MINISTRY OF HEALTH CARE OF THE REPUBLIC OF UZBEKISTAN

TASHKENT MEDICAL ACADEMY

"INTRODUCTION TO CYTOLOGICAL DIAGNOSIS"

Study guide

TASHKENT-2023

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TABLE OF CONTENTS

INTRODUCTION

Cytological diagnosis is an integral part of clinical laboratory diagnosis and helps to control the effectiveness of clinical diagnosis and treatment.

The textbook "Introduction to cytological diagnosis" contains modern information about the development of cells, their activity, morphological structure and properties. The first chapter provides information on the importance of cytological examinations in preventive and diagnostic medicine, safety of techniques in working with cytological material, types of cytological examination, rules for obtaining material for cytological examination, preparation of cytological material.

The second chapter provides information on cellular structural components, epithelial tissue cytomorphology, cytological classification of cervical diseases, reactive changes, pre-tumor diseases, benign and malignant tumors.

The third chapter presents methods of cytological examination in hematology, anemias, thrombocytic line pathology, cytological diagnosis of acute and chronic leukemias, leukocytosis, leukemic reaction and cytological differential diagnosis of leukemias.

The "Introduction to cytological diagnosis" training manual is intended for general clinical and cytological laboratory workers, students of medical-biological faculty of medical universities, master's students and clinical supervisors of "Clinical laboratory diagnosis" direction.

CHAPTER 1. INTRODUCTION TO CYTOLOGICAL DIAGNOSTICS.

1.1. Importance of cytological examinations in preventive and diagnostic medicine. Safety techniques when working with cytological material.

The purpose of the training: to provide information about cytological diagnostics, to familiarize with the importance of cytological examinations in preventive and diagnostic medicine, to learn the requirements for ensuring the safety of medical personnel during cytological examination, biological safety rules, technical safety rules, rules for working with a microscope.

Cytology is the science of cell structure and function. Cytology is derived from the Greek words "cytos" meaning cell and "logos" meaning science, teaching. Cytology studies the cellular structure of biological materials using a microscope:

1. Features of cell structure, organs, tissues, cellular composition of natural body fluids.

2. Cell activity.

3. Cell reproduction processes.

4. Cell aging and death processes.

5. Cell structures and their participation in physiological processes.

6. Methods of regulation of physiological processes.

7. Reproduction of cells and their parts.

8. Adaptation of cells to the environment.

9. Cell reactions to various factors.

10. Changes in the nucleus, cytoplasm, formation of structures and cell complexes in pathology.

Clinical cytology evaluates the morphological structure of cell elements by microscopy of a cytological preparation (smear) in order to determine pre-tumor or

tumor transformation.Cytological examination is currently one of the most accurate examination methods of modern medicine, and the accuracy of the results is close to 100%. Sensitivity - false-negative results of testing methods are about 94% for all types of cytological analysis. Specificity - the ability to give positive results in the presence of the disease is not less than 99%.

Guidelines for recommending cytological examination:

• suspicion of the inflammatory process;

• suspicion of a malignant tumor;

• accurate diagnosis of viral infection;

• confirmation of oncological diagnosis during surgery;

• monitoring the effect of treatment of various diseases;

• preventive screening;

• monitor the possibility of relapse in oncological diseases.

Morphological examination is based on cytological examination, but unlike biopsy, in the process of cytological examination:

- a very small amount of biological material is required;

- no special equipment is required to obtain cytological material (smear or scrapings) and the process is carried out in a few minutes;

- is a non-invasive, painless treatment;

- vaginal smear helps to check the hormonal dysfunction of the ovaries;

- examination of vaginal dome and cervical smear helps to identify cancer and pre-cancer conditions;

- allows to detect malignant tumors of lungs, stomach, bladder, prostate gland and other organs in a short time;

- allows to determine the cytological form of the tumor, to determine the spread of malignant tumors, to determine metastases;

- viral diseases, inflammatory diseases and autoimmune pathologies can be accurately diagnosed.Inspection materials may vary. The method of their preparation depends on the nature of damage to organs and tissues. The following materials are examined cytologically:

- blood;

- urine;

- sputum;

- swabs from the cervix, uterus and cervical canal;

- smears from wounds, fistulas, erosions, wounds;

- smears from prostate fluid;

- spinal fluid;

- amniotic fluid (pre-fetal water);

- smears and scrapings from the surface of some tumors;

- fluids of joints and serous spaces (abdominal cavity, pleural cavity, pericardial cavity);

- materials obtained during endoscopic examination of the bronchus, stomach, intestine;

- secretions of mammary glands;

- smears of tissues, organs or punctured organs (for example, mammary gland, lymph node) removed during surgery.

The results of cytological examination are affected by the quality of the obtained material, its correct preparation, and moderate staining.

For the accuracy and reliability of the check, the following rules must be observed:

- taking biological materials from two or three points;

- it is necessary to follow the rules of the correct preparation of the sample: preparing a smear from the material, fixing and painting the smears;

- choosing the right method of obtaining biological material.

Various cytological analysis methods can be used in different laboratories, but the main ones are as follows:

1. Light microscopy;

2. Electron microscopy;

3. Immunocytochemical examination.

Clinical cytology is a part of laboratory diagnostics based on examination of cells (blood, bone marrow, exudates, transudates, secretions of various organs). Cytological examinations are widely used in mass preventive examinations, especially in groups prone to the development of malignant tumors.

Organization of screening for the purpose of early and timely diagnosis of tumors consists of two stages:

1. Mass screening of the population in order to determine tumor or pre-tumor conditions (examination of all population groups).

2. Carrying out examinations in subgroups selected as a result of screening (examination of a group with a high risk).

The use of cytological examination as a screening for cervical cancer is considered a highly effective method, the possibility of detecting tumors is 10 times higher than visual diagnosis; especially with the possibility of detecting cancer in its early and asymptomatic stages is even more important.

Requirements for ensuring occupational safety of medical personnel during cytological examination.

Ensuring labor safety is based on general safety rules in clinical and diagnostic laboratories. Biological safety measures, waste collection and safety, rules for working with electrical equipment and reagents, fire safety should be ensured.

Biological safety rules.

All samples of biological material (aspirate, smear) are sources of infection. To ensure biological safety, the following rules must be observed:

1. Opening of the biological material brought to the cytological laboratory is carried out in special personal protective equipment (gowns, rubber gloves).

2. Smears brought to the laboratory are placed in special metal or plastic containers, unfixed smears are not left on the table.

3. At the end of the work, employees disinfect the workplace and laboratory room in rubber gloves. For the purpose of disinfection, specially recommended means for neutralizing virus and bacterial flora are used.

4. Hazardous residues of biological material, waste generated during the implementation of technology are collected in hermetic disposable containers and delivered to special places of the institution.

5. All employees working with electrical equipment must follow the safety techniques specified in its technical passport and instructions.

6. All laboratory workers working with chemical reagents must follow the rules of working with reagents, personal hygiene rules, and use special protective equipment.

7. Fire safety rules must be followed for fire prevention in accordance with the procedure specified in special normative documents.

Technical safety rules:

1. In order to attract students to laboratory work, it is necessary to provide information on the rules of technical safety.

2. It is necessary to work in the laboratory in a white coat and have a personal towel.

3. There must be a student on duty assigned to each activity, who is responsible for cleanliness and order.

4.Each student should have a workplace attached to it, responsible for its cleanliness and order.

5. Foodstuffs and drinking water cannot be stored in the laboratory, it is forbidden to eat and drink in containers intended for chemical agents.

6. It is necessary to check heating equipment, ventilation, protective equipment before work. Equipment and apparatus should be used only by a special employee.

7. The use of broken containers, the use of reagents without labels is prohibited.

8. Prepared solutions are placed in specially labeled containers.

9. Added equipment and electrical equipment cannot be left unattended.

10. To measure acid, alkali and toxic reagents, it is necessary to use rubber cylinders or pipettes with a cotton swab or a closed end.

11. Protective glasses, rubber gloves, aprons should be used when working with alkaline substances.

12. Alkaline and acidic reagents must be neutralized before disposal.

13. To heat flammable and volatile reagents, a water bath should be used, it is impossible to heat them over an open flame or hold them near a flame.

14. In the event of a sudden power outage, all electrical equipment must be turned off.

15. When flammable liquids burn, a special fire extinguisher, earth should be used.

16. When electrical wires catch fire, disconnect it from the electrical network, extinguish the fire max

17. Be careful when working with mercury thermometers.

18. At the end of the work, it is necessary to clean the workplace (remove reagents and equipment from the table, collect waste, wash the table and wipe it with a dry cloth) and hand it over to the student on duty.

Rules for working with a microscope.

1. To clean and protect the microscope from damage, the microscope must be covered with a special folder when not in use.

2. Lenses and other optical equipment should be cleaned.

3. Do not touch the surface of the lenses with your fingers. To protect optical equipment from dust, eyepieces should be stored in tubes or covered with caps.

4. Eyepieces, lenses and the optical surface of the condenser can be cleaned with clean cotton soaked in a special liquid. It is necessary to send the lens to an optical workshop to clean the inner surface of the objective lens. It is impossible to dial an independent lens, eyepiece, condenser without an engineer.

Basic mistakes in working with a microscope limit the capabilities of the microscope. These errors include:

1. Using a curved mirror and a condenser at the same time will spoil the illumination of the microscope.

2. Using high-aperture condensers with low-aperture lenses reduces image quality. To eliminate this error, the condenser aperture is initially reduced, that is, its upper lens is removed.

3. Unloading the condenser without taking into account the thickness of the glass of the object leads to the appearance of artifacts.

4. The illumination of the field of view can be controlled by lowering or raising the light condenser of the microscope and changing the size of the condenser aperture.

5.The use of neutral light filters and special glasses affects the illumination of the microscope and the medical worker preserves his vision.

6. The use of thick objective lenses prevents light from entering high-aperture lenses, resulting in the condenser not being able to focus on the subject.

Safety techniques when working with a microscope.

Safety techniques should be followed when working with a microscope illuminator. To replace the microscope lamp, it is done after 15 - 20 minutes after disconnecting from the power supply. The microscope cannot be left unattended when it is switched on.

Control questions:

1. What does cytology study?

2. Instructions for cytological examination.

3. Materials used in cytological examination.

4. Rules of cytological examination.

5. Safety techniques when working in cytological laboratories.

6. Rules for working with a microscope.

7. Mistakes in working with a microscope.

8. Technical safety of working with a microscope.

1.2. Cytological laboratories and their equipment. Organizing the work of cytological laboratories, keeping their documents. Types of cytological examination.

Purpose of training: Types of cytological laboratories, types of cytological examination, organization of work of cytological laboratories, tasks of cytological

laboratory employees, work scheme of cytological laboratory, documentation in cytological laboratory, delivery of biological material to the laboratory, registration and marking, and familiarization with equipment in cytological laboratory.

The cytological laboratory is part of the clinical-diagnostic laboratory and works as central cytological laboratories in oncological dispensaries and large multidisciplinary hospitals. Complex, automated bulk checks requiring special equipment are checked in central laboratories.

Special cytological laboratories are organized in dispensaries, women's consultations, maternity hospitals, sanatoriums, pathological-anatomical bureaus, and special laboratory analyzes are checked at the request of the organization.

The following cytological examinations are carried out in clinical diagnostic laboratories:

1. Cytological examination of puncture material.

Tumors in the head, neck, mammary gland, thyroid gland, lymph nodes, bones, soft tissues of the limbs, skin, lungs, chest cavity, abdomen and retro-abdominal cavity, taking a punctate through a fine needle for cytological examination from dense neoplastic formations (fine needle biopsy));

2. Cytological examination of exfoliative material.

Cytological examination of secretions, excreta, erosions, wounds, wounds, cuts and separations on the surface of fistulas.

3. Cytological examination of endoscopic material.

Cytological examination of the material obtained during bronchoscopy, bronchial catheterization, esophagoscopy, gastroscopy, duodenoscopy, laparoscopy, rectomanoscopy, colonoscopy, cystoscopy and other types of endoscopic examination.

4. Cytological examination of biopsy and operative material.

Cytological examination of biopsy fragments and smears from operative material, cuttings.

5. Cytochemical examination of the material, including glycogen, lipids, DNA (deoxyribonucleic acid), RNA (ribonucleic acid), enzymes, etc.

6. Identification of sex chromatin in tumor cells.

The main purpose of cytological analysis is to determine whether there is a malignant tumor (oncocytology). During the differential diagnosis, the nature of the pathological process, inflammatory, reactive, proliferative changes or precancerous conditions, as well as benign tumors are identified. The importance of morphological examinations in the diagnosis of tumors is increasing. The morphological characteristics of the tumor also help to choose the right treatment method (surgical, light, chemotherapeutic and their combination), because the effectiveness of treatment procedures depends on the structure, origin and degree of atypia of the tumor cells.

Cytological analysis helps to assess the nature and degree of epithelial proliferation, to diagnose precancerous conditions (dysplasias), and to identify and distinguish groups with a high risk based on it. Cytological examination is of great value in monitoring epithelial cell changes in high-risk groups, which cannot be observed by other morphological methods. The greatest achievement of this method is the detection of cancer in the early uncomplicated stages. The development of endoscopic techniques and ultrasound examination methods paved the way for more widespread use of cytological analysis in the diagnosis of tumors.

Duties of cytological laboratory workers.

Duties of the head of the cytological laboratory:

- organizes and ensures the work of the department, prepares the work plan of the department and distributes the duties of employees;

- organizes and controls the delivery of cytological material and test results from the preventive treatment institutions to the laboratory. The chief physician of the institution sending the material, the chief physician of the main institution in the centralized laboratory is responsible for the delivery of cytological material;

- attached treatment provides sending of cytological laboratory staff for urgent cytological examinations to preventive institutions, puncture, urgent consultations in severe cases, participation in clinical-biopsy conferences;

- selects cases to be analyzed at clinical-biopsy conferences, makes a plan for treatment with the deputy chief physician, organizes conferences (supervises speakers, reviews cytological preparations, slides, etc.);

- Analyzes the annual work of the cytological laboratory and presents it to the management of the institution;

- organizes the continuous replenishment of the collection of micropreparations;

- advises doctors of clinical departments on issues of clinical cytology;

- organizes training of cytological laboratory doctors and laboratory assistants.For this purpose, it holds periodical and thematic conferences, supervises the examination of cytological material; ensures the acquisition of new cytological and cytochemical methods; analyzes complex problems of cytological diagnosis;

- ensures the readiness of the department when infectious material is received for cytological examination;

- ensures compliance by employees with safety rules, fire safety, rules for the storage of toxic reagents.

Duties of a doctor-cytologist:

- conducts cytological examination of prophylactic, diagnostic, hormonal, cytogenetic material; if necessary, he conducts an urgent cytological examination, the endoscopist participates in the collection of biological material together with the surgeon and other specialists, performs a puncture biopsy independently;

- prepares micropreparations for clinical - biopsy conferences, archives, exhibitions;

- advises the laboratory technician on cytological material processing, staining methods, quantity of cytological preparations;

- controls the quality and training time of laboratory assistants, gives them medical recommendations;

- consults with other doctors of the department and the head of the department in case of unknown or doubtful results;

- examines the cytological material microscopically, describes the microscopic picture and makes a cytological diagnosis.When the diagnosis of dangerous tumor, severe epithelial dysplasia, hormonal therapy, diseases requiring surgery is confirmed, the result form is signed by the head of the cytological laboratory and two doctors-cytologists;

- informs the head of the cytological laboratory about the deficiencies caused in the work process;

- carries out organizational and methodical work;

- reports on the work performed month by month.

Duties of senior laboratory technician:

- middle and junior employees of the laboratory fill in the tables, calculate the monthly salary and apply for the chemical reagents, materials and other necessary equipment needed for the laboratory;

- prepares solutions of basic chemical reagents, makes accounting and stores chemical reagents;

- provides education and training of middle and junior employees in the laboratory;

- helps the head of the department to fill out reports and questionnaires about chemical reagents, equipment and apparatus;

- controls the sanitary-epidemiological condition of the laboratory.

Duties of a laboratory assistant:

- fills in documents for recording cytological materials;

- processes cytological material using additional methods;

- prepares urgent cytological preparations;

- controls and documents the issuance of micropreparations from the archive;

- controls equipment and apparatus;

- prepares chemical reagents;

- conducts organizational and methodical work to improve the quality of material;

- reports on the work performed month by month.

Work scheme of the cytological laboratory:

- obtaining biological material for examination;

- marking and registration;

- paint smears;

- microscopic examination of cytological preparations;

- write a response to a referral for inspection;

- keep a copy of the answers in the laboratory;

- distribution of answers to clinical departments.

At all stages, the material and its routing must be well preserved. Answers should be given in duplicate if necessary. Cytological preparations with pre-tumor and tumor processes, special inflammation should be kept in the archive.Other smears are washed off and glassware is reused to make smears.

Delivery of biological material to the laboratory, registration and marking (marking).

The biological material taken for cytological examination is brought to the laboratory in a short time in a special container.

Vials and smears in which biological material is stored must be marked with the patient's last name or serial number.

The referral is filled in a special form. The following information is written on the referral:

- patient's name, surname, father's name, gender and age;

- in which method and from which organ the biological material was obtained;

- the form being sent (liquid, smears on the glass of the product), quantity;

- a brief history of harmful effects and their nature, previous examination results, treatment procedures (especially hormonal, light and chemotherapy);

- results of other examinations (x-ray, endoscopy, etc.), in case of suspicion of blood system disease (hemoblastosis) - blood analysis;

– definition of status localis;

- clinical diagnosis.

The marking on the drug and the referral form must be clear and appropriate. The laboratory employee who received the biological material can check the labeling of the preparations and the instructions. The laboratory assistant writes the number of smears sent on the referral form, records the materials received in the laboratory journal.

Equipment of cytological laboratories: binocular microscope, fluorescent microscope; centrifuge for preparation of cytological preparations; smear fixation and painting apparatus; glassware, laboratory containers.

Cytological laboratory documents:

- a journal of incoming analyzes and recording their results;

- laboratory tests workbook;

- journal of serious pathology.

Archive, registration and distribution of archival materials.

- the cytological report is stored in the laboratory on electronic or paper carriers for 3 years;

- the results of cytological tests are stored for 25 years in the patient's medical history;

- when using computer technology, cytological conclusions are stored in the electronic medical history;

- preparations without pathological changes are not stored, they are cleaned in special disinfectant solutions in accordance with the rules of biological safety;

- drugs with pathological changes (inflammation or cancer) are archived and stored for 20 years;

- the archive of cytological preparations is kept according to the decision of the head of the laboratory;

- drugs in the archive are issued with a written application from the doctor.

Control questions:

1. Types of cytological laboratory.

2. Types of cytological examination.

3. Organization of cytological laboratory work.

4. Duties of cytological laboratory staff.

5. Necessary information in the referral.

6. Documents supporting cytological laboratory work.

7. Archive, record and provide archival material.

1.3. Methods of obtaining cell material for cytological examination

Purpose of training: ensuring the quality of the drug, general requirements for cytological examination, exfoliative material, puncture material, endoscopic material, biopsy and surgical materials, rules for supplying biological material to the laboratory, obtaining gynecological material, cytological examination of breast material, cytological diagnosis of thyroid pathology, introduction to obtaining urological material, obtaining pulmonological material, and obtaining gastroenterological material.

