation and how they are transformed into oncogenes.
- To describe the main antioncogenes known at present: retinoblastoma, p53, APC, WT1, DCC, NF1, NF2, VHL, BRCA 1 and 2.

Topic 34

- To define the *benignity* and *malignancy* with respect to neoplasias.
- To learn about tumours of intermediate malignancy.
- To understand the key importance of pathoanatomical study in the diagnosis of benignity and malignancy.
- To describe the main macroscopic, microscopic and developmental characteristics of benign and malign tumours, with special emphasis on the general differential characteristics.
- To define the concept of *cell differentiation* from different histological perspectives (cell architecture and morphology), ultrastructural and functional. To explain the importance and limitations of evaluating the degree of cell differentiation when assessing the prognosis of malignant tumours.

Topic 35

- To study the different types of tumour spreading: to define the concepts of *local invasion* and *distance metastasis*.

Topic 36

- To study the characteristics of neoplasias in the incipient stage: to define the concepts of *in situ carcinoma* and *microinvasive carcinoma*.

Topic 37

- To list and describe the different routes of metastatic dissemination of malignant tumours.
- To study the general characteristics of hematogenous metastasis. To describe the importance of vascular anatomy and the characteristics of the recipient organ and those of the tumour itself in the distribution of metastasis.
- To study the general characteristics of lymphatic metastasis, its biological significance and the pathoanatomical characteristics.
- To determine the importance of pathoanatomical assessment of tumour extension. To learn about the different methods for classifying tumour extension: TNM system and staging.
- To study the biological mechanisms of tumour infiltration and metastasis.
- To describe kinetic aspects of tumour growth.

Topic 38

- To list and describe the different pathoanatomical methods used in studying neoplasias: cytological diagnosis, diagnostic biopsy and examination of surgical pieces.

- To describe the new pathoanatomical techniques used in the study of neoplasias: electronic microscopy, immunohistochemistry, flow cytometry and molecular biology. To consider their importance and utility in diagnosis and the assessment of aggressiveness.

Topics 39-42

- To define the concepts that enable a histogenetic classification of tumours.
- To list the nomenclature of benign and malignant tumours arising in different tissues.
- To study the general characteristics of epithelial, soft-part, haematopoietic, bone and nerve tumours.
- To distinguish between the basic kinds of tumour and their degree of aggressiveness.

Special class 1

- To explain the differences and similarities between arteriosclerosis and atherosclerosis.
- To explain the different stages in the formation of atheroma plaque and the pathogenic mechanisms.
- To explain the complications associated with atheroma plaque and the consequences.
- To explain the importance of arteriolar hyalinosis in the perpetuation of benign arterial hypertension.
- To explain the association between arteriolar necrosis and malignant arterial hypertension.

Applied objectives

- To understand that any tissue removed surgically or expelled naturally must be subjected to pathoanatomical examination.
- To know how to carry out and interpret a macroscopic description of a surgical piece or autopsy material.
- To know how to distinguish macroscopically between a thrombus and a clot.
- To infer the benignity of a tumour, for example, of a uterine leiomyoma, from the macroscopic characteristics of clear delimitation, absence of necrosis and localization.
- To infer the malignancy of a tumour, for example, of a pulmonary carcinoma, from the macroscopic characteristics of infiltrating margins, necrosis, haemorrhage and locoregional ganglion metastasis.
- To know how to distinguish a solid tumour from a cyst.
- To know how to distinguish a primitive hepatic tumour from metastasis.
- To be able to recognize microscopically a malignant tumour from its cell atypia, the abundance of atypical mitosis, necrosis and infiltrating margins.
- To be able to recognize microscopically an adenoma, an adenocarcinoma and a squamous carcinoma.
- To know how to distinguish microscopically between acute and chronic inflammation.
- To be able to recognize microscopically a granuloma.
- To know how to diagnose pneumonia microscopically.
- To know how to diagnose aortic atheromatosis macroscopically.

SYLLABUS

Theory

1. Concept of pathological anatomy

Origin, importance and development of knowledge about the morphological substrate of disease.

2. Normal cells and adapted cells

Structural and ultrastructural characteristics of normal cells. Concept of *cell adaptation*. Induction of the endoplasmic reticulum. Autophagia. Wear-and-tear granules and other endogenous adaptation pigments.

