

## CLINICAL CYTOLOGY

### GENERAL INFORMATIONS

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Assistant/Associate	Assoc. Prof. Valerija Miličić, MD, PhD Asst. Prof. Marija Perić, MD, PhD Adela Benkotić, MD
Study Programme	Undergraduate University Study of Medical Laboratory Diagnostics
Status of the course	mandatory
Year of study, semester	3 <sup>rd</sup> year, 5 <sup>th</sup> semester
ECTS	<b>4</b>
Workload (hours)	Lectures: 30; Seminars: 5; Laboratory exercises: 3
Expected number of students	30-35

### COURSE DESCRIPTION

#### Course objectives

The main goals of this course are introducing students with the basic facts about clinical cytology, to introduce and understand the indications for the application of cytology and the possibilities of applying diagnostic cytology in various fields of medicine through familiarization with the working methods and organization of cytology laboratories.

#### Enrolment requirements and entry competencies

The basis for knowing, performing, and understanding cytological skills is a good knowledge of pathology, and to achieve consistency and applicability of cytological findings in clinical practice, it is necessary to know the clinical manifestations of the disease.

#### Learning outcomes at the Programme level

**1.1, 1.2, 2.1, 2.2, 2.3, 2.6, 3.1, 3.2**

#### Learning outcomes

After completing lectures, seminars and exercises, independent study and passing the exam, students will be able to:

1. explain the interdisciplinary approach to clinical cytology, the importance of the cytology team, the role of the cytotechnologist in the organization of the work of the cytology laboratory.
2. know the methods of obtaining material for cytological analysis.
3. apply the methods of technical processing of material for cytological analysis.
4. apply the methods for archive and process liquid samples.
5. stain cytological preparations (by May-Grünwald-Giemsa and Papanicolaou methods)
6. recognize basic cellular and non-cellular elements in cytological smears.
7. use the laboratory information system for patient registration, sample registration, accurate patient and sample identification.
8. explain the methods for taking and processing cytological preparations in the cytology of the respiratory system, urinary tract and breast.

#### Course content

**Lectures:** A brief history of the development of clinical cytology in our country, an interdisciplinary approach to clinical cytology. Quality control - internal and external control mechanisms. Cytology-based screening programs (opportunistic and organized). Cytological team, role of cytotechnician (cytoscreener), organization of work in cytological laboratories, all of which affects the accuracy of cytological findings, advantages and disadvantages of cytological analysis, indications and contraindications, classification of cytological findings, cytological criteria of malignancy, characteristics of normal-benign cells in cytological preparations, the problem of

differential diagnosis of tumors, the causes of false positive and false negative cytological findings. Methods of obtaining material for cytological analysis - aspiration and exfoliative cytology, "imprint" method, cytological puncture - palpable formations, non-palpable under US control, under CT control, exfoliative samples - (VCE smears, swabs, excochleates, extracts, brushing, washing, effusions, urine, sputum), cytology. Technical processing of material for cytological analysis: preparation of smears, centrifuge, cytocentrifuge, labeling of preparations. Basic and special staining in cytology, method of analyzing cytological preparations, elements of cytological findings. Numbering of samples. Basic principles of sample interpretation. Reception and proper identification of patients. Management of medical records. Archiving samples. The value and place of cytology in clinical work. Accuracy of cytology (sensitivity, specificity). Advantages and disadvantages. Quality control - internal and external control mechanisms. Cytology-based screening programs (opportunistic and organized). Indications for the application of cytology in gynecology and perinatology, samples for cytological analysis, methods of sample collection, instruments for taking a cytological sample, transfer to a coverslip, fixation of samples, staining and mounting.

*Bone Marrow and Lymph Nodes Cytology.* Organs of hematopoiesis; structure and function of hematopoietic organs, bone marrow, lymphatic system, normal lymph node, blood cells; erythrocytes, leukocytes, platelets. Granulopoiesis - developmental stages of cells of the granulocytic order, morphology of leukocytes, morphological changes of granulocytes - congenital anomalies of granulocytes, toxic granules, alkaline phosphatase in leukocytes. Erythropoiesis - developmental stages of cells of the erythrocyte order, morphological changes of erythrocytes - hemolytic anemia, megaloblastic anemia, sideropenic anemia. Thrombopoiesis - developmental stages of cells of the platelet order. Diseases of erythropoiesis; anemias, polycythemias, classification of anemias, deficiency anemias; macrocytic, sideropenic, hemolytic anemia. Hematopoietic malignant diseases; Myelodysplasias, Chronic myeloproliferative diseases. Acute leukemias, cytochemistry, immunocytochemistry.

*Gynaecological Cytology.* Indications for the application of cytology in gynecology and perinatology, samples for cytological analysis, methods of sample collection, instruments for taking a cytological sample, transfer to a coverslip, fixation of samples, staining and mounting. Microscopic analysis of finished preparations (principle and technique of preparation analysis, assessment of sample adequacy, description, cytological opinion and diagnosis, recommendations), normal cells of the female genital tract at different ages of a woman's life, cytohormonal analyses. Benign proliferative changes of the cervix and cell changes during radiation and/or chemotherapeutic therapy. Degrees of purity regarding the number of leukocytes and *Bacillus vaginalis* flora, the causative agent of sexually transmitted diseases in the Pap smear. Cytology of intraepithelial and invasive lesions of the cervix, vagina and vulva.