Material for cytological examination is taken by doctors of various fields (gynecologists, surgeons, oncologists, endocrinologists, endoscopy doctors, hematologists, etc.).

The complexity of ensuring the quality of the drug is as follows:

1) different methods of obtaining material from different organs and tissues;

2) use of several sampling methods (sputum, aspiration, puncture, etc.);

3) obtaining various biological material (excretions and secretions of various organs, aspirates from cavities, tumors and tumor-like growths, smears, scrapings from the surface of erosion, sections of removed tissues, etc.).

Material extraction time and patient preparation depend on the type and method of extraction material.

Methods of obtaining material for cytological examination:

1. Exfoliative;

2. Puncture;

3. Endoscopic;

4. Biopsy and operation.

General requirements for cytological examination:

- cellular materials are applied with a thin layer to clean, degreased, dry, single-use glasses using a dry tool;

- containers for supplying materials (test tubes, Petri dishes, etc.) must be disposable, dry and clean;

- drying of cytological smears is carried out at room temperature;

- if the staining method (Papanikolau, etc.) requires wet fixation, the material is fixed with an aerosol as soon as it is obtained or placed in 96% alcohol for 10 minutes, and then the preparation is air-dried;

- preparation of cytological preparations from a tissue fragment is performed before treatment with formalin;

- materials sent for cytological examination cannot be divided into parts and sent to different laboratories, because changes may be present in one part of the material and not in another part;

- obtained liquids are centrifuged, the supernatant is poured and smears are prepared from the precipitate.

Exfoliative material.

Exfoliative materials include:

- discharges of various organs (mammary gland, vaginal discharge, bladder, etc.);

- erosions, wounds, injuries, separations and cuts of fistulas;

- cuttings from the cervix and uterine canal, aspirates from the uterine cavity;

- glandular secretions, excreta, sputum, transudate, exudate, washing water, etc.Getting exfoliating materials:

- a smear for cytological examinations is prepared from cell elements that are easily separated from the surface of the mucous and serous layers and fall into various secretions (fluids, sputum, pathological secretions of the mammary gland, pleural exudate, urine, fistula secretions, etc.);

- to prepare the drug, a drop of separation is applied to the glass of the object and a smear is prepared;

- printing - smears: glass of the product is applied to the damaged area and a certain amount of cell elements remain on its surface (mammary gland, exit of fistula, mucous membrane, surface of wounds);

- the material can be removed from the damaged area with a cotton swab and applied to the glass of the product.

Smears are prepared with the help of a spatula, the edge of a glass, a scalpel: the smears are taken from the easily removable focus of wounds, the abundance of mucus and necrotic masses in the biological material interferes with the correct preparation of the smear, so the purulent layer and necrotic masses are removed.

Fluids of serous cavities and cysts are obtained by puncture of the pleura, pericardium, abdominal cavity and cysts. To prevent coagulation, a preservative is added to the liquid (1 g of sodium citrate per 1 liter of liquid) and mixed thoroughly. All the fluid taken is sent to the laboratory for examination. If the amount of liquid is very large (several liters), then the liquid is left for an hour, the upper layer is poured, and the lower layer (1 liter) is delivered to the laboratory.

Tumor tissue is often covered with a necrotic layer, a fibrinous layer, or mucus, which prevents cell detachment and uptake. Cytological examination is qualitative only if a sufficient amount of material is obtained.

Puncture material.

Puncture materials with a thin needle from tumors, pre-tumor and neoplastic formations (skin, mammary gland, lung, chest cavity, liver, kidney, abdominal

cavity, thyroid gland, prostate gland, testicle, ovary, lymph nodes, tonsils, salivary glands, soft tissues, bones, etc.). is taken.

For the purpose of cytological examination, a number of rules must be followed for obtaining material by diagnostic puncture method:

1. Puncture is performed by a doctor under the control of ultrasound or X-ray examination.

2. Puncture is performed in accordance with the rules of asepsis and antiseptics.

3. When melanoma is suspected, it is impossible to puncture the tumor.

4. Before puncture, the tumor is carefully palpated, its mobility, connection with the surrounding tissues and convenient fixation are determined.

5. The needle and syringe must be completely dry for puncture.

6. During the puncture, the cells are not anesthetized so that there is no change in the elements.

7. A mandrel is not used for tumor puncture, because the needles used for diagnostic points have a very small diameter and the end is curved, so the needle easily penetrates the tissues above the tumor (skin, subcutaneous tissue, muscles).

8. Tumors rich in blood vessels (thyroid gland, vascular tumors, bones, etc.)) a mandrel must be used to prevent the needle from clogging. After the mandrel is inserted into the tissue, it is removed.

9. Puncture of various tumors is performed with a thin needle (outer diameter 0.6-0.7 mm) and it is connected to a 10 or 20 ml syringe.

10. Dense, pulsating tumors should be inserted while holding the nasal plunger.

Endoscopic material.

Endoscopic examination methods allow visual examination of body cavities and hollow organs using laryngoscopy, bronchoscopy, esophagoscopy,

gastroscopy, duodenoscopy, laparoscopy, colonoscopy, etc. using optical devices equipped with a lighting device.

During endoscopic examination, materials for cytological examination are taken using special devices. Materials can be obtained during endoscopy:

- with a brush;

- with washing water;

- with tampon;

- with biopsy.

The choice of the method of obtaining the material is determined by the nature of the damage, its localization, and the possibility of conducting instrumental tests.

Washed water aspirates are taken using a suction device. Cytocentrifuge technology is used to prepare a smear from the material obtained during bronchoscopy.

With the help of endoscopy, scrapings from the tumor or mucous membrane are removed with the help of a special brush and loop. The material is evenly distributed over the product glass.

Biopsy and surgical materials

Biopsy and surgical materials include:

- materials obtained during surgery (smears, smears from removed tissue, fluids);

- cytological preparations (smear and cuttings) are prepared from the material obtained by biopsy.Obtaining biopsy and surgical materials:

- prints are made by applying a glass to the biopsied or removed tumor tissue;

- cutting a tumor or lymph node should be done with a dry scalpel, preventing the cell from disintegrating in water;

- if the tissue is dense (bone, cartilage) and smearing is not possible, scraping is taken from the surface of the tumor (by light scraping with a glass or a scalpel).

If fluid is taken for cytological examination, it should be sent to the laboratory in a sterile container.

Rules for preparation of preparations (smears) for cytological examination.

To accurately assess the morphological characteristics of the cells in the smear, it is necessary:

- properly made smear;

- quality fixation;

- good painting.

Incorrect assessment and misdiagnosis in cytological examination are caused by:

- uneven distribution of cells;

- not fully assessing the morphological characteristics of cells;

- "missing" important diagnostic information on the smear;

- lack of important clinical data on the product window.

Rules for delivery of biological material to the laboratory:

1. Vials with material and ointment must have identification (marking): it must contain the serial number or surname of the patient, the code on the referral must match the patient's surname.

2. Cytological material should be delivered to the laboratory as soon as possible. This is especially true of fluids, sputum, cysts, and bloody material.

3. There should be special containers for the transportation of glassware, test tubes, Petri dishes and containers of different sizes. Cytological material is not allowed to touch the referral.

4. Received materials are delivered to the laboratory with a referral. The referral will contain the following information:

a) patient's surname, first name, first name, age;

b) presumptive diagnosis;

c) date of receipt of material;

d) the member from whom the material was received;

e) the institution where the biological sample was taken.

5. The laboratory employee who received the material must check the marking of the drug, the instructions, the nature and quantity of the biomaterial, and the number of smears sent.

Obtaining gynecological material

Obtaining the correct material is of great importance for an effective cytological diagnosis, because obtaining the wrong material can lead to an incorrect cytological diagnosis.

Before the examination, the woman should be fully informed about the importance and necessity of the cytological examination, as well as the conditions.

Cervical cancer often develops in the transformation zone, before which precancerous conditions develop. Since the dysplastic area can be located in small, limited areas, it is very important to take the material from the entire surface of the cervix, especially from the transformation area. Cytological examination of smears allows early detection of intraepithelial precancerous conditions. In countries with well-established mass screening programs, deaths from cervical cancer have been significantly reduced due to timely detection and treatment of pre-cancerous conditions and early forms of cancer. At the same time, in order for the cytological examination to be effective, it is necessary to observe the conditions for obtaining the material, correct fixation, staining, careful consideration of the entire cellular composition of the preparation and its correct interpretation.

Conditions for full receipt of material.

1. The material is taken by a gynecologist.

2. All instruments must be dry, sterile, or disposable.

3. Before taking smears from the uterine cavity, it is necessary to make sure that there is no pregnancy, vaginitis or cervicitis.

4. It is not possible to take material during menstruation.

5. For women of reproductive age, smears should be taken after the 5th day of menstruation and 5 days before the expected onset of menstruation.

6.After treating the cervix with acetic acid or Lugol's solution, the smear is not removed, because the cells change and become useless.

7. Within 24 hours after sexual intercourse, when using vaginal preparations, creams, cytological examination is not possible.

8. The material should be taken from the entire surface of the cervix, especially from the transformation zone.

9. The number of cells in the cytological smear should be sufficient - on average 8000-10000.

10. The smear should contain a sufficient number of endocervical cells.

11. Removal of material from the cervical canal is carried out only after removing the cervical mucus.

12. All procedures in the uterine cavity can be performed only after removing vaginal mucus and after complete treatment of infectious diseases.

13. The dried ointment must be marked.

The referral to the laboratory should indicate the following:

a) surname, first name, first name, age;

b) information about the start date of the menstrual period and the menstrual cycle (day of the cycle, post-menopausal period, pregnancy);

c) gynecological information (bleeding from the genitals, hormonal therapy, etc.);

d) presumptive diagnosis, if there is no pathology, the norm should be indicated;

e) date of receipt of material;

f) smear type (ecto, endocervical, endometrial);

g) the institution where the biological sample was taken.

Cytological material is invalid if:

1. If the material is not taken from both the transformation zone and the cervical canal.

2. If a very small amount of cell material is obtained.

3. If the preparations contain a large amount of blood elements or inflammatory elements.

4. Apply too thick or too thin.

5. If the material is not evenly distributed in the product window.

Features of evaluation of biological material for cytological examination:

1. Quality material is a material containing a sufficient number of flat cells, endocervical cells, and metaplastic cells. This material contains little or no admixture of blood and mucus.

2. Somewhat poor quality material - the smear lacks endocervical cells and metaplastic cells, flat cells are sufficient. This material contains little or no admixture of blood and mucus.

3. Poor quality material - it will not be possible to assess whether there are pathological changes in the material. The reason for this is the presence of thick smear, low number of cells, blood, mucus, inflammatory elements.

Cytological examination of breast material

Material for cytological diagnosis can be obtained using the following methods:

1. Punctate mammary glands.

2.Bioptat printing - smears.

3. Separations.

4. Material from erosive surfaces.

Cytological diagnosis of thyroid pathology.

To determine the pathological changes of the thyroid gland, the material is performed with a puncture needle or by examining the tissue removed during surgery.

A puncture of the thyroid gland with a thin needle is performed when a dangerous process is suspected.

Obtaining urological material.

Used for cytological examinations:

1. Daily urine deposition.

2. Aspiration of urine from the bladder cavity.

3. Aspiration from a bladder tumor.

4. Cytological examination of prostate secretion.

5. Biopsy - taking a tissue sample from the body.

Indications for kidney biopsy:

1) detection of tumors;

2) diagnosis of diffuse and focal diseases;

3) chronic glomerulonephritis, nephrotic syndrome, connective tissue systemic diseases, systemic vasculitis, diagnosis of kidney damage in diabetes, etc.

Obtaining pulmonological material.

Rules for taking sputum:

1. Sputum should be taken in the morning, before eating.

2. Sputum is collected in a 20-50 ml sterile disposable vial with a tight-fitting cap.

3. 3-5 ml of sputum is enough for examination.

4. Sputum analysis should be done within 2 hours.

5. During transportation, sputum should be protected from direct sunlight and heat.

Factors affecting the test results:

1. Improper collection of sputum.

2. Failure to deliver sputum to the laboratory on time. In stale sputum, saprophytic flora increases, and shaped elements disappear.

3. Carrying out sputum analysis after using antibacterial, antihelmintic drugs.

Obtaining gastroenterological material.

The following can serve as material for cytological examinations in gastroenterology:

1. Material obtained during esophagogastroduodenoscopy.

2. Gastric lavage.

3. Sections of the mucous membrane taken with biopsy forceps during esophagogastroduodenoscopy.

4. Taking a microbiota from dangerous tumors.

Leukocytes and epithelial cells are found in native and stained preparations, and atypical cells are found in malignant tumors.

Cytological examination of gastrobioptat allows early diagnosis of malignant tumors.

Evaluation of cytological preparations according to the classification of Papanikolaou and Cooper:

1 class. Normal epithelial cells.

2 class. Degeneratively changed epithelial cells.

3rd and 4th grade. Epithelial cells with enlarged nuclei are found in peptic ulcer disease.

Class V - dangerously changed atypical cells.

Control questions:

1. Exfoliative material.

2. Puncture material.

3. Endoscopic material.

4. Biopsy and surgical materials.

5. Preparation of preparation from biological material for cytological examination.

6. Rules for delivery of biological material to the laboratory.

7. Obtaining cytological material in gynecology.

8. Cytological examination of mammary gland and thyroid gland material.

9. Taking cytological material in urology

10. Obtaining cytological material in pulmonology.

11. Obtaining cytological material in gastroenterology.

1.4. Paints. Classification of paints. Methods of painting the smear.Evaluation of coating quality, artifacts

The purpose of the training: dyes, classification, smear staining methods, azur-eosin staining, gram staining, hematoxylin-eosin staining, Pap smear staining, cytochemical methods.

A variety of natural and synthetic dyes are used to stain fixed cells.

According to the chemical composition, paints are divided into the following types

a) Alkaline paints.

Alkaline dyes (hematoxylin, azur 2, carmine) stain acidic (basophilic) substances of cells - nuclei and basophilic inclusions of cells. Basophilic substances of cells contain nucleic acids (DNA and RNA) and include the ribosome and RNA-rich branches of the cytoplasm.

b) Acid paints.

Acid dyes (eosin, acid fuchsin) mainly stain alkaline (acidophilic or oxyphilic) parts of cells - cytoplasm, internal and external proteins, erythrocytes, cell wall.

c) Neutral paints.

Neutral paints are a mixture of alkaline and acid paints. Alkaline dyes stain the cell nucleus purple, and acidic dyes stain the cytoplasm pink-yellow.

d) Fluorochromes.

Some substances fluoresce at a certain wavelength of light.

e) Cytochemical dyes.

Special inclusions of the cell undergo a cytochemical reaction with the help of cytochemical dyes.

f) Immunochemical reactions.

Immunochemical reactions are used to detect specific proteins using fluorescent antibodies. This method has high specificity and sensitivity.

According to tinctorial properties, paints are divided into the following types:

1. Nuclear paints.According to the staining mechanism, nuclear dyes are divided into two groups:

- Alkaline dyes form salts with DNA and RNA. These include safranins, brilliant cresyl blue, azure, methylene blue, toluidine blue, methyl green, and others.

- Binding dyes form brightly colored lacquers with lithium, iron, chromium ions. This group includes hematoxylin, carmine, alizarintianin and others. Depending on the type of metal ion, the paint color varies from red to green-black.

2. Cytoplasmic dyes. These dyes bind to cellular proteins and stain non-nuclear structures. They include eosin, picrofuchsin, auramine and others.

Methods of painting the smear.

There are many methods of staining cytological smears:

1. Azur - with eosin (Romanovsky, Leishman, May-Grunwald, Papengheim method);

2. With hematoxylin and hematoxylin-eosin;

The advantage of hematoxylin-eosin dyes is clear staining of the nuclei of atypical cells, so this method is widely used in screening.

3. Staining by the Papanikolaou method.

Papanicolaou staining is the best method for staining gynecological smears, because in this method, cell cytoplasm is stained in different colors according to the degree of maturation.

Staining with azure-eosin dyes.

1) Romanovsky-Gimza staining.

The dye consists of alkaline azur 2 and acidic eosin. Before work, Romanovsky paint is titrated: several dilutions of the paint with paint and distilled water in the

ratio of 1:1, 1:2, 1:3 ... 1:10, 1:20 are prepared. The time and ratio of dye is written on each dye. It is painted for 20-25 minutes. Wash in running water and dry. The highest quality dye titer is determined by smear microscopy. The Romanovsky-Giemza method stains the nucleus, chromatin structure, bacterial flora well and is widely used for staining peripheral blood.

2) Painting by the dot method.

Initially, 2 types of dyes are prepared: 0.1% aqueous solution of azur 2 and 0.1% aqueous solution of eosin (1 gram of dry dye is mixed with 1 liter of distilled water with a neutral medium). The paints will be ready in 2 weeks after preparation. It is painted for 20-25 minutes. In the dot method, the cell and its nucleus are well stained. This method is used to stain blood and bone marrow punctate smears. The smear for staining platelets is stained for up to 1 hour by the Romanovsky-Gimza or Nokhta method.

3) May-Grunwald staining.

Dry non-fixed smears are placed in May-Grunwald solution for 3-5 minutes. Then the smears are washed in running water and dried. Due to the presence of methyl alcohol in May-Grunwald dye, it is both fixed and stained at the same time. This method is used to stain granulocytes.

4) Painting by Papengheim method.

This method is a combination of Romanovsky-Giemza and May-Grunwald methods. Dry, unfixed smears are placed in May-Grunwald solution for 3-5 minutes. Then the smears are stained in Romanovsky-Giemza solution for 20-25 minutes. The ointment is washed in running water and dried. This method is used to study the cells of blood and blood-forming organs: their nucleus and cytoplasm are best seen.

5) Staining by the Leishman method.

Dried preparations are placed in Leishman stain for 3 minutes for fixation and partial staining. Then it is washed in running water and stained with azure-eosin mixture for 15-20 minutes. This method is used to detect malaria plasmodia.

6) Painting by Wright's method.

1 ml of dye is poured into the unfixed smear, after 1 minute 1 ml of distilled water is added. After 2-3 minutes, it is washed with distilled water and dried.

7) Express staining of cytological preparations - Alekseev's method.

5 - 8 drops of Romanovsky-Giemza dye are applied to the fixed smear, after 60 seconds 10 - 16 drops of neutral distilled water at 50-60°C are added and mixed. After 1-2 minutes, it is washed with distilled water.

Gram staining.

A few drops of crystal violet solution (Genizian violet) are added to the drug. Wash off in water after 30-60 seconds.Iodine solution is dripped for 60 seconds and washed. In order to clean it, put it in 96° alcohol for 10-15 seconds and wash it. Contrast dye safranin or fuchsin is injected into the smear for 45 seconds and washed.

Hematoxylin-eosin staining.

Hematoxylin-eosin staining is widely used in histology. It is widely used in the diagnosis of removed tissue biopsy and oncological pathology.