3. Cell lesions

Concept of *reversible* and *irreversible cell lesion*. Causes of cell lesion. Pathogenetic mechanisms responsible for cell lesions. Ultrastructural changes in cell lesions.

4. Cell degeneration

Concept. Changes in cell water content. Hyaline degeneration. Fat breakdown. Fat infiltration or lipomatosis. Intracytoplasmic deposit of cholesterol esters. Mucoid and mixoid degeneration.

5. Cell death

Cell necrosis. Apoptosis. Genes and products (proteins) involved in cell death and survival. Forms of tissue necrosis: coagulative, liquefactive, caseous, gummatous, enzymatic and traumatic (in fatty tissue), fibrinoid, waxy. Gangrene. Development and consequence of necrotic foci. Calcification.

6. Changes in liquid circulation in the organism

Definition of hypoxia, anoxia and ischemia. Definition of passive and active congestion. Local, regional and systemic passive congestion. Macroscopy and microscopy of changes in acute and chronic passive congestion in the lungs and liver.

7. Oedema

General features. Localized and generalized oedema. Physiopathology. The most important morphological changes in different organs.

8. Thrombus and thrombosis

Definition. Macroscopic and microscopic aspects of the thrombus. Normal development of a thrombus towards more unusual organization and development. Thrombus migration. Aetiological factors in thrombosis. Consequences of arterial thrombosis for tissue.

9. Embolus and embolism

Definition. Different types of embolus. Usual origin of pulmonary embolisms and systemic arterial embolisms.

10. Definition of infarct and gangrene

Differences between white and red infarct. Macroscopic and microscopic aspects, physiopathology, evolution of infarcts.

11. Haemorrhage

Morphological substrate of the different kinds of haemorrhage. Pathogeny and nomenclature. Different developmental possibilities of a localized interstitial haemorrhagic focus and blood accumulation inside a serous cavity.

12. Concept of inflammation and its purpose

Clinical signs (redness, tumour, heat, pain and functional limitation) and their correlation with morphological and biochemical changes. Components of the inflammatory process: alterations, vascular aspects, exudation, proliferation. Initiation of alterations and chemical mediators in the inflammatory process.

13. Vascular exudation

Haemodynamic changes in inflammation. Vascular changes and permeability. Exocytosis: margination and surfacing, emigration, chemotaxis, phagocytosis. Inflammatory exudation cells. Changes in the leukocyte count and formula.

14. Classification of inflammation

Classification of inflammation according to duration: acute and chronic. Classification according to the kind of exudation: serous, fibrinous, purulent, haemorrhagic.

15. Non-specific and specific chronic inflammation

Granulomas. Concept. Mechanisms of formation. Classification according to cause: foreign body, viral agents, hyperergic, unknown origin. Types of giant cell in granulomas and their diagnostic significance: Langhans, foreign body, Touton, Aschoff, Virchow, Warthin-Finkeldey. Tuberculous and tuberculoid granulomas.

16. Lesions produced by mycobacteria

Tuberculosis. Leprosy. Atypical mycobacteria.

17. Healing of tissue wounds

Regeneration: labile, stable and permanent cells. Repair via connective tissue.

18. Healing of skin wounds

Healing by first and second intention. Healing of bone fractures. Healing of nervous system lesions. Healing of lesions in parenchymal organs.

19. General and local factors that affect the healing of tissue wounds

Complications in wound healing.

20. Alterations in cell growth and differentiation

Agnesia, aplasia, atrophy, hypoplasia, hypotrophy, hyperplasia, hypertrophy, metaplasia, dysplasia.

21. Immunopathology

Defence mechanisms against insult. The acquired immune system, its morphological and functional substrate. Types of anomalous immune response and their role in different pathological processes.

22. Hypersensitive reactions

Type I (anaphylaxis), type II (cytotoxic), type III (via immunocomplexes) and type IV (deferred).

23. Morphological changes in congenital and acquired immunodeficiency

Autoimmunity: concept. pathogenic mechanisms. Organ-specific and systemic autoimmune diseases.

24. Pathology of rejection in tissue and organ transplants

Adverse reaction of the graft against the host.

