



MEDICINE AND SURGERY

Course: Pathology

Year (1st-2nd-3rd-4th-5th-6th): 4th

Period (1st-2nd semester – annual): 2nd

Credits: 4 CFU

Objectives

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 personalized medicine, with particular regard to molecular biology and digital pathology; how does Pathology integrate in the management of a patient. The final goal will be to interpret all the information listed in the pathological report. In particular, students should be able to:

- Interpret the terminology used in the report (histotype, grade; diagnosis, prognosis and prediction)
- Explain the basic principles and clinical significance of immunohistochemistry and molecular pathology
- Illustrate and exemplify the role of histology and immunocytochemistry in the management of an oncological patient.
- Discuss the advantages and limits of cytology in the diagnostic workflow and in the screening.
- Explain why, when and how they should use cytology, histology or both.
- Interpret the impact of molecular pathology in the management of oncological diseases.
- Comment on processing, diagnosis and clinical significance of sentinel lymph node procedure.
- Discuss the significance of intraoperative examination in guiding surgeon's hand.
- Explain the role of biopsy sampling and surgical resection as regard the pathological staging and grading of tumors.
- The role of imaging and of clinical informations in the diagnostic pathological process.
- Interpret and discuss a pathology report of a patient with a tumoral lesion.

Prerequisites

Knowledge of:

- normal anatomy and histology;
- physiology;
- biochemistry
- foundation of pathology

Contents

Breast pathology: from cytology to molecular pathology

- Epidemiology of a breast nodule.
- Define the pathological (cytology, histology and gross findings) and clinical features of fibrocystic disease
- Define the pathological features and the clinical significance of the followings:
 - a. non-proliferative fibrocystic changes
 - b. proliferative fibrocystic changes
 - c. ductal hyperplasia
 - d. sclerosing adenosis
- Compare and contrast the major clinical and pathological features of the following breast diseases:
 - a. fibroadenoma
 - b. phyllodes tumor
 - c. intraductal papilloma.
- Describe the epidemiological features of invasive and not invasive carcinoma of the female breast.
- Describe the potential impact of family history of breast cancer on a patient with a breast nodule.
- Compare and contrast the pathological (cytology, histology and gross findings) and clinical features (relative incidence and prognosis) of the following types of breast carcinoma:
 - a. high-grade in situ ductal carcinoma
 - b. low-grade in situ ductal carcinoma
 - c. in situ lobular carcinoma
 - d. infiltrating ductal carcinoma
 - e. infiltrating lobular carcinoma.
- Describe the role, if any, of special types (tubular, medullary, mucinous, etc) of breast cancer.
- Discuss the role of fine needle aspiration (FNA) in the diagnosis of a patient with a breast nodule.
- Discuss the role of core-biopsy in the diagnosis of a patient with a breast nodule.
- Describe the role of intraoperative examination in a patient with a breast nodule.
- Describe how stage and grade impact on the clinical course of breast cancer.
- List the main clinical or pathologic features that predict poor survival in breast cancer.
- Illustrate the role of biomolecular profile (estrogen, progesteron, MIB1 and HER2 expression) on the management of a patient with breast cancer.
- Know the correlation between the morphological and the molecular classification of breast cancer.
- Define the pathological and clinical features of gynecomastia.
- Know the main pathological and clinical features of invasive male breast cancer.



Female genital system 1. Prevention of cervical carcinoma: from pap test to HPV genotyping

- 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

Female genital system 2: ovarian and endometrial tumors and non-neoplastic pathology

- List the settings that may lead to chronic endometritis (questo non è tumore)
- Describe the incidence, common locations, pathogenesis and clinical features of endometriosis. (questo non è tumore)
- Define adenomyosis. (questo non è tumore)
- Explain the relationship between endometrial hyperplasia and endometrial adenocarcinoma.
- Illustrate risk factors, pathogenesis, clinical features, and spread of endometrial carcinoma.
- Describe and compare the typical clinical presentation and microscopic features of uterine leiomyoma and leiomyosarcoma.
- Define malignant mixed mullerian tumor and endometrial stromal tumor.
- Describe the pathogenesis and clinical features of polycystic ovarian disease. (questo non è tumore)
- Illustrate the basis of the classification of ovarian tumors and incidence of main histological types.
- Describe and contrast the pathologic and clinical features of ovarian surface tumors (serous and mucinous cystadenomas, borderline tumors, and carcinomas).
- Illustrate the issue of peritoneal involvement in the staging of ovarian surface tumors.
- Describe the usual clinical presentation and pathologic features of mature cystic teratomas.
- Describe the two most common types of sex cord-stromal tumors: granulosa-theca cell tumors and fibrothecomas.
- Define Krukenberg tumor.

Central and peripheral nervous system: gliomas and more.