Hematoxylin, an alkaline dye that stains basophilic structures, and eosin, an acidic dye that stains eosinophilic structures, are used for staining.

Hematoxylin-eosin staining technique:

1. Paraffin from the tissue section is dissolved with ortho-xylene or toluene for 3-5 minutes, stored in 96° ethanol for 3 minutes, 80° ethanol for 3 minutes, 70° ethanol for 3 minutes, and distilled water for 5 minutes.

2. It is stained with hematoxylin for 7-10 minutes.

3. Wash in distilled water for 5 minutes

4. Hold in 1% hydrochloric acid in ethanol at 70° until brown.

5. Washed with distilled water and kept in 0.5% ammonia solution until the sections turned blue.

6. It is stained with an aqueous solution of eosin for 0.5-1 minutes.

7. Wash three times in distilled water.

8. Sections are stored in 70° ethanol, twice in 96° ethanol for 2 minutes.

9. Cuts are stored twice in carbol-xylol for 1 minute.

10. Stored twice in xylene or toluene for 2 minutes to dry.

Papanicolaou staining.

Necessary reagents: Nikiforov's mixture, 95°, 90°, 80°, 70° and 50° alcohols, Harris hematoxylin, 0.25% hydrochloric acid, G yellow dye, EA-36 dye, absolute alcohol, xylene, Canadian balsam.

Painting procedure:

- fixed smears are passed through 80°, 70° and 50° alcohols and distilled water;

- stained in Harris hematoxylin for 6 minutes;

- washed in distilled water and immersed in 0.25% hydrochloric acid 6 times;

- put it in a bowl of running water for 6 minutes and wash it in distilled water;

- passed through 50°, 70°, 80° and 95° alcohol;

- dehydrated preparations are stained with G yellow dye for 1.5 minutes;

- washed 2 times in 95° alcohol;

- painted in EA-36 paint for 1.5 minutes;

- smears are washed 3 times in 95° alcohol;

- passed through absolute alcohol, xylene mixture and xylene 2 times;

- covered with Canadian balsam.

Cytochemical methods

Cytochemical methods are based on a color reaction between a chemical reagent and a specific component of the cell. Substances in the cytoplasm are stained under the influence of specially selected reagents, the amount and activity of these substances can be determined according to the degree of staining.

Control questions:

1. Classification of paints.

2. Staining with azure-eosin dyes.

3. Romanovsky-Gimza staining.

4. Dot painting.

5. May-Grunwald staining.

6. Painting by the Pappenheim method.

7. Staining by the Leishman method.

8. Painting by Wright's method.

9. Gram staining.

10. Staining with hematoxylin-eosin dyes.

11. Staining by the Papanikolaou method.

13. Cytochemical dyes.

1.5. Rules for preparation of cytological smear.

Liquid and dry cytology.

The purpose of the training: to introduce the rules of material selection in cytological examination, the method of preparation of preparations from

cytological materials, dry and liquid cytology, assessment of the quality of cytological preparation, methods of studying live (intravital) and fixed cells.

Currently, the success and quality of cytological examinations is mainly related to the correct acquisition of pathological material, the correct reception, processing and sending of pathological material to the laboratory. Errors at the preanalytical stage in the laboratory average 70%. In order to reduce the number of errors at this stage, doctors with special training in obtaining, processing and sending materials are needed, with good experience.

The quality of the cytological preparation depends on:

1. Choosing the right place for sampling (different organs and tissues).

2. The sample should be taken from the affected area and not from the surrounding tissue.

3. If necessary, it is necessary to take material from different parts of the tumor.

4. Use of several sampling methods (scraping, aspiration, smearing, etc.).

5. Preparation of cytological material according to the nature of the biological material (blood, sputum, fistula and secretions of various organs, aspirate of cavities, tumors and tumor-like formations) (smears, scrapings from the surface of organs, erosions, etc.);

Correct preparation of cytological preparation.

There are three stages in the process of cytological examinations:

1. Selection of biological materials (by specially trained clinical staff).

2. Preparation of the drug (ointment) is carried out by clinical or laboratory staff.a) the tools used for the preparation of the drug must be new;

b) Smear preparation: cell material is smeared on a clean glass slide with a dry instrument in a transverse direction or a tissue sample is taken. Drying of cytological smears is carried out at room temperature;

c) materials obtained in liquid cytology are placed in a liquid medium. Test tubes, Petri dishes, and containers for transportation must be clean and dry;

g) if necessary, wet fixation is performed immediately after receiving the material (Papanikolau method). The smear is fixed in aerosol fixative or 96% alcohol for 10 minutes and air-dried;

e) preparation of cytological preparation from tissue pieces is carried out before processing with formalin;

f) Materials must be numbered and marked.

3. Evaluation of the drug, study of the morphological characteristics of the cells in it is carried out by laboratory staff.

There are certain rules for sampling for cytological examination:

- sampling is not performed during menstruation;

- material is not taken during the treatment of infectious and inflammatory diseases;

- it is recommended to use special brushes and spatulas to remove cells;

- if there is no visible change in the organ, the material is taken in one window, pathologically changed materials are taken in several windows.

Method of preparation of cytological preparation.

Rules for preparation of ointment:

1. The smear is made by using a special spatula, the edge of the glass, a scalpel, etc.

2. When taking sputum, it is taken carefully in order not to damage the blood vessels and not to allow red blood cells to fall into the smear.

3. Mucous and necrotic masses on the surface of the organ prevent the correct preparation of smear, therefore purulent crusts and necrotic mass should be removed with a special cotton swab.

4. The coating is applied leaving about 1 cm from one side of the window and 1.5 cm from the other side.

5. So that all areas of the smear are clearly visible, the cells in the smear should be evenly distributed, there should be no "thick areas" containing invisible cell complexes.

Assessing the quality of cytological preparation.

High-quality staining helps to accurately assess the microscopic characteristics of the cells in the smear.

Characteristics of a quality painted coating:

- is evenly painted;

- there should be no artifacts (dark traces of paint) and unswollen cells;

- there should be enough cells in the smear and they should be evenly distributed (the entire area of the smear should be well visible and there should be no thick areas;

- cytoplasm, nucleus, nuclear chromatin, nucleoli should be well stained.

Cell staining is based on physico-chemical processes (diffusion, adsorption, absorption, solubility, etc.) in dyes and microstructures.

In high-quality painting of the smear, it is necessary to attach great importance to the sequence, the rules for the preparation of solutions and the time.Factors that cause poor quality materials to be obtained:

- neglect to perform various stages of drug preparation;

- non-compliance with the terms of obtaining the material;

- that the material in the furnace is not removed from all surfaces;

- poor distribution of materials on the glass;

- preparation of very thin or very thick smear;

- drying of the grease required for wet fixation;

- poor-quality coating;

- presence of blood and inflammatory elements in the smear.

Liquid cytology.

Liquid cytology is the most effective method introduced into clinical practice in 2004. In liquid cytology, a special brush is used during material collection. To preserve all the cells, the brush is immediately placed in a special preservative liquid and sent to the laboratory. A special preservative removes mucus, leukocytes, red blood cells, and detritus for easy cell separation. The material is centrifuged in the laboratory, all cells are collected in a sediment, and high-quality monolayer preparations are prepared from it. This method does not change the shape of the cells. Smudges are painted with special paint. The accuracy of liquid cytology is 95%.

However, like any diagnostic method, liquid cytology has its drawbacks:

1. Liquid cytology does not allow to identify diseases associated with the inflammatory process.

2. Liquid cytology method requires expensive equipment and reagents. In addition, the doctor must undergo special training. All this increases the cost of the analysis.

Dry cytology.

The ointment should be distributed with a thin layer. If the smear is stained by the Papanicolaou method, the preparations are immediately fixed and dried in the air (wet fixation). If the smears are painted by the Romanovsky method, they

are fixed after drying (dry fixation). If staining with hematoxylin-eosin, both dry and wet fixation can be used.

Dry cytology can have a high rate of false negatives and false positives. The accuracy of smear diagnosis is 40-60%. In many cases, the reason for incorrect results is:

• large amounts of blood and inflammatory elements make it difficult for cell microscopy;

• a part of the cell is lost when the glass is transferred to the glass;

• Some cells change shape during drying and staining.

As a result, a mistake can be made when examining the smear: missing a cancer or mistaking a healthy cell for a cancer cell.

Live (intravital) study of cells.

A light microscope allows you to see living cells. For short-term observation, cells are placed only in a liquid medium on a glass slide. As objects, living cells of simple animals, blood cells, or broken down tissues of multicellular organisms can be chosen.

When studying living cells, they try to stain them using vital or fluorescent dyes. In this method, a 1:200,000 dilution ratio of native drug or acidic dyes with minimal effect on cell activity is used.When living cells are stained, the dye accumulates in the cytoplasm in the form of granules, while in injured or dead cells, diffuse staining of the cytoplasm and nucleus occurs.

Studies of fixed cells.

After the cell is removed from the body, autolytic enzymes are activated in them, and this leads to irreversible changes in the composition of the cell. The function of fixation is to kill the cell, to stop the activity of intracellular enzymes, to prevent cell disintegration, as well as to preserve cell structures and substances,

to prevent the appearance of properties (artifact structures) that are not present in a living cell.

It is widely used for fixation:

a) aldehydes and their mixtures;

b) alcohols (methyl alcohol, ethyl alcohol) that cause irreversible denaturation of proteins, precipitation of nucleic acids and polysaccharides;

c) sulema and picric acid fixatives that have a settling effect;

d) fixatives containing osmium tetraoxide (OsO4), which preserves lipids well.

There are mixed complex combinations such as Nikiforov mixture, May-Grunwald fixator, Leishman fixator. After fixation, cells can be subjected to further processing. The main processing is the coloring of the cells, which allowed us to reveal many details.

Control questions

1. What does the quality of a cytological preparation depend on?

2. Correct preparation of cytological preparation.

3. Method of preparation of cytological preparation.

4. Evaluation of the quality of the coating.

5. Dry cytology.

6. Liquid cytology.

7. Live (intravital) study of cells.

8. Study of fixed cells.

CHAPTER 2. BASIS OF CYTOLOGICAL DIAGNOSTICS.

2.1. Cell structural components. Cytomorphological signs of cell cycle, apoptosis, necrosis, inflammation

The purpose of the training: to familiarize with the components of cells, cell division, proliferation, differentiation, aging and cell death, apoptosis, necrosis, morphological signs of inflammation, pathogenetic stages of inflammation, forms of inflammation.

A cell is an element that reflects the structure and function of all living things. Cells exist as part of the tissues of unicellular organisms (bacteria, protozoa) or multicellular organisms.

Cells differ in shape, size and internal structure. The shape of the cells can be as follows: spherical, oval, ovoid, cylindrical, branching, curved, star-shaped, polygonal, etc. Cell size ranges from 0.01 mm (nerve cell) to 0.2 mm (egg cell). However, cells have similarities in the basic characteristics of vital activity, metabolism, excitation, growth, development and reproduction.

The average cell volume is approximately 80% water, 15% protein, 3% lipid, 1% carbohydrate, 1% nucleic acid, and minerals.

Different cells have different life spans. For example, neurons and muscle cells live for 100 years or more, liver cells live for 480 days, red blood cells for 120 days, intestinal cells for 5 days.

The cell theory was developed by Matthias Schleiden and Theodor Schwann in 1838: the cell is the elementary unit of living organisms.According to him:

- all organisms, both multicellular and unicellular organisms, consist of cells;

- a cell is an elementary unit of life, capable of self-repair, self-management and self-reproduction;

- the structure of cells in different organisms is similar;

- the cellular structure of organisms shows the unity of their origin;

- the combination of cells has the ability to form complex structures (tissues, organs, organisms);

- new cells appear as a result of division of previous cells.

All types of cells consist of three main, interrelated components:

1. Cytoplasmic membrane - the outer shell of the cell.

2. Organoids, cytoplasm containing special cell inclusions.

3. The nucleus is separated from the cytoplasm by a membrane and contains chromatin, nucleolus.

Cytoplasmic membrane.

Cytoplasmic membrane or plasmalemma is the shell of the cell that separates the cell from the external environment. At the same time, the cytoplasmic membrane has a selective permeability that keeps the internal environment constant, and participates in the process of substance exchange with the environment and neighboring cells. The membrane consists of 2 layers of lipid and protein layers located on the outer and inner surfaces. There are different receptors on the cytoplasmic membrane.

Functions of the membrane:

- maintaining the shape of the cell;

- protection;

- regulation of metabolism: there are many pores in the cytoplasmic membrane through which ions and molecules enter the cell;

- maintenance of the internal environment: the passage of substances through the cytoplasmic membrane is selective, that is, substances are selectively passed;

- are receptors in the cytoplasmic membrane and interact with special molecules;

- recognize other cells and intercellular substance: connections between cells are made at the expense of a large number of folds and protrusions, hivchins;

- ensuring cell movement.

Cytoplasm

Cytoplasm is the internal environment of the cell between the cytoplasmic membrane and the nucleus, in which the processes of substance exchange and maintaining a constant internal environment are carried out. This colloidal system can change its physical and chemical properties, its different parts can be different - from liquid to solid state. Cytoplasm contains:

1) cytosol or hyaloplasm.

The main substance in the cytoplasm (matrix, internal environment) is called cytosol or hyaloplasm. Hyaloplasm contains organelles and inclusions, as well as water, protein, lipids, polysaccharides, nucleic acids, enzymes, ions, vitamins and other products. Many biochemical processes take place in the cytoplasm (glycolysis, fatty acids, proteins, cholesterol synthesis, gluconeogenesis).

2) Organelles.

Organelles are cellular structures that have a specific function and specific shape. Types of organelles:

Common organelles. They are present in all cells and are necessary for their vital functions. These include mitochondria, endoplasmic reticulum, Golgi complex, lysosome, peroxisome, cytocenter, ribosome, proteosome, plastids, vacuoles.

Special organelles. These organelles are present in some cells and perform special functions. Special organelles: cilia, chivchins, microvilli, myofibrils, acrosome.

Most cell organelles can only be examined with an electron microscope.

3) Cytoskeleton.

Cytoskeleton is the supporting apparatus of the cell, which ensures the movement of the cell and organelles. The cytoskeleton consists of a network of protein filaments that give the cell its shape.The main types of cytoskeleton are microtubules and filaments.

These structures are connected to the cytoplasmic membrane and the nuclear envelope, forming a complex network in the cytoplasm, providing the movement of intracellular structures and the shape of the cell.

Nucleus

The nucleus is an organelle that stores the main genetic material of the cell. Core Functions:

- control of cell activity;

- due to the presence of chromosomes containing genetic information in the nucleus, it functions as a center that controls all vital activities and development of the cell;

- storage and transmission of genetic information;

- information, transport, synthesis of ribosomal RNA;

- ensuring cell division.

The most important process in the nucleus is the production of genetic material necessary for cell division or to enhance its synthetic activity. The production of genetic material consists of a chain of synthetic processes that ensure the synthesis of vital proteins.

The kernel contains the following components:

1. Kernel shell (caryolemma).

The nuclear envelope consists of two membranes - outer and inner. The outer membrane is fused with the membranes of the granular endoplasmic reticulum and contains ribosomes on its surface. There are many pores in the nuclear envelope

through which synthesized proteins enter the nucleus from the cytoplasm and RNA molecules are released.

2. Chromatin (chromosomal material).

Chromatin (from the Greek chroma - color) is a chain made of DNA and protein complex. DNA segments that contain specific information about the type of protein are called genes.Genes contain information about a specific protein, therefore determine specific characteristics - skin, eye, hair color, nose shape, vocal cords and other characteristics.

3. Nucleus.

The nucleus is an integral part of the cell nucleus and is the optically dense part. This is the area of synthesis and accumulation of ribosomal RNA, and then the RNA is released into the cytoplasm. The nucleus does not have a membrane and is surrounded by a layer of condensed chromatin (heterochromatin). The type of nucleus depends on the type of cell and its metabolic state: large and dense nuclei are characteristic of cells with high activity, that is, intensively dividing embryonic cells and cells with strong protein synthesis. In reactively altered cells, the number and size of nuclei increases significantly.

4. Karyoplasm.

Karyoplasm is the liquid part of the nucleus. It provides biochemical processes. A cell usually has a single nucleus, but binucleated and multinucleated cells also exist. The nucleus is located in the center of the cell (centric) or in one of its poles (eccentric).

In most cells, the nucleus is round, sometimes elliptical, in some cells it is multilobed (monocytes, neutrophil leukocytes).

The size of the nucleus depends on the type of cell. The ratio of the size of the nucleus to the cytoplasm is a relatively specific value for each cell type. The

characteristics of the nucleus are especially strongly changed in pre-tumor and malignant tumors.

Organelles.

Mitochondria. Mitochondria are energetic organelles. The shape of mitochondria can be different: oval, spherical, linear, rod-shaped, filamentous. Mitochondria consist of membrane, matrix and crystals. Inside the mitochondria are RNA, DNA and ribosomes. Its membranes contain special enzymes, with the help of which the energy of nutrients is converted into the energy of ATF (adenosine triphosphate), which is necessary for the vital activity of the cell and the organism as a whole. The number of mitochondria depends on the functional activity of the cell and can be up to ten thousand.

Endoplasmic reticulum. The endoplasmic reticulum consists of a structure of interconnected spaces, designed for the synthesis and transport of organic substances in the cytoplasm of the cell. It makes up 10% of the cell volume. Endoplasmic reticulum consists of cavities, channels, membrane tubules and ribosomes.The activity of the endoplasmic reticulum is as follows: synthesis of carbohydrates, lipids and proteins, detoxification of drugs, loss of activity of steroid hormones.

According to the activity, the endoplasmic reticulum is divided into two types:

1) smooth endoplasmic reticulum (leading importance in lipid biosynthesis and up to 5 mmol of calcium ions accumulate in it);

2) granular endoplasmic reticulum (holds a large number of ribosomes and protein synthesis is carried out).

Ribosomes. Ribosomes are attached to the membrane of the endoplasmic reticulum or are freely located in the cytoplasm, are arranged in groups and provide protein biosynthesis. The composition is protein and ribosomal RNA.

They consist of large and small, dense, spherical units, which combine amino acids into polypeptide chains and provide protein synthesis.

Golgi complex. The Golgi apparatus is a net around the nucleus and consists of 4-6 cisternae. The Golgi apparatus is usually located near the endoplasmic reticulum. Duties: collection and condensation of secretory products developed by the endoplasmic reticulum, protein transport, membrane wrapping of newly formed granules, synthesis of polysaccharides and glycoproteins, formation of lysosomes.

Lysosomes. Lysosomes are oval membrane-bound organelles that contain more than 50 different hydrolytic enzymes. Tasks: break down organic matter, dead organelles, old cells, changed cell components, various bacteria.The membrane of the lysosome is very strong and prevents the release of its enzymes into the cytoplasm of the cell, but if the lysosome is damaged by external influences, the whole cell or its part is destroyed.

Peroxisomes. Peroxisomes are separate membrane organelles that contain about 50 enzymes. They contain oxidases, enzymes that break down fatty acids and neutralize alcohol absorbed in hepatocytes. The main function of the peroxisome is to carry out biochemical reactions with the help of oxygen. Peroxisomes are often located near the membranes of the endoplasmic reticulum. The proliferation of peroxisomes in cells is an adaptive response to external influences necessary for cell survival.