*Respiratory tract cytology.* Epidemiology of lung cancer. History of pulmonary cytology. Types of samples in pulmonology cytology: exfoliative - swab of the nasal mucosa for eosinophils, sputum, bronchial secretion, BAL, impression (brushing of the bronchus, biopsy material of the bronchus, lung, surgical material, pleural biopsy), pleural effusion; aspiration - punctate (transbronchial - transtracheal, transthoracic, punctate lymph nodes). Cytomorphology of respiratory system cells. Cytology of inflammatory (granulomatous reaction and inflammation) and other non-tumor changes in pulmonology. Lung cancer cytology and immunocytochemistry of lung cancer. Molecular methods.

*Breast Cytology.* Structure of the breast, indications for cytological puncture of the breast and taking breast samples (limitations and complications), types of samples, method of taking samples (exfoliative, aspiration and impression cytology), preparation of cytological preparations (liquid and solid). Aspiration cytodiagnosis: microscopic analysis of preparations, normal cells in breast punctate, cytomorphology of cystic and solid non-neoplastic formations. Cytomorphology of benign and malignant growths in breast puncta, diagnostic parameters benign/malignant. Exfoliative cytodiagnosics: analysis of breast explants/secretions, physiological and pathological

appearance of explants, technique of taking explants (selective sampling of explants), macroscopic description of explants, microscopic appearance of normal explants, description, cytological opinion and diagnosis, recommendations.

*Urine Cytology.* Structure of the urinary system. Indications for cytological examination of the urinary tract and types of material. Risk factors and incidence of urothelial tumors. Collection and processing of samples for cytodiagnosis. Cytological analysis of supravital and permanently stained samples. Cytomorphology of cells in urine. Cytomorphological changes in cells during inflammation. "Decoy" cells and cytomorphology in acute renal rejection. Morphological changes in urolithiasis and iatrogenic changes. Hematuria. Atypia and dyskaryosis of the urothelium - cytomorphology. Tumors of the urinary tract system - cytomorphology.

**Seminars:** 1. Standard approach to laboratory diagnosis of acute leukemias. 2. G.N. Papanicolaou – meaning for the development of gynecological cytology, 3. Cytology of pleural effusions. Tumors of the mediastinum. 4. Place and value of cytology in the early diagnosis of breast cancer. 5. New technologies in the diagnosis of urinary tract tumors.

**Exercises:** 1. Introduction to the organization of work in the cytology laboratory. Work in the outpatient clinic for the collection of materials - patient reception and assistance to the doctor when performing a puncture. Work in the outpatient clinic for punctures of palpable formations and bone marrow - patient reception and assistance to the doctor during the puncture. Punctures under the control of UZV.

2. Punctures under ultrasound control. Reception and technical processing of material for cytological analysis - making a smear, concentrating the sample (centrifugation), fixing the material (two methods of fixation). Technical processing of material for cytological analysis - staining and microscopy (supravital and intraoperative staining).

3. Technical processing of material for cytological analysis - staining: MGG., Papanicolaou. Cytochemical staining (Fe, PAS, POX, ANAE, NASD, acid phosphatase). Immunocytochemical staining. Numbering of preparations, archiving of preparations; knowledge with keeping medical records.

#### **Mode of teaching**

Lectures, Problem solving seminars, Laboratory exercises

#### **Student obligations**

Regular attendance and active participation in classes is mandatory. It is justifiable to miss 30% of each form of teaching, and uncompleted exercises and seminars must be passed. The student is obliged to take all forms of knowledge testing.

#### **Monitoring student work (Connectivity of learning outcomes, teaching methods and grading)**

Exam method: written exam.

*Evaluation of the final written exam:*

Teaching activity	ECTS	Learning outcome	Student activity	Assessment methods	Grade points	
					Min.	Max.
Attending classes		1-8	Class attendance	Attendance record	1	5
Seminars	0.75	1-8	Preparation of seminar	Seminar presentation	4	15
Exercises	1.25	3-7	Exercises attendance, performing exercises	Attendance record, active participation	15	30
Final exam	2	1-8	Studying for the final exam	Written exam	30	50
<b>Total</b>	<b>4</b>				<b>50</b>	<b>100</b>

Percentage of correct answers (%)	Grade points
60.00-64.99	5
65.00-69.99	10
70.00-74.99	15
75.00-79.99	20
80.00-84.99	25
85.00-89.99	30
90.00-94.99	38
95.00-100	50

*Calculation of final grade:*

Grade points earned in the final exam are added to the grade points earned during the course. Grading in the ECTS system is done by absolute distribution, i.e. based on total achievement and is compared to the numerical system in the following manner: A - excellent (5): 90-100 grade points; B - very good (4): 80-89.99 grade points; C - good (3): 65-79.99 grade points; D - sufficient (2): 50-64.99 grade points.

**Required reading (available in the library and through other media)**

Title	Number of copies in the library	Availability through other media
At the beginning of the lecture, students will receive written materials that form the base of the exam		
Pajtler M. Metode detekcije, rane dijagnoze i prevencije neoplastičnih promjena vrata maternice, Medicinski fakultet Osijek, 2007.	8	

**Additional reading**

1. Gray W, Kocjan G. Diagnostic Cytopathology. Churchill Livingstone Elsevier, 2010.
2. Loffler H, Rastetter J, Haferlach T. Atlas of Clinical Hematology. Springer, Sixth Revised Edition
1. Selected journal articles.

**Course evaluation procedures**

Anonymous, quantitative, standardised student survey on the course and the teacher's work implemented by the Quality improvement office of the Faculty of Medicine Osijek.