- Distinguish the histologic from the biologic malignancy in primary brain neoplasms.
- Compare and contrast the clinical manifestations of a localized mass effect and the generalized increased intracranial pressure.
- Compare the incidence and distribution of meningiomas and gliomas and illustrate the main histological subgroups of glial tumors.
- List the histologic features to be evaluated when grading a glial neoplasm.
- Describe the clinical course and prognosis of glial neoplasms.
- Illustrate the role of intraoperative examination in the diagnosis of primary and metastatic brain tumors
- Illustrate the main prognostic features of glial tumors with emphasis on immunocytochemical and molecular markers
- Indicate the putative cell of origin of medulloblastoma, the age group most likely to develop this neoplasm, and typical routes of dissemination.
- Indicate the main neoplasms that can metastasize to the brain and discuss the main clinico-pathological features of help in the differential diagnosis with primary tumors
- Explain the similarities and the differences between schwannomas and neurofibromas.
- Describe the major clinical features of neurofibromatosis 1 and 2.
- Illustrate the clinico-pathological features of intracranial hematoma (intraparenchymal, subdural, extradural).
- Illustrate the main histopathological features of Alzheimer and Parkinson diseases.

Tumor of the prostate: From indolent adenocarcinoma to molecularly damaged aggressive variants

- Describe the different anatomical regions of the prostate.
- Illustrate the main morphological features of adenocarcinoma of the prostate.
- Illustrate the epidemiology of prostatic neoplasm.
- Describe the diagnostic strategy of prostate cancer.
- Illustrate the definition of not-clinical significant tumor and active surveillance in prostate cancer patients.
- List the prognostic histological parameters of prostate cancer.
- Illustrate the value of germline and somatic mutations of DNA repair genes in developing prostate carcinoma.
- Define the role of mutations in BRCA genes in prostate carcinoma.
- Synthetic lethality of PARP inhibitors in prostate cancer.

Melanocytic and not melanocytic lesions of the skin

- Illustrate the significance of the following terms: Macule, Papule, Plaque, Pustule, Vesicle, Bullae, Blisters; acantholysis, acanthosis, dyskeratosis, erosion, exocytosis, hydropic swelling, hypergranulosis, hyperkeratosis, lentiginous growth, papillomatosis, parakeratosis, spongiosis, ulceration, vacuolization and illustrate in which pathological context these alterations are more likely to take place.
- Discuss the role of immunofluorescence in the diagnosis of bullous lesions of the skin
- Describe the nonmelanocytic pigmented disorders of the skin.
- Define a melanocytic nevus in terms of clinical manifestations.
- List the variant forms of melanocytic nevi.
- Know the importance of the family history of patients with multiple nevi.
- Define a dysplastic nevus in terms of architectural and cytologic features and clinical significance.
- Discuss the concept that some dysplastic nevi are precursors of malignant melanomas.
- Define a malignant melanoma in terms of architectural difference from a melanocytic nevus.
- Describe the risk factors for the development of a malignant melanoma.
- List the clinical early warning signals for melanoma and the main histological variants of melanoma.
- Discuss the concept of horizontal and vertical growth in melanoma.
- Illustrate the main phenotypic features of melanoma cells.
- Discuss the significance of tumor regression as prognostic parameter related to the staging of melanoma
- Illustrate the Breslow and Clark criteria and their significance in the staging of melanoma.
- Illustrate the role of sentinel node dissection in the evaluation of melanoma staging
- Discuss the predictive significance of b-raf mutation in melanoma cells
- List all the information that need to be reported in a diagnosis of melanoma.
- Illustrate the potential sites of a metastasis for a melanoma
- Define actinic keratosis in terms of clinical presentation, etiology and behaviour.
- Define squamous cell carcinoma of the skin in terms of etiology, pathogenesis, and prognosis.
- List the predisposing factors for the development of a squamous cell carcinoma of the skin.
- Illustrate criteria useful to define the grading of squamous cell carcinoma.
- Discuss whether keratoacantoma is a nosologic entity
- Define a basal cell carcinoma in terms of frequency, pathogenesis, localization, and clinical outcome.
- Illustrate the differential diagnosis of basal cell carcinoma
- Describe the treatment of basal cell carcinoma and how it differs from the treatment of squamous cell carcinoma