Cell inputs. Cell inclusions are temporary components of the cytoplasm, formed as a result of the accumulation of metabolic products. Cell inclusions include granules, vacuoles, glycogen granules, pigments, lipids, etc. will be in the form

Cell inputs are divided into trophic, secretory, excretory, pigment types. Trophic inputs store reserve nutrients (starch, proteins, sugars, fats) in dense granules. Secretory inputs include the product produced in the cell. Excretory inputs include metabolic products released from the cell. Pigment inclusions are

accumulations of endogenous or exogenous pigments (hemoglobin, hemosiderin, melanin, lipofuscin).

The functions of cell membranes are to store organic matter and energy. Cellular inclusions can be seen under a light microscope, and their presence allows identification of certain cells (melanocytes, mucus-producing cells, macrophages sequestering hemosiderin).

Cell cycle

The repetitive process by which eukaryotic cells divide is called the cell cycle. Different organisms have different cell cycles. For example, 18 hours in leukocytes, 28 hours in skin. In adults, some cells in the body (lung, kidney and liver cells) divide only when damaged. Intestinal epithelial cells divide throughout a person's life, while neurons stop dividing completely when they mature.

In the early stages of development, the cells of the body divide a lot, then the cell cycle becomes longer. The biological significance of the mitosis cycle is the generation of young cells and the transfer of genetic information from generation to generation.

The cell cycle consists of interphase, mitosis and quiescent period.

Interphase is the period between cell divisions. In interphase, chromosomes are in the form of chromatin in the cell nucleus.

Mitotic (proliferative) cycle. The following stages are distinguished in mitosis:

1. Division of the cell nucleus

- **prophase**, metaphase, anaphase, telophase.- in the prophase, a large number of cytoplasmic microtubules of the cytoskeleton are disintegrated and bipolar mitotic spirals are formed;

- **metaphase** (all chromosomes are located at the same level (metaphase plate) and ends with the formation of two chromatids;

anaphase is the division of each chromosome into two chromatins and their distribution at different poles of the cell;

- in **telophase**, separated odd chromatins move closer to the poles, a new nuclear envelope appears.

2. Division of cytoplasm - cytokinesis (cell division).

Proliferation. The main method of cell division is mitosis. As a result of the increase in the number of cells, there are groups or populations of cells that are located in the same place and have the same cytological characteristics.

Differentiation is the process of formation of morphological characteristics of cells, which ensures the performance of specific activities. According to the degree of maturation, cells are divided into differentiated and undifferentiated types. However, only differentiated cells can fully perform their functions. Therefore, any violation of differentiation leads to a violation of cell activity (tumor cells of endocrine organs, the appearance of immature cells in the blood).

Aging and cell death.

The normal functioning of the body depends on the cell cycle. The duration of this period is different for each cell. After normal functioning for a certain period of time, cells morphologically enter the aging period: the cell size decreases, large lysosomes increase, pigment and fatty inclusions accumulate, vacuoles appear in the cytoplasm and nucleus.

All cells of the body have their own life span, when it ends, they stop functioning, die, and new cells appear in their place. Cell death is programmed into their genetic makeup.

Two different mechanisms are distinguished in cell death: necrosis and apoptosis.

Apoptosis

Apoptosis is genetically programmed cell death. This is the most important physiological process that allows the body to maintain the functions of its structural structures at a certain level.

Apoptosis is important in the following processes:

- formation of organs during embryonic development;

- to prevent the appearance of pathological cells that differ from the cells of the body, resulting from genetic errors and mutations;

- after the end of the physiological functions of organs and tissues (thymus gland atrophy, reproductive system in old age, atrophy of organs and tissues, etc.);

- destruction of old cells when the morphology and function of organoids changes, etc.

Stages of apoptosis:

- loss of communication with neighboring cells;

- the size of the cell decreases: the chromatin in the nucleus condenses, the nuclei crack, are dense and divided into separate fragments. At the same time, the cytoplasm breaks down;

- the cell turns into apoptotic bodies surrounded by a membrane;

- apoptosis bodies are engulfed by surrounding cells, usually macrophages.

However, in response to apoptosis, the inflammatory response never develops, and instead of dead cells, new cells appear. It is important to note that only cells undergo apoptosis, not tissues.

Necrosis

Necrosis - under the influence of harmful factors (temperature, hypoxia, chemical and mechanical effects, etc.), the cell breaks down. At the initial stage,

there is a change in cell organoids (mitochondria swell and the number of cristae in them decreases), the permeability of the plasma membrane increases, the membrane of lysosomes breaks down and hydrolases are released.Changes are also observed in the cell nucleus - karyopyknosis, karyorrhexis, karyolysis. Cell decay products attract leukocytes and macrophages, an inflammatory reaction - swelling, hyperemia, pain - occurs around the necrosis site.

Inflammation

Inflammation is the most complex protective and adaptive process that occurred in the course of evolution, aimed at maintaining the stability of the organism. It is changes in the peripheral blood vessels, blood, connective tissue aimed at eliminating the damaging agent and restoring tissues.

Importance of inflammation:

1. The body is protected from the influence of foreign and harmful factors.

2. Eliminates or limits pathogenic factors that cause inflammation and damage developed as a result, and prevents the spread of infection.

3. Due to exudation, the concentration of toxic substances in the focus of inflammation decreases.

4. The inflamed area provides detoxification of toxic substances.

5. Unfavorable conditions are also created for the life of microorganisms in the ignition source.

Pathogenic factors are exogenous and endogenous.

Exogenous factors include:

1. Biological factors - microorganisms (bacteria, viruses, rickettsiae), worm infestations, foreign proteins, insect and snake venoms).

2. Chemical substances (acids, hydroxides, heavy metal salts).

3. Physical factors: mechanical (injury, foreign body, pressure), thermal (cold, heat), electrical (natural electricity, industrial and household current) and radiation effects (X-rays, radiation, ultraviolet rays).

Endogenous factors include tissue breakdown caused by disease in the body, blood clots, infarcts, hemorrhage, gallstones or urinary stones, and antigen-antibody complexes. Inflammation can be caused by saprophytic microflora.

Pathogenetic stages of inflammation:

1. Alteration is a complex of tissue damage, metabolic, physical, chemical and structural-functional changes. It is the first response to damage of the organism and is manifested as local biochemical and vascular reactions. These reactions are aimed at localizing and limiting the aggressive agent with the help of blood cells. At this stage, the tissue shows various degrees of dystrophic changes, even necrosis.

2. Exudation is characterized by vascular reactions and changes in blood circulation in the center of inflammation, liquid part of blood coming out of veins - exudation, release of leukocytes in the center of inflammation and development of phagocytosis. Blood plasma is exudated, migration of phagocytes, blood cells occurs, exudate and inflammatory proliferations appear. Macrophages at the site of inflammation perform bactericidal and phagocytic functions. At the same time, some of these cells die. At the peak of the exudative inflammatory reaction, a large number of neutrophilic leukocytes and a necrotic mass are seen in the materials sent for cytological examination.

3. Proliferation.During this period, the cellular composition of the inflammatory infiltrate is formed. In the proliferative phase, macrophages enter the inflammatory site, multiply and secrete substances that stimulate fibroblasts and repair blood vessels. Cells of the immune system appear in the infiltrate (lymphoid and plasma cells), as a result of the proliferation process, a new connective tissue is formed - granulation tissue.

Forms of inflammation:

1. Acute inflammation can last from several hours to 2 weeks. In acute inflammation, neutrophil leukocytes, eosinophils and macrophages predominate.

2. Chronic inflammation occurs when it is impossible to eliminate the damaging factor. In chronic inflammation, lymphoid elements, plasmatic and fibroblastic cells, and histiocytes prevail.

3. Proliferative inflammation. Focal or diffuse infiltrates appear in proliferative inflammation and may have a lymphocytic - monocytic, macrophage, epithelial cell, large cell, plasma cell structure.

As with any pathological process, during inflammation, harmful effects can be observed along with the protection of organs.

Control questions:

1. Understanding the cell.

2. Cell theory.

3. Cell structure.

4. Cell cycle.

5. Mitotic cycle.

6. Phases of mitosis.

7. Morphological signs of necrosis.

8. Morphological signs of apoptosis.

9. Inflammation, etiology, mechanisms.

2.2. Epithelial tissue cytomorphology. Cytological and histofunctional characteristics of epithelium of different organs.

Purpose of training: to provide information on epithelial tissue properties, epithelial tissue function, classification, classification of exocrine glands.

Epithelial or epithelial tissue - covers the surface of body cavities, mucous and serous layers of internal organs (esophagus, respiratory system, urinary tract) and includes the epithelium of glandular organs. In this regard, the epithelium is divided into two types: covering and glandular.

Epithelial tissue has the following characteristics:

1. Demarcation: covers the outer surfaces of the organs and the inner surfaces of the cavities, that is, it separates the internal environment of the body from the environment.

2. Epithelial layer consists only of layers of epithelial cells, there is almost no intercellular substance, they are close to each other and connected to each other by various contacts.

3. Epithelium is separated from other tissues by a dense basement membrane.

4. Epithelial tissue does not have blood vessels, it is fed diffusely.

5. Epithelial cells are divided into basal and apical parts, and the structure of these parts differs sharply from each other.

6. Epithelium has strong regeneration properties.

7. Epithelial cells can have special organoids:

- cilia (airway epithelium);

- microvilli (intestinal and kidney epithelium);

- tonofibrils (skin epithelium).

Function of epithelial tissue:

- protection;

- limitation;

- participation in the exchange of substances between the organism and the environment;

- secretary.

Classification.

The following classification is used for epithelial tissues:

According to the shape of surface cells:

1) flat;

2) cubical;

3) cylindrical.

According to the presence of special structures on the apical surface of the cell:

a) there are microvilli on the apical surface of the bordered epithelium;

b) there are cilia on the apical surface of the floating epithelium.

Histogenetic classification:

1. Skin epithelium (ectodermal) multi-layered flat freezing and non-freezing epithelium; epithelium of salivary, sebaceous, mammary and sweat glands; epithelium of the ureter; multilayered squamous epithelium of the respiratory tract; lung alveolar epithelium; thyroid and parathyroid gland, thymus and adenohypophysis epithelium.

2. Intestinal epithelium (enterodermal) - single-layer cylindrical epithelium of the intestinal tract; liver and pancreas epithelium.

3. Kidney epithelium (nephrodermal) - nephron epithelium.

4. Epithelium of serous layers (cellodermal) - single-layer flat epithelium (peritoneum, pleura, pericardial shell); epithelium of gonads; adrenal gland epithelium.

5. Neuroglial epithelium - epithelium of cerebral ventricles; epithelium of brain shells, anterior chamber of the eye; retinal pigment epithelium; olfactory epithelium; glial epithelium of the auditory organ; taste epithelium; chromophobe epithelium, perineural epithelium.

According to morphofunctional characteristics:

1. Single-layer epithelium - all cells are located in the basement membrane.

1.1 Single-row single-layer epithelium - all cells are located on the basement membrane, have the same size, so the nuclei are located at the same level.

1.1.1. Single-layer flat epithelium forms kidney tubules, outer layer of kidney capsule, mesothelium and endothelium.

1.1.2. A single-layer cuboidal epithelium covers some tubules of the kidney.

1.1.3. A single-layered columnar epithelium covers some tubules of the kidney, stomach, small and large intestines.

1.2. The nuclei of multi-row single-layer epithelial cells are located at different levels, because the cells have different shapes and sizes.

2. Multilayered epithelium - only the cells of the basal layer lie on the basement membrane.

2.1. Non-condensable stratified epithelium

2.2. Frozen multi-layered epithelium (keratinization is observed in the surface layer);

2.3. Transitional epithelium.

Single-layered flat epithelium consists of a layer of single-layered cells of a polygonal shape. The diameter of the cells is several times greater than the height.

These cells have few organoids. Single-layered squamous epithelium is located in some tubules, mesothelium and endothelium of the kidneys. Mesothelial serous layers - pleura, epi- and pericardium, cover the peritoneum. Endothelium covers blood vessels, lymphatic vessels and heart cavity. Its function is to limit and prevent friction of internal organs.

Single-layer cuboidal epithelium - the diameter of the cells is equal to the height. It is located in the excretory ducts of exocrine glands, kidney tubules.

Single-layer cylindrical epithelium - the diameter of the cells is less than the height.According to the structure and functional characteristics, it is divided into the following types:

1. Single-layer cylindrical epithelium of the kidney. In a series of tubules, the epithelium is cylindrical. Nuclei are located in the basal part of the cells.

2. Cylindrical epithelium with a one-layer border. Due to the presence of borders on the apical surface of the cells, the absorption surface of the small intestine increases.

3. Single-layer cylindrical glandular epithelium is located in the stomach, cervical canal and specializes in mucus production.

4. Single-layer floating cylindrical epithelium is in the fallopian tubes, and there are cilia in the apical part.

Regeneration of single-layer single-row epithelium takes place at the expense of cambial stem cells.

Single-layer multi-layered squamous epithelium is located in the respiratory tract. Cilia are visible on the apical surface of the cells. The task is to clean and humidify the passing air.

Multilayered epithelium consists of several layers of cells, and only the bottom row of cells is located in the basement membrane.

Multilayered flat non-coagulated epithelium covers the mucous membrane of the cornea of the eye, oral cavity, larynx, esophagus, rectum, anus.

Multilayered squamous epithelium forms the epidermis and covers the skin. Its task is to protect against mechanical damage, radiation, bacterial and chemical effects, to isolate the body from the environment. Keratin is synthesized and accumulated in epidermal cells. Therefore, the cells are frozen.

Passing epithelial walls are located in hollow organs (kidney cup, ureter, urinary bladder) with a strong stretch feature.

The glandular epithelium specializes in the production of secretions and is located in the glands:

1. Endocrine glands (or endocrine glands) produce hormones or biologically active substances into the blood or lymph. Hormones, even in small amounts, have a powerful effect on organs and systems.

2. Exocrine glands (external secretory glands) produce secretions to the external environment - on the surface of the skin or in the cavity of organs covered with epithelium.

Classification of exocrine glands.

I. According to the structure of the output channels:

1. Simple - the excretory duct does not branch.

2. Complex - the excretory duct branches.

II. According to the structure (forms) of the secretory part:

1. Alveolar - secretory part in the form of an alveolus.

2. Tubular - secretory department in the form of a tube.

3. Alveolar-tubular - mixed form.

III. According to the ratio of excretory channels and secretory parts:

1. Unbranched - one secretory part opens into one excretory duct.

2. Branched - several secretory parts open into one excretory duct.

IV. By type of secretion:

1. Merocrine - integrity of cells is not disturbed during secretion. Characteristic of many glands.

2. Apocrine (apex - peak, crinio - separation) - during secretion, the apex of the cells partially breaks down (mammary glands).

3. Holocrine - during secretion, the cell completely breaks down (sebaceous glands of the skin).

V. By localization:

1. Endoepithelial glands - single-cell glands in the epithelial layer (gland cells in the epithelium of the intestine and respiratory tract).

2.Exoepithelial glands - the secretory department is located outside the epithelium, in the tissues.

VI. According to the nature of the secretion: protein, mucus, mucus-protein, sweat, fat, milk, etc.

Control questions

1. Definition of epithelial tissue.

2. General characteristics of epithelial tissue cells.

3. Classification of epithelial tissue.

4. Single layer epithelium.

5. Multilayered epithelium.

6. Epithelium of the skin and gastrointestinal tract.

7. Epithelium of the respiratory tract.

8. Epithelium of the urinary tract.

2.3. Cytological classification of cervical diseases. Compensatory - adaptive processes.

The purpose of the training: to introduce the cells of the cervix, normal cytogram, compensatory - adaptive processes, regeneration, inflammation, atypical changes after chemotherapy and radiation.

Cytological examination has a special place in the diagnosis of gynecological diseases. 70% of examination in cytological laboratories is cytology of gynecological material.

Public gynecological examinations are conducted in order to detect cervical cancer early. Mass gynecological examinations are conducted to detect "atypical cells". However, cytological examination also detects other pathological processes, including precancerous conditions. In this regard, during gynecological examinations, in addition to diagnosing cancer, background and pre-tumor diseases are also detected and treated.

Screening is aimed at detection and prevention of pathology without clinical symptoms, but it also allows early diagnosis of dysplastic changes and cancer.

Cytological classification, which includes pathological changes of the cervix, is the terminology of Bethesda (Appendix 1).

The following cells are found in the cervix:

1) Multilayered squamous epithelial cells.

Multilayered flat non-coagulated epithelium is located in the vaginal part of the cervix (exocervix). A cytological smear is taken from the surface of the mucous membrane, so its cellular composition consists of epithelial cells. Multilayered squamous epithelium consists of the following layers of cells:

a) Surface cells are large, flat, polygonal cells with a diameter of about 50 μm. The nucleus is 6 microns, oval or round, structureless, pyknotic structure. Superficial

cells are cells that are mostly isolated. When stained by the Papanicolaou method, the cytoplasm is pink-yellow, eosinophilic, clear, and lipid and glycogen granules are detected in some cells. Surface cells are found in a normal cytological smear of the cervix.

b) Intermediate cells - 30-45 μm diameter, usually polygonal or round cells. Cytoplasm is stained cyanophilic. Nuclear chromatin is vesicular. Intermediate cells are found in a normal cytological smear of the cervix.

c) Parabasal cells are round, 15-30 μm in diameter, the nucleus with fine chromatin occupies half of the cell, sometimes there are nucleoli. Cell cytoplasm is stained green-blue, rich in tonofilament and glycogen, cells can be located separately or in a plast.Parabasal cells can often be detected in atrophy, in the postpartum period and against the background of inflammatory diseases.

d) Basal cells are small and have a high nuclear-cytoplasmic ratio. The nucleus is round or oval, located in the center of the cell and has granular chromatin, nucleoli and karyosomes. Cytoplasm is basophilic. Basal cells, due to their deep location, rarely fall into the smear in the form of chains or bundles.

2) Single-layer cylindrical epithelial cells.

Single-layer cylindrical epithelial cells are located in the cervical canal (endocervix). Cylindrical epithelial cells are normally arranged in small groups in the form of ribbon-like or beehive-like structures. Cells are cylindrical in shape, the nucleus is located eccentrically. "Package" cells can be found: the cytoplasm is full of mucus, sometimes the cells contain secretory granules.

3) Metaplastic epithelial cells.

Metaplastic epithelial cells are located in the transformation zone (in the transition zone of the endocervix to the cervical vaginal part. Metaplastic epithelial cells are mostly scattered, rarely in small groups. The nucleus is slightly hyperchromic, the chromatin is evenly distributed. The size of the nucleus is more than half of the cell. The cytoplasm is intensively stained and contains vesicles.

Sometimes light areas or vacuoles are detected around the nucleus.Cell borders are clear.

Normal cytogram

Normally, the cervical preparation contains the following cells:

(1) surface and intermediate squamous epithelial cells; parabasal cells appear during menstruation and after atrophy;

(2) a small amount of metaplastic epithelium;

(3) cylindrical epithelial cells;

(4) a small number of leukocytes, the number of which increases before menstruation;

(5) endocervical mucus.