25. Amyloidosis

Biochemical and structural characteristics of the amyloid substance. Clinicoanatomical types of amyloidosis. Lesions in the most commonly affected organs.

26. Neoplasia

Definitions: tumour, neoplasia, cancer, oncology. Strict concept of *neoplasia* and distinction from pseudotumoural processes. Concept of *tumour benignity* and *malignancy*. Most common types of cancer.

27. Nomenclature and classification of tumours

The suffix *-oma*. Histogenetic terminology and that depending on tumour benignity and malignancy. Distinction between parenchyma and tumour stroma. Simple tumours: epithelial and mesenchymatic. Mixed and embryonic tumours. Hamartomas and choristomas.

28. Biological characteristics of the neoplastic cell: growth rate

Membrane changes. Antigenic modifications. Hybridation. Morphological and biochemical dedifferentiation. Mechanisms of invasion and metastasis.

29. Carcinogenesis

Tumour monoclonality and multiclonality. Mutagenesis and the epigenetic theory. The initiation-promotion sequence. Predisposing factors: inheritance, chronic irritations, embryonic remains, immunodepression.

30. Chemical carcinogenesis

Main types of carcinogen. Cancers related to tobacco, diet, hormones and other factors.

31. Viral carcinogenesis

Main DNA viral oncogenes: human papilloma virus, Epstein-Barr virus, hepatitis B virus. RNA viral oncogenes: HTLV1.

32. Carcinogenesis due to radiation

Ultraviolet rays. Ionizing radiation. Radiation and DNA repair defects.

33. Molecular bases of cancer

Oncogenes and their proteins. Antioncogenes. Genes that regulate apoptosis, tumour progression and metastasis.

34. Macroscopic and microscopic pathoanatomical criteria of benignity and malignancy

Concept of *cell differentiation*. Histological evaluation of the degree of tumour differentiation.

35. Types of neoplastic extension: local infiltration and distance metastasis

Routes of metastatic dissemination.

36. Tumour progression

In situ and microinvasive carcinoma. Prognostic importance of determining tumour extension. TNM classification and staging.

37. Biology of invasion and metastasis

Concepts of tumour growth kinetics.

38. The pathoanatomical method in studying neoplasias

Cytological diagnosis, diagnostic biopsies and the examination of surgical pieces. Other pathoanatomical techniques used in studying tumours: immunohistochemistry, electronic microscopy, flow cytometry and molecular biology.

39. Study of benign epithelial tumours

Adenomas, papillomas, pseudotumoural lesions.

40. Study of malignant epithelial tumours

Squamous carcinoma, adenocarcinoma, neuroendocrine carcinoma, transitional carcinoma, undifferentiated carcinoma and basocellular carcinoma.

41. Connective tumours of soft parts common to all organs

Classification. Fibroma, fibromatosis and fibrosarcoma. Benign, malignant and intermediate malignant fibrohistiocytic tumours.

Tumours derived from adipose tissue: lipoma and liposarcoma. Tumours of muscular tissue: leiomyoma, leiomyosarcoma, rhabdomyoma and rhabdomyosarcoma.

42. Vascular tumours

Hemangioma, lymphangioma, glomangioma, angiosarcoma, Kaposi's sarcoma and hemangiopericytoma. Tumours originating in bone and cartilage: chondroma, chondrosarcoma, osteoma and osteosarcoma.

Practice

1. Autopsy pathology.
2. Macroscopic pathology.
3. Basic interpretation of lesions in histological preparations observed under the microscope.
4. Clinical experience in a hospital department of pathological anatomy.
5. Basic principles for applying special immunohistochemical techniques, electronic microscopy, molecular biology and flow cytometry to pathoanatomical diagnosis.

LEARNING RESOURCES AND TEACHING METHODS

Theory classes

Clinicopathological papers

Practical classes

Seminars for discussing morphological changes

Interactive videos and videodiscs

Students must take part in all the teaching activities on offer as each one is designed to help them achieve a specific objective.

LEARNING REQUIREMENTS

Students must have sufficient knowledge of cell biology, general histology and human anatomy of organs and systems in order to be able to follow correctly the pathological anatomy teaching program.