Hard & Soft tissue neoplasms: a molecularly heterogenous field

- Illustrate the role of epidemiological and clinical features in the preliminary evaluation of a soft tissue neoplasm
- Discuss the frequency and the prognosis of benign fibrous histiocytoma and dermatofibrosarcoma protuberans of the skin
- Illustrate the main histotypes of soft tissue tumors which emphasis on the distinction between benign and malignant tumors.
- Discuss the more frequent tumor histotypes and related sites of origin
- Illustrate the role of morphology in the characterization of soft tissue tumours and the main criteria to define the grading of a malignant tumor
- Justify the role of immunohistochemistry in the diagnosis of soft tissue tumors
- Justify the role of molecular biology techniques in the diagnosis of soft tissue neoplasms.
- Discuss the significance of the evaluation of surgical margins in the diagnosis of soft tissue tumors
- Understand the difference between primary and secondary cancer of bone
- List factors that predispose to secondary bone cancer
- Discuss the role of a correct epidemiological, clinical and radiological evaluation in the diagnosis of bone tumors.
- Describe the following aspects of osteoma, osteoid osteoma, osteosarcoma, osteochondroma, chondroma, chondrosarcoma: morphology, bones affected, age of patient, prognosis.
- Describe the following aspects of Ewing sarcoma and giant cell tumor of bone: morphology, pathogenesis, bones affected, age of patient, prognosis.
- Describe the following aspects of metastatic tumors to bone: incidence, route of metastasis, tissue of origin, diagnostic immunocytochemical markers

Intraoperative exam: guiding surgeon's hand

- Illustrate advantages and limits of frozen sections (including those performed for biobanking)
- Discuss the diagnostic role of cytological smears in combination with frozen section
- Illustrate advantages and limits of Intraoperative gross examination
- Illustrate the main indication of frozen sections with regards to breast and female genital system tumors, skin tumors, soft tissue tumors, thyroid nodules, CNS tumors
- Discuss which are the main pathologies that are unsuitable to be investigated with intraoperative exam

The clinical significance of a molecular pathology lab

- Illustrate which are the main tumor categories where a molecular analysis can significantly contribute to the patient management and why.
- Illustrate and exemplify the diagnostic role of a molecular analysis
- Illustrate and exemplify the prognostic role of a molecular analysis
- Illustrate and exemplify the predictive role of a molecular analysis
- Illustrate tissue characteristics which make a specimen suitable to be examined in a pathology lab (pre-analytical features)
- Discuss the critical role of morphology as a guide for the execution and for the correct interpretation of a molecular test
- Illustrate the role of pathologist in a molecular pathology lab
- Illustrate which are currently the main technologies of a molecular pathology lab
- Discuss general principles of quality control in a molecular pathology lab

Morphological and Molecular approach to Lung cancer

- Illustrate epidemiology, clinical features and risk factors of lung cancer
- Genetic features
- Illustrate precursor lesions of lung cancer
- Histological classification of lung cancer
- Illustrate gross findings, histology and immunohistochemical features of lung cancer
- Diagnostic, prognostic and predictive molecular features of different subtypes of lung cancer
- Describe the clinical course and prognosis of lung cancer
- Cytological and bioptic approach to lung nodule

Morphological and Molecular approach to Colorectal cancer

- Illustrate epidemiology, clinical features and risk factors of Colorectal cancer
- Genetic features
- Illustrate precursor lesions of colorectal cancer
- Adenoma-carcinoma sequence
- Histological classification of colorectal cancer
- Illustrate gross findings, histology and immunohistochemical features of colorectal cancer
- Diagnostic, prognostic and predictive molecular features of colorectal cancer
- Describe the clinical course and prognosis of colorectal cancer



Haematopathology: a matter of multidisciplinary integration

- Illustrate the normal morphology and the physiology of lymph nodes, spleen, and bone marrow
- Illustrate the role of multidisciplinary integration of clinical, epidemiological, radiological, histopathological, and genetic data in the preliminary evaluation and diagnosis of blood cancers.
- Illustrate the indication of nodal excision and bone marrow biopsy
- Describe the histopathological changes and the main genetic alteration that occur in the bone marrow of patients with myelodysplastic syndromes, myeloproliferative neoplasms, acute myeloid leukemia, and systemic mastocytosis
- Describe the general principles of the current (2022) classification of acute myeloid leukemia
- Discuss the importance of immunohistochemical markers in the differential diagnosis of lymphomas
- Illustrate the main architectural patterns in the pathological (neoplastic or reactive) lymph node
- Illustrate the most important immunohistochemical and molecular markers in “small B-cell lymphomas”
- Illustrate the most important immunohistochemical and molecular markers in aggressive large B cell lymphoma and their prognostic relevance
- Illustrate the most important immunohistochemical and molecular markers in T cell lymphoma
- Discuss the clinical and histopathological peculiarity of Hodgkin lymphoma, its subtypes, and prognosis
- Illustrate the clinico-pathological and molecular features of Langerhans cell histiocytosis, Juvenile Xanthogranuloma, and Erdheim-Chester disease.



Teaching Methods

- Lectures
- Tutorial activities with digital slides.

Verification of learning

Oral assessment.

Texts

Kumar, Abbas, Ester: Robbins and Cotran, Pathologic Basis of Disease, 10th Edition, Elsevier