The cell composition of smears taken at different stages of a woman's cycle and at different periods of a woman's life is different.

Compensatory - adaptive processes

Compensatory - adaptive processes are morphological and functional changes in the organism, aimed at restoring lost activity. Unlike damage, these processes allow the organism to adapt to the changed conditions by normalizing or increasing the level of vital activity.

Compensatory adaptation processes include: regeneration, hypertrophy, hyperplasia, metaplasia, atrophy.

Regeneration

Regeneration is the regeneration of structural elements instead of dead tissue and restoration of function. The reparative regeneration phase is the proliferative phase of inflammation.

There are the following forms of regeneration:

1. Cellular regeneration: cells reproduce by mitosis. Cellular regeneration is mainly characteristic of bone, epidermis, gastrointestinal tract, mucous membrane of respiratory and urinary tracts, connective tissue, endothelium, mesothelium, hematopoietic system, and lymphoid tissues. In this case, young cells multiply in the cytological smear.

2. Intracellular regeneration: an increase in the number (hyperplasia) and size (hypertrophy) of nuclei and ultrastructures. Cells, their nuclei are enlarged, cellular and nuclear polymorphism appears. Intracellular regeneration is characteristic of myocardium and skeletal muscles.

3. Cellular and intracellular regeneration: cells, their nuclei, cellular and nuclear polymorphism are observed. It is characteristic of liver, kidney, pancreas, endocrine glands, lungs, smooth muscles.

All tissues and organs have the ability to regenerate, but it differs structurally and functionally according to the specialization of the tissue or organ.These changes should not be considered pre-tumor proliferation.

The regenerative process consists of two interrelated stages:

1. Proliferation is the proliferation of young, immature cambial stem cells. Each tissue has its own cambial cells, which differ in the degree of proliferative activity and specialization, but several types of cells can arise from the stem cell (hematopoietic tissue, connective tissue).

Hypertrophy is an increase in the size of organs, tissues, cells, and intracellular structures. Hyperplasia is an increase in the number of structural elements of tissue and cells.

2. Differentiation is the formation, structural and functional specialization of cell structures that goes along with proliferation.

Atrophy

Atrophy is a decrease in the size of cells, tissues, organs or the end of their activity. Atrophic smear is observed in women during premenarche and postmenopause. The following atrophic changes are distinguished:

1) Mild atrophy: there are cyclical changes; but there is no menstruation.

2) Moderate atrophy: smear consists of intermediate cells without cyclic changes.

3) Severe atrophy: complete atrophy of the epithelium develops, characterized by the presence of parabasal cells and pseudoparakerotic cells with small, strongly basophilic shiny cytoplasm, small pyknotic nuclei, and karyorrhexis.

Inflammatory atypia.

A combination of degenerative, reparative, proliferative changes can lead to inflammatory atypia.

Causes of inflammatory atypia can be:

a) Special infectious agents (trichomonad vaginitis, amoebic vaginitis, candidiasis, gonococcal infection);

b) Nonspecific infectious agents (bacterial vaginosis, actinomycosis, leptotrichosis, mixed bacterial flora, chlamydia, simple herpes virus).

Cytological inflammatory atypia is manifested by:

1. Enlargement of cell and nucleus.

2. Hyperchromia.

3. Presence of multinucleated cells.

4. Uniform distribution of chromatin.

5. Chromatin contours are unclear.

6. In the nuclei, one or two enlarged nuclei, a large number of chromocents are found.

7. Multinucleated cells and fragmented cells may have nuclei.

Changes after chemotherapy and radiation.

Cells changed as a result of radiation and chemotherapeutic effects are similar to cells of good and bad quality: disruption of DNA synthesis, loss of the ability to divide normally, inactivation of enzyme systems, chromatin coagulation, denaturation of nuclear and cytoplasmic proteins are observed. Young cells in the premitotic and mitotic phases are damaged first.

In the early stages of chemotherapy and acute radiation, the following changes occur in cells:

1. Cytoplasm vacuolization. Vacuoles of different sizes are unevenly located, do not merge with each other and can occupy a third of the cell volume.

2. Increase in cell size.

3. An increase in the size of the cell nucleus.The nucleus may be enlarged due to swelling, the chromatin structure is light, the membrane is thin, and folded.

4. Presence of multinucleated cells, pseudomitosis, pathological mitoses;

5. Nuclear vacuolization, chromatin condensation, karyorrhexis, appearance of "extra nuclei";

6. The shape and color of the cytoplasm changes;

7. Cannibalism of cells, increase of leukocytes.

The effect of radiation therapy on the body begins a few days after the start of therapy. Observed under the influence of long-term radiation therapy:

1) Destruction stage:

a) large multinucleated cells (light giants);

b) odd-shaped cells with elongated cytoplasm with signs of karyorrhexis and/or karyolysis;

c) eosinophilic homogenization of cytoplasm, karyolysis, cytolysis;

g) presence of a large number of leukocytes, erythrocytes, mainly necrobiotic changes.

2) Lymphoid reaction:

a) the appearance of large cells of the "foreign body" type;

b) scar tissue-forming fibroblasts are identified in the smear.

Acute radiation changes often disappear 6 months after the end of radiation therapy. Sometimes there are signs of chronic damage to the epithelium in the form of atrophy or dysplasia. In contrast to atrophic changes associated with estrogen deficiency, signs of radiation pathomorphosis are observed: two and multinucleated, large cells.

In contrast to papillomavirus infection, radiation-induced vacuoles in human cells are small and unevenly distributed in the cytoplasm, with no distinct light zone around the nucleus.

Control questions:

1. Cytological examination in the diagnosis of gynecological diseases.

2. Bethesda terminology.

3. Multilayered flat non-coagulating epithelial cells.

4. Single-layer cylindrical epithelial cells.

5. Metaplastic epithelial cells.

6. Normal cytogram.

7. Compensator - adaptation processes.

8. Regeneration.

9. Proliferation. Hypertrophy. Hyperplasia.

10. Differentiation.

11. Inflammatory atypia.

12. Changes after chemotherapy and radiation.

2.4. Pre-tumor processes, etiopathogenesis, cytological characteristics.

The purpose of the training: to introduce cytological pathologies of the cervix, cervical precancerous conditions and development factors, specific cytological signs of human papillomavirus infection, cervical dysplasia, cancer in situ, invasive cancer, metaplasia, dystrophy, hyperkeratosis, parakeratosis, dyskeratosis.

Among the gynecological diseases of women of reproductive age, uterine pathology is observed in 10-15%. Today, cervical cancer is the most common oncological disease of the female genital organs and accounts for approximately 12% of all malignant tumors diagnosed in women. In the development of cervical cancer, certain stages of pathological processes of the cervix are noted.

The following vitological pathologies of the cervix are distinguished:

a) cervical background diseases;

b) cervical precancerous diseases;

c) cancer of the cervix in situ;

d) invasive cervical cancer.

Background diseases of the cervix are changes in the vaginal part of the cervix, in which normoplasia is observed, that is, the mitotic division of epithelial cells, their differentiation, proliferation is normal. These diseases include: pseudo erosion, ectropion, polyp, endometriosis, leukoplakia, erythroplakia, papilloma, cervicitis, true erosion.

Precancerous conditions of the cervix include epithelial dysplasia - pathological processes that lead to hyperplasia, proliferation, differentiation, maturation of epithelial cells.

Etiopathogenesis of cervical diseases.

Cervical precancerous conditions, and later cervical cancer appear against the background of multi-layered squamous epithelial diseases (ectopy, metaplasia).

Factors of the development of cervical background and precancerous diseases:

1. Inflammatory diseases of the genitals.

As a result of inflammatory diseases, necrobiosis and desquamation of the multilayered squamous epithelium of the cervix, and later eroded areas appear.

2. Human papilloma virus infection.

Mild changes in the epithelium infected with human papillomavirus disappear over time in the majority of patients, but 15% of patients have the possibility of transition to intraepithelial cancer.

Today, the human papilloma virus (HPV) has been proven to be the main etiological factor in the development of cervical cancer.

OPV 16 and 18 are included in the high-risk groups of human papillomavirus in the development of cervical cancer. In squamous cell cancer, in more than 50% of cases, OPV 16 is detected, in adenocarcinoma, OPV 18 is detected. The infection is usually sexually transmitted.

Specific cytological signs of human papillomavirus infection:

1) Koilocytic atypia:

Koilocytes are flat epithelial cells of various shapes, they are mostly scattered or in small groups, uneven, hyperchromic nucleus is enlarged and can be two, cytoplasm is wide, there is a pale perinuclear zone around the nucleus.

2) amphophilic cytoplasm;

3) dyskeratosis, parakeratosis, hyperkeratosis.

The development of dysplasia and cancer in human papillomavirus infection is a complex process depending on many factors and is closely related to infections, genetic characteristics and immune status.

Cervical dysplasia.

Dysplasia is the development of precancerous conditions as a result of the violation of epithelial differentiation: atypical signs appear in the cambial stem cells, the histological structure of the epithelium is disturbed, but the basement membrane is intact, and this process can be completely restored. Hyperplasia of basal cells, hyperkeratosis, appearance of atypical mitoses, increased mitotic activity can be observed in multi-layered flat epithelium; glandular epithelium is characterized by polymorphism and hyperchromia of nuclei, increased nuclear-cytoplasmic ratio, increased functional activity of cellular elements (pathological freezing, mucus formation).

The sequence of tissue changes in the process of cervical blastogenesis is expressed as follows:

- irregular diffuse hyperplasia;

- epithelial weak dysplasia (LSIL);

- severe epithelial dysplasia (HSIL);

- non-invasive cancer (CIS);

- invasive cancer.

Epithelial weak dysplasia - LSIL.

In weak epithelial dysplasia, atypical basal cells occupy one third of the epithelial layer in histological preparation, and the ability to differentiate is slightly impaired:

- there are pathologically changed surface and intermediate cells;

- the polarity and character of layered arrangement of epithelial cells has not changed;

- connections between cells are intact;

- cell differentiation is preserved, therefore, cytological changes are mainly detected in mature cells;

- dyskaryotic cells are few and separate, located between normal cells;

- Cytoplasm is usually polygonal, abundant, as in superficial or intermediate cells;

- there are signs of infection with the human papilloma virus;

- there are signs of mild dyskaryosis in the nucleus:

(a) The shape of the nucleus is usually round;

(b) contours are flat, single concavities may be present;

(c) chromatin is evenly distributed;

(d) the size of the nucleus is 3-6 times larger than that of normal interstitial cells;

(e) the nuclear-cytoplasmic ratio is increased, but the nucleus occupies less than half of the cell volume;

(f) nucleus normochromic or slightly hyper chromic;

(g) chromatin is relatively evenly distributed;

(h) chromatin structure is fine-grained, small chromo cents are identified;

(i) Nucleus absent.

Epithelial weak dysplasia - changes in LSIL can be associated with inflammatory, reparative, degenerative, atrophic and other damage, besides, the indicated pathological processes can hide real dysplasia.

Strong epithelial dysplasia - HSIL.

In severe epithelial dysplasia, atypical basal cells occupy up to two-thirds of the epithelial layer. Their ability to differentiate is strongly impaired:

- in addition to pathologically changed surface cells, intermediate and parabasal atypical cells are also identified;

- cells are often oval or round in shape;

- many cells are scattered;

- increased nuclear-cytoplasmic ratio;

- cell contours are uneven;

- chromatin granular, moderate hyperchromia characteristic;

- nuclear changes are characteristic of small cells, nuclear-cytoplasmic ratio is characteristic of large cells;

- metaplastic cells with a small nucleus, small, polygonal, flat cells and oval or round, basophilic cytoplasm;

- the number of pathological cells increases according to the degree of dysplasia.

Cancer in situ.

In severe dysplasia, the ability of cells to differentiate is almost lost, and only a small number of cells can be differentiated into intermediate cells. In intraepithelial cancer, almost the entire epithelial layer consists of atypical cells, but the integrity of the basement membrane is preserved.

In severe dysplasia and intraepithelial cancer (carcinoma in situ), the following symptoms occur:

• symptoms of severe dyskaryosis:

a) the nuclear-cytoplasmic ratio shifts a lot towards the nucleus;

b) there are chromocenters, that is, places where chromatin accumulates;

c) nuclei are usually absent;

d) the contours of the membrane are uneven, sometimes disintegrating, and cell borders appear wavy;

e) changed cells are located as plastids, syncytium.

Invasive cancer.

In invasive cancer, there is a strong polymorphism in the cells, and the integrity of the basement membrane is broken. In intraepithelial cancer, numerous syncytial clusters of cells with coarse chromatin are found.

Metaplasia.

Metaplasia is the transformation of one type of tissue into another. In the process of regeneration, metaplasia can also be observed: the process of transformation of spare cells into flat epithelium. Squamous cell metaplasia is associated with the proliferation of reserve cells, which is a necessary factor for malignant transformation. The appearance of precancerous diseases is caused by the covering of the cylindrical epithelium with flat epithelium.

Metaplasia is observed in the respiratory tract, salivary glands, pancreas, and cervical epithelium. Squamous metaplasia, squamous and glandular metaplasia can be observed in transitional epithelium.

Dystrophy.

Degeneration is a quality change associated with a metabolic disorder of tissues and cells.

Dystrophy is a degenerative change, a morphological and structural manifestation of metabolic changes. In most cases, dystrophy is reversible. However, if the effect of the unfavorable factor is continuous and strong, irreversible damage and death of cells is observed.

Symptoms of dystrophy at the cellular level:

1) the appearance of granularity;

2) uneven staining of cytoplasm;

3) vacuolization - intracellular swelling, sometimes cells turn into a large vacuole filled with liquid;

5) nuclear pyknosis or lysis is observed;

6) first there are changes in the cytoplasm, then changes in the nucleus;

7) when the cell dies, a change to the nucleus is observed:

(a) Swelling, cracks in the nuclear membrane appear, and chromatin accumulates at the periphery of the nucleus.

(b) the nuclear membrane may form paranuclear vacuoles;

(c) the nucleus enlarges due to swelling, the image of chromatin fades, and the nuclear composition becomes homogeneous;

(d) nuclear pyknosis - the nucleus shrinks due to leakage of nuclear juice or turns into a homogeneous spherical mass due to dilution of chromatin;

(e) nucleoli become dense or, on the contrary, expand;

(f) fragmentation of the nucleus - "karyorrhexis": the nucleus forms folds and breaks into fragments connected by chromatin bridges, eventually tearing;

(g) vacuolization of the nucleus.

Fatty degeneration is the accumulation of lipids in the cytoplasm in the form of small or large vacuoles.

Hyperkeratosis.

Epithelial response to chronic injury or impact (chronic inflammation, hormonal influence, disruption of trophic processes, etc.) is manifested in the quality of strong proliferation of cells. Rapid proliferation of multi-layered squamous epithelial cells can lead to thickening of the epithelial layer. The proliferation of cells of the parabasal layer leads to freezing of the surface layer (hyperkeratosis).

It is characterized by the presence of flat epithelial horns without a hyperkeratosis core in cytological preparations of the cervix.

Parakeratosis.

Epithelial response to trophic processes or influences can be manifested as increased differentiation. This leads to the development of parakeratosis. The term parakeratosis of the epidermis is manifested by the preservation of the nucleus in the frozen layer. In cervical parakeratosis, cells with a pyknotic nucleus, small, surface frosted cells appear. Parakeratosis is a protective reaction of the epithelium and is not clinically significant. However, parakeratosis can be an indirect sign of viral damage, under which dysplasia and cancer are hidden. Parakeratosis can develop when taking long-term estrogen and oral contraceptives.

Parakeratosis is characterized by the presence of small, round, oval, elongated or polygonal flat epithelial cells in the form of scattered or plastids. Cell nuclei are pyknotic, round, oval or rod-shaped and located in the center of the cell. Cytoplasmized, its color is shiny, pale when stained by the Poppenheim and Leishman method, pink or orange when stained by the Romanovsky method, pink or orange when stained by the Papanicolaou method.

Dyskeratosis.

Dyskeratosis is characterized by the appearance of small epithelial cells of elongated or polygonal shape, the nucleus is hyperchromic, and the cytoplasm is dense and shiny. Dyskeratosis is often caused by human papilloma virus infection.

Review Questions:

1. Cervical precancerous diseases.

2. Etiopathogenesis of cervical precancerous diseases.

3. Developmental factors of background and precancerous diseases of the cervix.

4. Dysplasia of the cervix.

5. Epithelial weak dysplasia - LSIL.

6. Strong epithelial dysplasia - HSIL.

7. In situ and infiltrative cancer.

8. Cytological signs of metaplasia.

9. Cytological signs of dystrophy.

10. Cytological signs of hyperkeratosis.

11. Cytological signs of parakeratosis.

12. Cytological signs of dyskeratosis.

2.5. Good and bad quality tumors.

Cell and tissue atypism. Tumor growth.

The purpose of the training: to familiarize with good and bad tumors, tumor cytology, convenient localization of tumors for cytological examination, appearance of tumors, tissue and cell atypism, classification of tumors, cytological diagnostic criteria and types of tumor growth.

Tumor, neoplasm, blastoma - (from the Greek blasto - tumor) is a pathological process characterized by non-stop cell proliferation.

Specific to tumor cells:

1. Hyperplasia - autonomous, uncontrolled proliferation of cells that does not obey the regulatory activity of the body;

2. Atypism - changes in cell structure, metabolism, activity, reproduction and differentiation;

3. Anaplasia (from the Greek ana - reverse and plasis - formation) - a tumor cell acquires characteristics different from normal cells under the influence of carcinogenic factors.

Tumor cytology is a microscopic examination of a smear of material taken from the surface of a tumor for the purpose of early diagnosis. Due to the ease and convenience of material acquisition and rapid implementation, this practice is used in mass screening for cancer diagnosis.

Tumor cytology is the first stage of diagnostic research when a malignant tumor is suspected, and along with its advantages, it also has its drawbacks, that is, there will not be 100% accuracy for diagnosis.

Tumor cytology is widely used in the following localization of malignant tumors:

1. Cancer of the vulva (prints);

2. Cervical tumor (oncocytology of the cervix);

3. Uterine body tumor (aspirate);

4. Breast tumor (aspiration biopsy);

5. Skin tumor (prints);

6. Lung cancer (sputum smear, obtaining material during bronchoscopy);

7. Colorectal cancer (smearing, rectoromanoscopy or colonoscopy material acquisition);

8. Esophagus, stomach, duodenum cancer (obtaining material in fibro-, esophagogastro-, gastro-, duodenoscopy);

9. Thyroid cancer (aspiration material);

10. Urinary tract cancer (smearing, lavage or aspiration).

When a malignant tumor is detected in the cytology of tumors, the next step is a tumor biopsy, which is used to make an accurate diagnosis of cancer. The tumor consists of parenchyma and stroma. Tumor parenchyma consists of tumor cells, formed as a result of malignant transformation of immature cells and their clonal proliferation. All structures of tumor cells - nucleus, cytoplasm, membrane, organelles and cytoskeleton are changed.

The appearance of tumors is different:

- can be in the form of a knot, mushroom, cauliflower;

- the surface may be smooth, bumpy, or sucker-like;

- the tumor is inside the organ and can diffusely occupy the entire organ;

- if the tumor damages blood vessels, it can cause internal bleeding;

– different sizes;

- the consistency is dense (a lot of stroma) or soft (a lot of parenchyma).

Tissue atypism is a violation of the ratio of tissues characteristic of a certain organ, characterized by organotypic and histotypic differentiation disorders - a violation of the shape and size of epithelial structures, a change in the ratio of parenchyma and stroma, a change in the thickness of fibrous structures and their chaotic arrangement. Tissue atypism is characteristic of benign tumors.

Cell atypism is a disorder of cell differentiation. The main morphological sign of atypia of tumor cells is polymorphism: the size, shape, nucleus and nucleoli of the cells are different. Nuclei hyperchromia, coarse chromatin, polyploid cells, increased nuclear-cytoplasmic ratio, multiple mitoses are also characteristic of malignant tumors. When the atypism is strong, the cells completely change their appearance and differ sharply from the cells of origin, as a result of which it is impossible to determine from which cells they originated. One of the main signs of atypism is mitotic pathology, which indicates the effect of carcinogenic factors on the cellular genetic apparatus. Cellular atypism is characteristic of immature, malignant tumors.

Ultrastructural atypism is characterized by an increase in ribosomes, changes in their shape, location, size, functional heterogeneity of mitochondria, cytoplasm reduction, nuclear enlargement, and chromatin changes. Ultrastructures are typical of stem cells without atypism.

Cytological diagnostic criteria of malignant tumor cell atypia.

Atypical cell-specific:

- increase in size (sometimes giant), in rare cases the cell does not increase in size and this makes cytological diagnosis difficult;

– change of shape and polymorphism of cell elements;

- anisocytosis - cells are different in size;

- nuclear-cytoplasmic ratio increases;

- dissociation of nucleus and cytoplasm (for example, young nucleus and frozen cytoplasm);

- appearance of multinucleated cells;

- detection of "empty" nuclei of fragmented cells of different sizes and shapes;

- different staining of different areas of cytoplasm;

- emergence of cell complexes - cell collections;

- loss of polarity - the location of cell nuclei in different directions.

- tumor diathesis or "ugly" drug background - appearance of granular masses, leukocytes, erythrocytes (tumor invasion).

Nucleus:

 nuclear polymorphism;

 atypical location of the nucleus;

 increase in the size of the nucleus;

 anisokaryosis - different nuclear sizes;

 nuclear membrane is uneven, crooked;

 uneven thickening of the nuclear membrane;

 uneven distribution of chromatin;

 changes in chromatin structure - rough chromatin, granules of different sizes, egalite chromatin;

 in undifferentiated and poorly differentiated tumors, chromatin may be thin and evenly distributed;

 nuclear staining is usually hyperchromic;

 presence of inclusions in the nucleus: detection of virus bodies, intranuclear bodies, tubular structures, vesicles, tumors, pockets in the nuclear membrane.

Nuclei:

- detection of normal nuclei;

- an increase in the number of nuclei compared to normal cells;

- increase in size;

- be incorrect, in different forms.

A medical conclusion is formed based on the sum of the above signs when there is enough cell material. Evaluating a drug that is incorrectly taken and prepared incorrectly, with insufficient cellular elements, will lead to an error.

The main tasks of cytological diagnosis of tumors:

1. Giving a conclusion before treatment.

2. Urgent intraoperative diagnosis.

3. Control of treatment effectiveness.

4. Forecasting the course of the disease.

Before treatment, it is necessary to give a cytological conclusion:

- determination of tumor histogenesis;
- determining the level of tumor differentiation;
- determining the level of tumor spread;
- study background changes;
- determination of some forecast factors;
- examination of bacterial flora.

Classification of tumors

The main feature of tumor classification is the nomenclature of tumors (terminology). In the nomenclature of tumors, the place of origin of the tumor is given: the suffix "-oma" is added to the stem of the word denoting the tissue. For example, fat tissue tumor - lipoma, fat tissue tumor - chondroma, muscle tissue tumor - myoma, smooth muscle tumor - leiomyoma, transverse muscle tumor - rhabdomyoma, etc.

Some tumors have preserved their historical names. For example, a connective tissue tumor is called a sarcoma (from the Greek "sarkos" - meat), because the cross-section of its tissue resembles fish flesh.

All tumors are divided by classification:

1. Good-quality tumors are composed of cells, and the tissue from which the tumor originated can be identified. In these tumors, only organotypic or histotypic differentiation is disturbed, tissue atypism, expansive and slow growth are characteristic. The tumor does not have a negative effect on the body and does not metastasize. However, benign tumors can cause dangerous complications when they are located in dangerous areas. For example, brain or spinal cord tumor, vascular tumor, etc. Sometimes benign tumors can turn into malignant tumors, that is, they can meet with malignancy.

2. Poor-quality tumors are tumors that arise from poorly differentiated or undifferentiated cells, which completely lose the resemblance to the tissue of origin. Not only organotypic and histotypic, but also cytotypic differentiation is disturbed in these tumors. Malignant tumors are characterized by cell and tissue atypism, infiltrative and rapid growth, metastasis, local and general negative effects on the body. Determining the level of differentiation, determining the level of danger is of great practical importance:

1. Highly differentiated - good quality tumors.

2. Moderately differentiated.

3. Undifferentiated - poor quality tumors.

International classification of diseases is widely used in oncological practice. In it, all diseases have their own morphological code, which indicates the nature of the tumor:

0 - tumors of good quality;

1 - pre-tumor conditions;

2 - cancer in situ or intraepithelial neoplasia;

3 - malignant tumors.

Modern classification is based on histogenetic features, taking into account the morphological structure of the tumor, localization, structural features of the organs, good or dangerous features. Based on this classification, 7 groups of tumors are distinguished:

1. Epithelial tumors without specific localization (organospecific).

2. Tumors of exocrine and endocrine glands, epithelial covers (organospecific).

3. Mesenchymal tumors.

4. Melanin-producing tissue tumor.

5. Tumors of the nervous system and cerebral cortex.

6. Tumors of the blood system.

7. Teratomas.

Cytological diagnostic criteria

Cytological diagnosis is the result of comparison with histological examinations as a factor of reliability. The most consistent cytological findings with histological

results are observed in metastatic lesions of the skin, mammary gland, thyroid gland, and lymph nodes. Conclusions of endometrial hyperplastic processes are unsatisfactory and correspond to 30-50%. Cervical pathology is suitable in 75-80%. 3 - 20% of smears come out of poor quality. Urgent cytological control is carried out during surgery, which allows to determine the metastatic damage of lymph nodes in 97-99% of cases.

The purpose of cytological examination of various organs:

1. Determination of the nature of the pathological process.

2. To determine the presence of a tumor.

3. Determination of the type of tumor (benign or malignant tumor).

4. To determine the tissue type, histological form and degree of differentiation of the tumor.

5. Cytological characterization of the tumor - studying the location, structure, structure of cells.

The specialist evaluates the following indicators based on cytological diagnostic criteria:

1. Number of cells.

2. Polymorphism - the appearance of different types of cells.

3. Arrangement of cells - formation of separate, complex and structures.

4. Size and shape of cells and their nuclei.

5. Nucleus and cytoplasm structure.

6. Nucleus - cytoplasm ratio.

7. Changes in the normal cellular composition of tissues.

8. Background of the drug (blood elements, non-structural substances, colloid, fat, etc.).

A solitary location of cells is a separate location relative to each other. When arranged in bundles, the cells touch each other but are separated from each other. Formation of structures - cells are connected to each other in different ways:

1. Plastics.

2. As a beehive structure.

3. Lattice structure.

4. Papillary papillary structures (cells surround each other).

5. Glandular structures (round structures, the nuclei are located eccentrically, there is a secret, structureless substance in the middle).

6. Spherical structures.

7. Follicular (follicular) structures - cells are located on the periphery, in the middle of the structure - secretion.

8. Rosette (several cells in the center, around which the cells are arranged in a circle).

In good-quality tumors, the cells in the structure are arranged in the correct order, the distance between them is the same, the cells and their nuclei are monomorphic. In malignant tumors, the structures form complexes (cancer, epithelial tissue tumor) or tufts (sarcoma, connective, muscle, nerve tissue). Cells in complexes are irregularly placed on top of each other.

Tumor growth

Tumor growth is divided into 3 different types:

1. Expansive growth.

In expansive growth, the tumor grows by displacing the surrounding tissue. Expansive growth is slow and characteristic of advanced, benign cell tumors. However, some malignant tumors (kidney cancer, thyroid cancer, fibrosarcoma, etc.) can grow expansively.

2. Appositional growth.

In appositional growth, normal cells touching the tumor become tumor cells due to neoplastic transformation.

3. Infiltrative or invasive growth.

In invasive growth, tumor cells destroy the surrounding tissue and grow into it. Invasion usually takes place along interstitial spaces, nerve fibers, blood vessels, and lymphatic vessels in areas of least resistance. Tumor complexes break them down and get into the blood and lymph flow, grow into the sparse connective tissue. In infiltrative growth, the border of the tumor is unclear, uneven.

Infiltrative growth is rapid and characteristic of immature, malignant tumors. According to the foci of tumor growth, unicentric (from one focus) and multicentric (from many foci) growth is observed.

Endophytic or exophytic growth is observed depending on the growth of tumors on hollow organs. Endophytic growth is an infiltrative growth of a tumor that grows along the wall of an organ. In this case, the tumor may not be noticeable from the surface of the mucous membrane (for example, stomach, bladder, bronchus, intestine), but the tumor growth is detected in the cross-section of the organ.

Exophytic growth is the expansive growth of a tumor into an organ cavity (for example, stomach, bladder, bronchus, intestine). In this case, the tumor grows into the cavity, fills the cavity and is attached to the wall of the organ at the peduncle.

Review Questions:

1. Understanding the tumor.
2. Tumor cytology.
3. Convenient localization of malignant tumors for cytological examination.
4. Appearance of tumors.
5. Morphological signs of atypia.
6. Tissue atypism.
7. Cell atypism.
8. Cytological criteria of atypia of malignant tumor cells.
9. Nuclear atypism.
10. Classification of tumors.
11. Criteria for cytological diagnosis of tumors.
12. Growth of tumors.

CHAPTER 3. METHODS OF CYTOLOGICAL EXAMINATION IN HEMATOLOGY.

3.1. Cytological examination methods widely used in hematology.

Purpose of training: to introduce cytological examination methods in hematology, morphological characteristics of pathological erythrocytes, erythrocytometry, reticulocytes, myelogram.

Hematology is the study of blood, blood-forming organs and blood diseases. Hematology is a branch of medicine that studies the etiology, diagnosis,

treatment, prevention and prognosis of blood diseases, the production of blood and its components (blood cells, hemoglobin, blood proteins, clotting factors).

Hematological diagnostic methods are traditionally the most common investigations. Currently, many clinical diagnostic laboratories use hematological analyzers of varying degrees of complexity to count and analyze blood cells.

Cytological examinations are important in the diagnosis of hematological diseases. Their implementation is carried out in clinical diagnostic laboratories and special hematology laboratories.

The most important diseases diagnosed by hematological methods are anemias, hemopoietic tissue tumors. Hematological tests are used to evaluate the response of the body in many diseases, to determine the severity of the disease and the effectiveness of their treatment.

Blood is a complex fluid consisting of plasma and blood-shaped elements: erythrocytes - red blood cells, leukocytes - white blood cells and platelets - blood platelets.

Methods of cytological examination of blood in hematology:

- morphological examination of erythrocytes in blood smear;

- count of reticulocytes;

- osmotic resistance of erythrocytes;

- examination of platelets in a blood smear;

- morphological examination of leukocytes;

- cytochemical reactions;

- myelogram.

Among the methods of quantitative and qualitative study of blood cells, the most common clinical blood test is: hemoglobin concentration, color index, number of erythrocytes, number of leukocytes, leukoformula, description of the morphological appearance of blood cells, assessment of the sedimentation rate of erythrocytes, determination of the number of reticulocytes and platelets.

The morphology of erythrocytes is examined using oil immersion at 1000 times magnification. The erythrocyte size, color, shape, color intensity, presence of inclusions are evaluated. A morphologically normal erythrocyte is called a normocyte, and its diameter is 7 - 8 μm, and it has the shape of a double concave

disk; normochromic staining - pink cytoplasm is intensively stained at the periphery, palely stained in the center, there are no inclusions.

Morphological characteristics of pathological erythrocytes.

1. Anisocytosis - the appearance of erythrocytes of different sizes. Normally, in peripheral blood, normocytes make up 68-70%, microcytes (diameter less than 6 μm) 15.5%, and macrocytes (diameter greater than 8 μm) 16.5%. When there are many microcytes in the blood, it is called microcytosis, and when there are many macrocytes, it is called macrocytosis. A large number of erythrocytes larger than 12 μm in diameter is called megalocytosis.

2. Poikilocytosis - erythrocytes have different shapes. Poikilocytes can be different in shape, for example:

Ovalocytes are formed due to defects in the membrane and are characteristic of hereditary ovalocytosis (hemolytic anemia), thalassemia, severe iron deficiency anemia, and megaloblastic anemia.

Stomatocytes are erythrocytes with a mouth-like light zone in the center of the cell. Stomatocytes are present after blood transfusion, liver diseases, infectious mononucleosis, hereditary stomatocytosis (hemolytic anemia).

Spherocytes are spherical erythrocytes that have lost their biconvex shape and do not have a central hollow zone. Spherocytes are called microspherocytes if their diameter is less than 6 μm. Spherocytes appear in hereditary microspherocytosis (hemolytic anemia), burns, incompatible blood transfusions, when artificial heart valves are placed, in the syndrome of disseminated intravascular coagulation.

Acanthocytes are stellate erythrocytes. Acanthocytes appear in the blood in hereditary acanthocytosis (hemolytic anemia), lipoproteinemia, liver disease (cirrhosis), during treatment with heparin, after splenectomy.

Echinocytes are erythrocytes that have similar protrusions in their cytoplasm. Echinocytes appear in severe anemia, stomach cancer, stomach ulcer, kidney failure, uremia.

Dacryocytes are drop-shaped erythrocytes, found in melofibrosis, severe anemia, and toxic liver damage.

Targeted erythrocytes are erythrocytes that accumulate hemoglobin in the center and are erythrocytes similar to the shape of the target and are detected in thalassemia (hereditary hemolytic anemia), severe iron deficiency anemia, liver diseases, after splenectomy.

Annulocytes are hollow, ring-shaped erythrocytes that appear in severe iron deficiency anemia.

Drepanocytes are sickle-shaped erythrocytes that appear in hereditary sickle cell hemolytic anemia.

Schizocytes are small fragments of erythrocytes, which appear in burns, after kidney transplantation, hemolytic anemia, hemolytic uremic syndrome, disseminated intravascular coagulation syndrome, vasculitis.

Degmatocytes are helmeted erythrocytes and appear in hereditary hemolytic anemia.

3. Anisochromia - appearance of erythrocytes stained with different intensity. The color of red blood cells depends on the concentration of hemoglobin, and the concentration of hemoglobin is 32-36% of the norm. Normally saturated with hemoglobin, normochromic erythrocytes have a pink color. Erythrocyte color change:

Hypochromia - pale colored erythrocytes. Hypochromia of erythrocytes is caused by low amount of hemoglobin in erythrocytes and is characteristic of iron deficiency anemia, lead poisoning, sideroblastic anemia, thalassemia. In iron deficiency anemia, hypochromia is usually accompanied by microcytosis.

Hyperchromia is a dark staining of erythrocytes due to an increase in hemoglobin in erythrocytes. Hyperchromia is characteristic of vitamin V12 deficiency anemia, folic acid deficiency anemia, hereditary spherocytosis (hemolytic anemia).

Polychromasia (polychromatophilia) - appearance of erythrocytes of different colors: gray-purple, dark gray. These erythrocytes are characteristic of vitamin V12 deficiency anemia, folic acid deficiency anemia, hemolytic anemia, posthemorrhagic anemia.

4. Inclusions in the cytoplasm of erythrocytes. Normally, erythrocytes do not contain inclusions in the cytoplasm.

Heinz-Ehrlich bodies are 1-2 μm inclusions located at the edge of erythrocytes and consist of denatured hemoglobin. Heinz-Ehrlich bodies are detected in fermentopathy (congenital hemolytic anemia).

Basophilic punctuation is the presence of mitochondria and RNA remnants in the form of diffusely located dark blue granules in erythrocytes. Basophilic punctuation can occur in toxic bone marrow damage, for example, poisoning with heavy metal salts, radiation treatment, treatment with cytotoxic drugs, activation of erythropoiesis, megaloblastic anemia, thalassemia.

Jolly-Govell bodies are 1-2 μm, red-purple, circular DNA remnants in the cytoplasm of erythrocytes. Jolly-Govell bodies appear in megaloblastic anemias, hemolytic poisons, after splenectomy, against the background of erythropoiesis activation.

Cabot's rings are remnants of the red-purple ring-shaped nuclear envelope located in the cytoplasm of erythrocytes. They are detected in poisoning with heavy metal salts, megaloblastic anemias and leukemias.

Schuffner's granularity is 20-30 small red-purple dots in erythrocytes and is detected in three days of malaria. Damaged erythrocytes increase in size and lighten in color.

Maurer's spots are large, pink-red spots of various sizes, consisting of 10-15 dots, on erythrocytes in patients with tropical malaria. Erythrocytes do not increase in size and do not change color.

Siderotic grains are blue-colored, small (0.5-1.5 micron) granules of non-hemoglobin iron (ferritin, hemosiderin). It is determined by cytochemical tests. Usually, 0.8-1.0% of siderocytes can be detected in peripheral blood. An increase in siderocytes is observed against the background of sideroblastic anemia, myelodysplastic syndrome, hemolysis of erythrocytes, after splenectomy.

Erythrocytometry.

Erythrocytometry is the measurement of the diameter of stained erythrocytes using a micrometer. Erythrocytometry is performed under maximum illumination of the field, using 1000 times magnification. The diameter of 100-200 erythrocytes located in the visible area is measured. The diameter of the erythrocytes obtained in the measurement results is expressed as a percentage. Normally, in peripheral blood, normocytes with a diameter of 7-8 μm are 68-70%, microcytes with a diameter of less than 6 μm are 15.5%, and macrocytes with a diameter of more than 8 μm are 16.5%.

Reticulocytes.

Reticulocytosis reflects the level of bone marrow regenerative activity and erythropoiesis activity. Determination of reticulocytes is used in the following cases:

1. Determination of hemolytic anemia.

2. Iron deficiency, vitamin V12, folic acid deficiency anemia therapy monitoring.

3. Therapy monitoring during treatment with erythropoietin.

4. Assessment of regenerative capacity after cytostatic therapy and bone marrow transplantation.

5. Doping control of athletes (taking erythropoietin).

Reticulocytopenia is observed in paroxysmal nocturnal hemoglobinuria, leukemia, myelodysplastic syndrome, cancer metastases to the bone marrow, aplastic, vitamin V12 deficiency anemia, red cell aplasia.

Myelogram

Bone marrow is taken by a doctor under aseptic conditions by means of a puncture. The cellular composition of the bone marrow depends on its dilution with peripheral blood, the state of the bone marrow, and the patient's age.

A myelogram is a ratio of bone marrow cells. 500-1000 cells are analyzed to calculate myelogram. All cells in the viewport are counted. In the myelogram, 60-70% of granulocytic cells, 20-25% of erythroid cells, 7-10% of lymphocytes, 2% of monocytes. Plasma cells, megakaryocytes, mast cells, macrophages, osteoblasts, osteoclasts are also considered in the myelogram.

In the assessment of myelogram, the cellular level of the bone marrow (multicellular, few cellular, normal cells) is first evaluated, and then the cells of each row of the bone marrow are evaluated.

Review Questions:

1. Cytological diagnostic methods in hematology.

2. Methods of quantitative and qualitative study of blood cells.

3. Morphology of erythrocytes.

4. Anisocytosis.

5. Poikilocytosis.

6. Anisochromia.

7. Inclusions in the cytoplasm of erythrocytes.

8. Erythrocytometry.

9. Reticulocytes.

10. Myelogram.

3.2. Bone marrow structure, activity.

Normal hematopoiesis. Hematopoietic factors.

The purpose of the training: introduction to hemopoiesis, bone marrow, bone marrow hematopoietic barriers, classes of hemopoietic cells, characteristics of blasts, regulation of hemopoiesis, necessary factors for normal erythropoiesis.

Hematopoiesis is a system that ensures constant renewal of blood-forming cells. In the process of hematopoiesis, blood cells - leukocytes, erythrocytes and thrombocytes are continuously formed, produced and broken down. Currently, the hierarchical model of hematopoiesis is confirmed, according to which blood cells are formed from hematopoietic multipotent stem cells. The main organ of hematopoiesis is the bone marrow, which has the following types:

1. Red bone marrow (consists of hematopoietic cells).

2. Yellow bone marrow (consisting of adipose tissue).

Red bone marrow serves as the only organ of blood formation from the 20th week of pregnancy. It is located in the epiphyses of skeletal flat bones and tubular bones. Red bone marrow has several hematopoietic barriers:

1. Erythrocyte line - produces erythrocytes.

2. Myelocytic line - produces eosinophils, neutrophils and basophils.

3. Lymphocytic line - produces lymphocytes.

4. Monocytic line - produces monocytes.

5. Megakaryocytic line - produces platelets.

Hematopoietic polypotent stem cells are class I cells, from which all cell lines of hematopoiesis are formed under the influence of cytokines. Under the influence of cytokines, stem cells become class II cells - colonies of polypotent cells - granulocytic - erythrocyte - macrophage - megakaryocytic colony-forming units and lymphocyte colony-forming units. Under the influence of cytokines, polypotent cells are transformed into class III oligopotent cells. Granulocyte-erythrocyte-macrophagal-megakaryocyte colony-forming units become 3 different types of cells: granulocyte and monocyte colony-forming unit, erythrocyte colony-forming unit, and megakaryocyte colony-forming unit. These processes are controlled by leukopoetin, erythropoietin and thrombopoietin.

Class IV cells are blasts, from which cells of class V are formed: lymphoblast, monoblast, myeloblast, erythroblast, megakaryoblast. Lymphoblast undergoes prolymphocyte (class V) and lymphocyte (class VI) stages during differentiation. A promonocyte (class V) and a monocyte (class VI) are formed from a monoblast. As a result of myeloblastization, eosinophil, basophil, or neutrophil passes through

promyelocyte, myelocyte, metamyelocyte, rod-nucleated (class V) and segment-nucleated (class VI) leukocyte stages.

Erythroblast differentiates into pronormocyte, basophilic, polychromatophilic and oxyphilic normoblast, reticulocyte (class V) and erythrocyte (class VI). A megakaryoblast becomes a megakaryocyte (class V), and platelets are released from the cytoplasm of a megakaryocyte (class VI).

Bone marrow cell content is assessed by a sternal or iliac puncture and a myelogram count.

Characteristics of blasts:

- the nucleus is large;

- nuclear-cytoplasmic ratio 1:4-1:8;

- the cell cytoplasm is pale yellow to dark basophilic in color;

- there is no perinuclear empty zone around the nucleus, there is no granularity in the cytoplasm;

- the chromatin structure of the nucleus is fine-reticulated;

- the nucleus may have 1-2 nuclei.

Acute and chronic leukemia, anemia, thrombocytopenia, lymphogranulomatosis, tuberculosis, Gaucher disease, Niemann-Pick disease, tumor metastases, visceral leishmaniasis can be diagnosed on the basis of myelogram. At the same time, it is of great importance in evaluating the effectiveness of the therapy.

Regulation of hematopoiesis

Blood formation is controlled by the following factors:

- growth factors - erythropoietin, leukopoetin, thrombopoietin;
- trace elements, vitamins, hormones (erythropoietin, thyroxine, androgen, corticosteroids, growth hormones).

Growth factors include colony-stimulating factors, interleukins, and inhibitory factors. Almost all growth factors affect stem cells and colony-forming cells. Necessary for normal erythropoiesis:

1. Hormones controlling protein metabolism (pituitary somatotropic hormone, thyroxine, etc.).

2. Hormones controlling calcium metabolism (parathormone, thyrocalcitonin).

3. Androgens stimulate erythropoiesis, and estrogen inhibits it.

4. Erythropoietin. Most of the erythropoietin is produced in the kidneys. Its formation is related to the lack of blood circulation and oxygen in the kidney. A decrease in the number of erythrocytes and a decrease in the partial pressure of oxygen are the basis for the increase in the production of erythropoietin. Erythropoietin production decreases in chronic kidney disease.

Thrombopoietin is synthesized in the liver, enhances the proliferation and differentiation of colony-forming megakaryocytic cells, platelet formation.

5. Microelements (iron, copper, zinc, selenium, etc.). Iron is included in heme and is necessary for the synthesis of hemoglobin. Iron deficiency in the body develops due to alimentary causes, malabsorption in gastrointestinal diseases, increased need for iron (pregnancy, athletes), bleeding. Copper is of great importance in the production of erythrocytes.

6. Vitamins. Folic acid, vitamins V12, V6, V2 and C are necessary for blood formation. Vitamin V12 and folic acid participate in the synthesis of nucleic acids in erythroblasts and increase their proliferation.

7. Cytokines (interleukin 1, 3, 6, 11 and 12, tumor necrosis factor) are involved in the differentiation of polypotent stem cells. Inhibitory factors reduce the production of hematopoietic cells. As a result of the lack of these factors, leukemia develops, an increase in leukocytes in the blood. Leukemia inhibitory factor inhibits monocyte-macrophage proliferation and differentiation

Review Questions:

1. Hematopoiesis.

2. Bone marrow.

3. Cells of hematopoietic classes.

4. Obstacles of hematopoiesis.

5. Development of hematopoiesis obstacles.

6. Regulation of hematopoiesis

7. Necessary substances for hematopoiesis

3.3. Cytological diagnosis of blood and bone breeding in differential diagnostics of anemias

Purpose of training: Anemia, classification of anemias, changes in blood and bone marrow in iron deficiency anemia, changes in blood and bone marrow in megaloblastic anemia, changes in blood and bone marrow in acute

posthemorrhagic anemia, changes in blood and bone marrow in hemolytic anemia, blood and bone in hypo-, aplastic anemia to introduce changes in the bone.

Anemia is a group of clinical and hematological syndromes, the common sign of which is characterized by a decrease in the amount of hemoglobin and erythrocytes in the blood.

Hemoglobin in erythrocytes transports oxygen from the lungs to the tissues and carbon dioxide from the tissues to the lungs. Patients suffering from anemia develop symptoms of hypoxia, a lack of oxygen in the tissues. In cases of mild anemia, patients are disturbed by general weakness, rapid fatigue, and impaired concentration. In severe anemia, shortness of breath, palpitations, headache, dizziness, ringing in the ears, loss of appetite are added to the slight physical exertion. In severe anemia, heart failure is added, especially when there is a concomitant pathology. Increased anemia is characterized by increased pallor of the skin and mucous membranes.

Classification of anemias:

1. According to erythrocyte size:

- microcytic anemia (iron deficiency anemia);

- macrocytic anemia (vitamin V12 deficiency, folic acid deficiency anemia);

- normocytic anemia (hemolytic anemia, aplastic anemia, metaplastic anemia).

2. According to the color indicator.

The color indicator shows that the erythrocyte is saturated with hemoglobin. Normally, RK is 0.85-1.05. Depending on it, the types of anemia:

1. Hypochromic anemia (color index less than 0.85):

- iron deficiency anemia;

- thalassemia.

2. Normochromic anemia (color index equal to 0.85-1.05):

- hemolytic anemias (due to excessive breakdown of erythrocytes);

- posthemorrhagic anemia (due to excessive bleeding);

- acute and chronic leukemias, lymphomas;

- aplastic anemia;

- tumor metastasis to the bone marrow;

- anemia developed due to reduced production of erythropoietin.

3. Hyperchromic anemia (color index more than 1.1):

- vitamin V12-deficiency anemia;

- folic acid deficiency anemia;

- refractory anemia in myelodysplastic syndrome.

3. According to severity:

- Mild anemia - hemoglobin 90-120 g/l.

- Moderately severe anemia - hemoglobin 90-70 g/l.

- Severe anemia - hemoglobin less than 70 g/l.

4. According to the regeneration feature of bone marrow:

The main sign of bone marrow regeneration is an increase in reticulocytes in the peripheral blood. Normally, reticulocytes are 1-10‰.

- aregenerator (aplastic anemia) - reticulocytes decrease sharply;

- hyporegenerator (vitamin V12 deficiency anemia, iron deficiency anemia) - reticulocytes decrease;

- normoregenerator or regenerator (posthemorrhagic anemia) - reticulocyte count is normal.

- Hyperregenerative (hemolytic anemias) - the number of reticulocytes increases sharply.

5. Etiopathogenetic classification.

- Anemia of chronic diseases: tuberculosis, bacterial endocarditis, bronchiectatic disease, lung abscess, brucellosis, pyelonephritis, osteomyelitis, collagenoses (systemic lupus erythematosus, rheumatoid arthritis, etc.).

- Iron deficiency anemia;

- Megaloblastic anemias: vitamin V12 deficiency anemia, folic acid deficiency anemia.

- Hemolytic anemias: congenital and acquired.

- Hypoaplastic anemia.

- Metaplastic anemias: leukemias, metastases of malignant tumors.

Iron deficiency anemia.

Iron deficiency anemia is the most common, accounting for 80% of all anemias. Cytological signs of iron deficiency anemia:

1. In peripheral blood:

- Reduction of erythrocyte and hemoglobin;

- Microcytosis of erythrocytes - 6 μm and smaller;

- Erythrocyte hypochromia - pale color;

- Poikilocytosis of erythrocytes - change in shape.

2. Normoblastic blood formation, erythroid row hyperplasia is observed in the myelogram.

Megaloblastic anemia

Megaloblastic anemia includes anemias of vitamin V12 and folic acid deficiency, and their cytological signs are as follows:

1. In peripheral blood:

- reduction of erythrocyte and hemoglobin;

- erythrocyte macrocytosis (9-12 μm), megalocytosis (increasing from 12 μm);

- erythrocyte hyperchromia - dark color;

- erythrocyte poikilocytosis - change in shape;

- Jolly-Govell bodies (nuclear remnants);

- Kebot rings (nuclear membrane);

- hypersegmentation of segmented neutrophils - 5 or more segments;

- reduction of reticulocytes.

In severe anemia:

- emergence of megaloblasts;

- reduction of thrombocytes, increase of macroplatelets;

- polychromaphilia - appearance of erythrocytes stained with polychromatophyll;

- formation of myelocytes and metamyelocytes;

- reticulocytes increase as a result of addition of hemolysis in splenic sinuses when megalocytes increase.

2. Megaloblastic blood formation, erythroid row hyperplasia is observed in the myelogram.

Acute post hemorrhagic anemia.

Acute post hemorrhagic anemia is characterized by heavy bleeding in a short period of time. In the diagnosis of acute post hemorrhagic anemia, the results of objective examination and instrumental examination are of great importance. In the cytological diagnosis of this type of anemia, the time that has passed after bleeding is of great importance:

1. In peripheral blood:

- normochromic, normocytic anemia is observed after bleeding;

- after 4-5 days, the number of reticulocytes increases, polychromaphilia - polychromatophilic stained erythrocytes, nucleated erythrocytes - normocytes appear;

- After 10 days, symptoms of iron deficiency anemia develop (erythrocyte microcytosis, hypochromia, poikilocytosis).

2. Normoblastic blood formation in the myelogram, erythroid row hyperplasia is observed after 4-5 days.

Hemolytic anemias

Hemolytic anemias are congenital and acquired. Cytological signs typical for hemolytic anemias:

1. In peripheral blood:

- reduction of erythrocyte and hemoglobin;

- normochromia of erythrocytes (hypochromia of erythrocytes is observed only in thalassemia and hyperchromia in microspherocytosis);

- normocytosis of erythrocytes (only in microspherocytosis, the diameter of erythrocytes decreases);

- reticulocytes increase sharply;

- in congenital hemolytic anemias, the shape of erythrocytes changes:

- small 5-6 μm, hyperchromic erythrocytes appear in microspherocytosis;

- oval-shaped erythrocytes appear in ovalocytosis;

- star-shaped erythrocytes appear in acanthocytosis;

- mouth-shaped erythrocytes with a hypochromic zone appear in stomatocytosis;

- in sickle cell anemia, the shape of erythrocytes does not change under normal conditions, only in the case of severe hypoxia, a hemolytic crisis occurs, and sickle erythrocytes - dacryocytes appear;

- in thalassemia, target-like, hypochromic erythrocytes - kodocytes appear.

In hemolytic crisis:

- a large number of normocytes with immature nuclei appear;

- amount of reticulocytes exceeds 30%.

2. Normoblastic blood formation, erythroid row hyperplasia is observed in the myelogram.

Hypo aplastic anemia

Hypo aplastic anemia is associated with a decrease in stem cells in the bone marrow, resulting in a decrease in all cell lines. Cytological signs of aplastic anemia:

1. In peripheral blood:

- pancytopenia (decrease of all types of cells): a sharp decrease in the number of erythrocytes, platelets and leukocytes;

- normochromic of erythrocytes;

- erythrocyte normocytosis;

- relative lymphocytosis (the absolute amount of lymphocytes decreases, the relative amount in the leukoformula increases).

2. In the myelogram, all types of bone marrow cells are sharply reduced, and the number of lymphocytes is relatively increased.

Cytological differential diagnosis of anemias is presented in Appendix 2.

Review Questions:

1. Definition of anemia.

2. Classification of anemias.

3. Blood changes in iron deficiency anemia.

4. Changes in bone marrow in iron deficiency anemia.

5. Blood changes in megaloblastic anemia.

6. Changes in bone marrow in megaloblastic anemia.

7. Blood changes in acute post hemorrhagic anemia.

8. Changes in bone marrow in acute post hemorrhagic anemia.

9. Blood changes in hemolytic anemia.

10. Changes in bone marrow in hemolytic anemia.

11. Blood changes in hypo aplastic anemia.

12. Changes in bone marrow in hypo aplastic anemia.

3.4. Thrombocytopoiesis. Platelet count methods. Thrombocytosis and thrombocytopenia. Cytological diagnosis of blood and bone marrow in platelet pathology.

Purpose of the training: familiarization with thrombocytopoiesis, methods of platelet counting, mastering cytological examination of thrombocytosis, thrombocytopenia, pathology of the platelet line of blood and bone marrow.

The process of formation of platelets in the body is called thrombocytopoiesis. The mother cell of platelets is a megakaryocyte cell.

Megakaryocyte cell elements originate, differentiate, and form from myeloid progenitor cells in the bone marrow. The main stimulators of megakaryocytopoiesis: IL-1, IL-3, IL-4, IL-6, IL-11, colony stimulating factors, erythropoietin, thrombopoietin.

Thrombocytopoiesis is based on the inverse garden principle: an increase in platelets in the blood stops thrombocytopoiesis, and thrombocytopenia stimulates the formation of platelets. In the bone marrow, the megakaryocyte cell undergoes several morphological differentiation stages: megakaryoblasts, promegakaryocytes, and megakaryocytes. Megakaryocytes make up 75-85% of the cells of the megakaryocytic line, megakaryoblasts make up 10%, and promegakaryocytes make up 15%.

A megakaryocyte is a giant polyploid cell with a diameter of 60-120 μm. A megakaryocyte is a large cell with a polymorphous nucleus, a large, pink cytoplasm, and a storage of platelets.

The main function of megakaryocytes is to form platelets and keep their number constant. From one megakaryocyte, up to 5000 platelets are released. Normally, 60-70% of megakaryocytes are active, that is, they form platelets. Approximately 80% of platelets are in the blood and 20% in the spleen. Platelets live 7-8 days.

A platelet is a cell without a nucleus, 2-4 μm in diameter, and is involved in hemostasis and blood clotting. The number of platelets in a healthy person is 180-320 x109/l.

Thrombocytes are round and oval in shape, the cytoplasm is composed of hyalomer and central pink-purple granulomer parts.

Platelet functions:

1. Angiotrophic: nourishes and strengthens the blood vessel wall.

2. Adhesion: platelets formed in primary hemostasis stick to the damaged blood vessel wall.

3. Aggregation platelets stick together.

4. Clot retraction: platelets stick together, resulting in the contraction of the blood clot and the formation of a thrombus.

5. Produces vasoconstrictors to reduce bleeding.

Thrombocytosis is an increase in the number of platelets in the blood, and thrombocytopenia is a decrease in the number of platelets.

Types of thrombocytosis and thrombocytopenia:

1. In primary (absolute) thrombocytosis, the number of platelets exceeds 400x109/l, the activity of megakaryocytic cells in the bone marrow increases. Primary (absolute) thrombocytosis occurs in the following cases:

a. In megakaryocytic leukemia (essential thrombocythemia).

b. In erythremia.

c. In chronic myeloid leukemia.

d. In myelofibrosis.

2. Secondary (absolute) thrombocytosis can occur:

a. When eating.

b. Boredom.

c. After bleeding.

d. In asphyxia.

e. In hemolysis.

f. In burning.

g. In sarcoidosis.

h. After surgery.

i. After splenectomy.

j. After treatment with corticosteroids.

k. In chronic inflammatory diseases (rheumatoid arthritis, non-specific ulcerative colitis, tuberculosis, osteomyelitis).

l. In low-grade tumors.

3. Causes of relative thrombocytosis:

a. Dehydration.

b. Blood transfusion.

Dangerous clinical signs of thrombocytosis are thrombosis at the level of 700-900x109/l of thrombocytes, the possibility of thromboembolism.

Absolute thrombocytopenia is a platelet count less than 150x109/l. Thrombocytopenia is observed when the clinical manifestation is less than 70x109/l. Absolute thrombocytopenia occurs in the following cases:

1. Hereditary pathology of thrombocytopoiesis.

2. Immune thrombocytopenia (autoimmune).

3. Blood diseases (aplastic, megaloblastic anemias, leukemias, paroxysmal nocturnal hemoglobinuria).

4. Heavy bleeding.

5. Bone marrow damage (in metastases, tuberculosis, radiation).

6. Hemolytic - uremic syndrome.

7. Kidney failure.

8. Liver diseases.

9. Vascular, spleen, tumors.

10. Eclampsia.

11. Hyperthyroidism, hypothyroidism.

12. Infectious diseases (virus, bacteria, rickettsiosis, malaria, toxoplasmosis, human immunodeficiency syndrome).

13. Eclampsia in pregnancy.

14. Menstruation.

15. Effects of drugs (cytostatics, analgesics, antihistamines, antibiotics, etc.).

16. Alcohol, heavy metal poisoning.

17. Hypersplenism, disseminated intravascular coagulation syndrome, after hemodialysis.

Morphology of platelets

In the blood of a healthy person, when stained by the Romanovsky-Giemza method, mainly 4 types of platelets are distinguished:

1. Mature platelets are 90-95%, round or oval in shape, 3-4 μm in diameter, hyalomeres and granulomeres are clearly distinguished.

2. Immature platelets are 0-1% and are 4-6 μm in size.

3. Old thrombocytes are 2-6%, 2-3 μm in size, round, oval, tooth-shaped and have a thin cytoplasm.

4. Damaged, degenerative thrombocytes are 0-1%, large, elongated, blue or pink cytoplasm, azurophilic granules, vacuolated cells.

Platelet count methods

1. Fonio method.

2. Counting in the Goryaev chamber.

3. Counting in an electronic automatic hematological analyzer.

Determination of the number of platelets by the Fonio method.

1. 14% magnesium sulfate solution or 6% ethylene diamine tetraacetate (EDTA) is taken into a Panchenkov capillary "up to the mark of 25 mm - R" and poured into a test tube.

2. Blood taken from the finger is taken up to the K line of the Panchenkov capillary and put into a test tube.

3. The test tube is thoroughly mixed and a smear is prepared from it, fixed and stained by the Romanovsky-Giemza method.

4. The number of platelets in the area magnified 1000 times is counted against 1000 erythrocytes (‰).

5. Knowing the number of erythrocytes in 1 μl of blood and the number of erythrocytes per thousand, based on the formula, the number of platelets in 1 μl of blood is calculated.

Platelet (x109/l) = Erythrocyte x platelet (‰)

Normally, according to the Fonio method, the number of platelets per thousand erythrocytes is 45-70‰.

Determination of the number of platelets in the Goryaev chamber.

1. 1% - 4 ml of ammonium oxalate solution is placed in a test tube.

2. 20 μl of blood is put into a test tube, mixed well and left for 25-30 minutes for erythrocyte hemolysis.

3. After re-mixing, the solution is poured into the Goryaev chamber.

4. The number of platelets is counted diagonally in 25 large squares.

5. The number of platelets is calculated by the formula

platelet count x 2000

Counting the number of platelets in an automatic analyzer.

In modern hematological analyzers, platelets are seen in sizes ranging from 2-30 fl. Automatic analyzers evaluate the size, structure, cytochemical and other characteristics of cells, analyzing approximately 10,000 cells in one sample.

Review questions:

1. Thrombocytopoiesis.

2. Characteristic of megokaryocyte.

3. Platelet functions.

4. Changes in the number of platelets.

5. Morphology of platelets.

6. Methods of counting platelets.

7. Determination of the number of platelets by the Fonio method.

8. Determination of the number of platelets in the Goryaev chamber.

9. Counting the number of platelets in an automatic analyzer.

3.5. Leukopoiesis. Leukopoiesis regulation. Leukopoietic factors.

Purpose of training: introduction to leukocytes, granulocytes, agranulocytes, granulocytopoiesis, monocytopoiesis, lymphocytopoiesis.

Leukocytes are nucleated blood cells that differ greatly in appearance and function. Leukocytes protect the body from external and internal pathogenic factors. The total number of leukocytes is 4-9 x109/l.

2 types of leukocytes differ according to the staining of granules in the Romanovsky-Giemza method:

1. Granulocytes. In the cell cytoplasm are special granules, which include neutrophils, eosinophils and basophils.

2. Agranulocytes. There are no special granules in the cytoplasm. They include monocytes and lymphocytes.

Leukopoiesis consists of granulocytopoiesis, lymphocytopoiesis and monocytopoiesis.

Granulocytopoiesis.

Colony-forming granulocytopoietic cells appear from pre-myelopoiesis cells in the bone marrow and mature into basophilic, eosinophil, and neutrophilic granulocytes. Types of granulocytes in bone marrow:

1. Proliferating cells - myeloblast, promyelocyte, myelocyte.

2. Proliferative cells - myelocytes, neutrophils with rod nuclei and segmental nuclei.

Granulocyte colony-stimulating factor (GM-KSF) and granulomonocytic factors (G-KSF) are involved in the regulation of granulopoiesis.

Neutrophils with a rod nucleus have a diameter of 12-16 μm. Nucleus-cytoplasm ratio is 1:1. The nucleus is pinkish-purple in color, rod-shaped, chromatin structure is large, dense, and the nucleus is absent. The cell cytoplasm is pink in color and has neutrophilic granularity.

Neutrophil with a segmented nucleus has a diameter of 12-16 μm, the cell nucleus is red-purple, the nucleus-cytoplasm ratio is 1:6-1:8. The structure of chromatin is large particles. The cell cytoplasm is pink in color and has neutrophilic granularity.

The main functions of neutrophils:

1. Phagocytosis.

2. Detoxification.

3. Invoking an inflammatory response.

4. Participation in the production of leukocytes.

5. Participation in blood clotting.

Normally, neutrophils with rod nuclei in peripheral blood are 0-6%, neutrophils with segment nuclei are 47-72%.

Eosinophils are round cells 12-16 μm in diameter with a nuclear-cytoplasmic ratio of 1:1. The nucleus is dark purple in color, usually consists of two segments, the chromatin structure is uneven, large fragments. The cytoplasm is oxyphilic, with large yellow-pink special granules. Eosinophils stay in the blood for 6-12 hours, then move to tissues. Eosinophils live 4 - 30 hours. Normally, leukoformula contains 0-5% eosinophils.

Function of eosinophils:

1. Limitation of allergic reactions.

2. Formation of antihelmintic immunity.

3. Phagocytosis.

4. Participation in the inflammatory process.

5. Participation in blood clotting.

Basophils are normally found in leukocyte formula 0-1%. Their function:

1. Improve vascular permeability.

2. Limitation of allergic reactions.

3. Participation in the anti-tumor process.

4. Anti-inflammatory effect.

5. Participation in blood clotting.

6. Participation in triglyceride metabolism.

Monocytopoiesis.

Monocyte and macrophage cells in the bone marrow, blood, and tissues are integrated into the mononuclear phagocyte system. Immature cells of the mononuclear phagocyte system arise from polypotent stem cells. As a result of maturation, these cells become macrophages, colony forming cells and

monoblasts. There are stimulators (IL-3, GM-KSF, M-KSF) and inhibitors (interferon alpha, beta, prostaglandins, IL-10) of monocytic cells.

A monocyte is a round cell with a diameter of 18-20 μm. The nuclear-cytoplasmic ratio is 1:1. The monocyte nucleus is bean-shaped, kidney-shaped, segmental or rod-shaped, eccentrically located. Chromatin structure is sparse. Monocyte cytoplasm is wide, air-gray. Features:

1. Phagocytosis.

2. Formation of special immunity.

3. Participation in reparative processes.

4. Regulation of hematopoiesis.

5. Participation in metal metabolism (iron, copper, zinc).

Normally, the number of monocytes in leukoformula is 3-11%. The absolute number is 0.09-0.60x109/l.

Lymphocytopoiesis

Lymphocytes are formed in the bone marrow from pre-lymphocytopoietic cells. V-lymphocytes are fully developed in the bone marrow and undergo antigen-dependent differentiation. T-lymphocytes migrate to the thymus and are there. Mature T-lymphocytes are collected in peripheral lymph nodes.

A lymphocyte is a round cell with a diameter of 9-15 μm. The cell nucleus-cytoplasmic ratio is 4:1-8:1, the nucleus is round, the chromatin structure is rough, fragmented, the cytoplasm is basophilic, thin. According to their morphology, lymphocytes are small, medium and large.

Normally, the amount of lymphocytes in the leukocyte formula is 19-37%, the absolute number is 1.2-3.0 x109/l.

Function of lymphocytes:

1. Transforms into a plasma cell and produces antibodies.

2. Cytotoxic effect against yeast, cancer cells, virus, simple animals.

3. Stores information about antigens.

Review Questions:

1. Leukocytes.

2. Granulocytopoiesis.

3. Neutrophil granulocytes.

4. Eosinophilic granulocytes.

5. Basophilic granulocytes.

6. Monocytopoiesis.

7. Monocyte.

8. Lymphocytopoiesis.

9. Lymphocyte.

3.6. Acute leukemias, classification,main clinical and laboratory markers.

The purpose of the training: introduction to leukemias, main cytological signs of leukemias, acute leukemia, types of acute leukemia, cytomorphological characteristics of blast cells, changes in peripheral blood in acute leukemia, changes in bone marrow in acute leukemia, cytochemical reactions.

Leukemia is a group of malignant tumors developed from hematopoietic cells. Tumor cells proliferate in bone marrow, blood, lymphoid and other tissues and acquire a systemic character from the beginning of the disease.

The main cytological signs of leukemia:

1. It proliferates uncontrollably.

2. Apoptosis disorder.

3. Cells lose their differentiation and maturation properties.

4. Morphological and metabolic atypism of cells.

5. Metaplasia in blood-forming organs.

6. Atypical cells are released from the peripheral blood.

7. Formation of foci of blood formation in organs and tissues not involved in hemopoiesis (liver, kidney, subcutaneous tissue, intestine, etc.).

Leukemias are divided into the following types according to the characteristics of tumor cell differentiation and maturation:

1. Acute leukemia (blast cells with immature tumor substrate).

2. Chronic leukemia (tumor substrate cells are matured).

Acute leukemia is a heterogeneous, clonal malignant neoplasm of the blood system consisting of immature cells.

According to the cytomorphological and cytochemical characteristics of leukemic cells, acute leukemias are divided into three groups:

1. Acute myeloblastic leukemia.

2. Acute lymphoblastic leukemia.

3. Undifferentiated leukemia.

According to WHO, blast cells in peripheral blood and bone marrow are 20% or more in acute leukemia.

Cytomorphological characteristics of blast cells:

1. Nuclear chromatin structure is fine mesh.

2. Having nuclei.

3. Basophilic cytoplasm.

4. Nuclear-cytoplasmic ratio 4:1-8:1.

Changes in peripheral blood in acute leukemia:

1. Normocytic anemia.

2. The amount of leukocytes varies from severe leukopenia to severe leukocytosis (from 1 to 300 x109/l):

a) aleukemic form - the number of leukocytes is 1-3 x109/l, there are no blast cells or 1-2%, relative lymphocytosis;

b) subleukemic form - the amount of leukocytes is 4-14 x109/l, blast cells are 5-10%;

c) leukemic form - the number of leukocytes is more than 15 x109/l, blast cells are more than 10%.

3. Thrombocytopenia.

4. "leukemic gap" in the leukocyte formula - the presence of blast cells in the blood, the absence of intermediate cells.

5. The increase of ECT.

Bone marrow changes in acute leukemia:

1. Bone marrow blast transformation (blast cells more than 30%).

2. Reduction of myeloid, lymphoid, erythroid barriers to blood formation.

3. A sharp decrease in megakaryocytes.

Cytochemical reactions.

Blood cytochemical reactions are based on a color reaction with metabolically active enzymes and substrates of blast cells in order to determine the type of acute leukemia. Determination of myeloperoxidase, acid and alkaline phosphatase, nonspecific esterase, glycogen and lipids is of great diagnostic value. Cytochemical reactions allow to determine the identification of blasts, the level of cell maturation and treatment tactics.

Review Questions:

1. The concept of leukemia.

2. Classification of leukemia.

3. The main cytological signs of leukemia

4. Blast cell-specific cytomorphological features

5. Acute leukemia.

6. Changes in peripheral blood in acute leukemia.

7. Changes in the myelogram in acute leukemia.

8. Cytochemical reactions in acute leukemia.

3.7. Chronic leukemia, classification, main clinical and laboratory markers. Blood and bone marrow in chronic leukemia cytological diagnosis.

The purpose of the training: to familiarize with cytological diagnosis of chronic leukemia, chronic myeloid leukemia, acceleration and terminal stage, cytological diagnostic criteria of chronic myeloid leukemia, chronic lymphocytic leukemia, chronic lymphocytic leukemia and cytological diagnosis of chronic and terminal stage.

Chronic leukemia is a neoplastic disease of hematopoietic organs, in which tumor cells differentiate into mature cells that retain the characteristics of maturation. Chronic myeloid leukemia and chronic lymphocytic leukemia are the most common among chronic leukemias.

Chronic myelogenous leukemia is a tumor disease of the hematopoietic system developed from pre-myelopoietic cells. The main cytomorphological substrate of

chronic myelogenous leukemia is granulocytes - promyelocytes, myelocytes, metamyelocytes, neutrophils with rod nuclei and segmental nuclei.

Chronic myelogenous leukemia occurs mostly in 30-60 years old. The clinical course consists of 3 stages:

1) chronic (good quality);

2) acceleration stage;

3) terminal stage (polyclonal, dangerous).

Cytological diagnosis of the chronic stage of chronic myeloid leukemia.

In peripheral blood:

1. Mild normochromic anemia.

2. Leukocytosis 50-1000x109/l.

3. Increase of neutrophils with rod nuclei.

4. Appearance of metamyelocytes, myelocytes, promyelocytes in the blood.

5. Granulocyte anisocytosis, nuclear and cytoplasmic vacuolization, nuclear polymorphism, absence of neutrophil granules (hypo- and agranulation).

6. A small amount of blasts can be released.

7. Eosinophil-basophil association (eosinophil and basophil increase).

8. Decrease in lymphocytes.

9. In 40% of cases, thrombocytosis is 600 x109/l and more.

In myelogram:

1. Bone marrow is multicellular.

2. A sharp increase in cells of the granulocytic line.

3. Eosinophil-basophil association.

4. Blasts up to 10%.

5. There are many megakaryocytes.

6. Erythrokaryocytes decreased.

Cytological diagnosis of accelerated stage of chronic myeloid leukemia.

In peripheral blood:

1. Moderate and severe normochromic anemia.
2. Leukocytosis 50-1000 x109/l.
3. Increase of neutrophils with rod nuclei.
4. The presence of metamyelocytes, myelocytes, promyelocytes in the blood.
5. Blood blasts increase up to 15%.
6. Eosinophil - basophilic association.
7. The number of platelets decreases.

In myelogram:

1. Bone marrow is multicellular.
2. A sharp increase in cells of the granulocytic line.
3. Eosinophil-basophil association.
4. Blasts up to 15%.
5. Megakaryocytes are reduced.
6. Erythrokaryocytes are sharply reduced.

Cytological diagnosis of terminal stage of chronic myeloid leukemia.

In peripheral blood:

1. Severe normochromic anemia.
2. Leukocytosis 50-1000 x109/l.
3. Reduction of neutrophils with segmental nuclei.
4. The presence of metamyelocytes, myelocytes, promyelocytes in the blood.
5. Blood blasts are more than 15-20%.
6. Eosinophil - basophil association.
7. The amount of platelets decreases sharply.

In myelogram:

1. Reduction of mature granulocytes.
2. Reduction of erythrocyte and megakaryocytic cells.
3. Increase in blast cells.

Cytological diagnostic criteria for chronic myeloid leukemia:

1. Normochromic anemia.

2. Leukocytosis 50-1000 x109/l.

3. Increase of neutrophils with rod nuclei.

4. Appearance of metamyelocytes, myelocytes, promyelocytes in the blood.

5. Blasts may appear in the blood.

6. Reduction of neutrophils with segmental nuclei.

7. Eosinophil - basophilic association.

8. The amount of platelets increases in 40%, decreases in the terminal period.

9. Myeloperoxidase positivity in tumor cells during cytochemical examination.

Chronic lymphocytic leukemia is a tumor of lymphoid tissue, the cytomorphological substrate of which is lymphocytes. Chronic lymphocytic leukemia affects people over 50 years old.

Cytological diagnosis of the chronic stage of chronic lymphocytic leukemia.

In peripheral blood:

1. Normochromic anemia.

2. Leukocytosis 50-600x109/l.

3. Absolute lymphocytosis.

4. Riedel cells (divided or kidney-shaped lymphocytes).

5. Botkin-Gumprecht shadows (traces of lymphocyte disintegrated during smear preparation).

6. Granulocytic cells - reduction of neutrophils with rod nuclei and segmental nuclei.

7. Thrombocytopenia.

8. Cytochemical examination: glycogen positivity in tumor lymphocyte cells.

In myelogram:

1. Bone marrow total lymphoid infiltration.

2. Reduction of granulocytic, erythrocytic, megakaryocytic cells.

Cytological diagnosis of terminal stage chronic lymphocytic leukemia.

In peripheral blood:

1. Normochromic anemia.

2. Leukocytosis 50-600x109/l.

3. Absolute lymphocytosis.

4. Increase the number of blasts by 15%.

5. Riedel cells (divided or kidney-shaped lymphocytes).

6. Botkin-Gumprecht shades (traces of lymphocytes broken up during smear preparation).

7. Granulocytic cells - reduction of neutrophils with rod nuclei and segmental nuclei.

8. Thrombocytopenia.

In myelogram:

1. Bone marrow total lymphoid infiltration.

2. Reduction of granulocytic, erythrocytic, megakaryocytic cells.

3. Blast cells increase by more than 15%.

Review Questions:

1. The concept of leukemia. Acute leukemias.

2. Classification of leukemias.

3. Changes in peripheral blood in acute leukemia.

4. Changes in the myelogram in acute leukemia.

5. Cytochemical reactions in acute leukemia.

6. Cytological diagnosis of the chronic stage of chronic myeloid leukemia.

7. Cytological diagnosis of the accelerated stage of chronic myeloid leukemia.

8. Cytological diagnosis of the terminal stage of chronic myeloid leukemia.

9. Cytological diagnosis of the chronic stage of chronic lymphocytic leukemia

10. Cytological diagnosis of terminal stage of chronic lymphocytic leukemia.

3.8. Leukocytosis, leukemic reaction and cytological differentiation of leukocytes.

Purpose of training: to provide information about leukocytosis, neutrophil, eosinophil, basophil, lymphocytic and monocytic leukocytosis, leukemic reactions, myeloid, lymphocytic, eosinophilic leukemic reaction, secondary erythrocytosis, reactive thrombocytosis.

Leukocytosis and leukemic reaction is an important clinical and hematological syndrome. The development of leukocytosis and leukemic reaction affects the course and outcome of the disease.

Leukocytosis is a clinical laboratory syndrome characterized by an increase in the number of leukocytes in the blood over 10x109/l. There are neutrophilic, eosinophil, basophilic, lymphocytic and monocytic types of leukocytosis. The most common leukocytosis is neutrophilic leukocytosis.

Neutrophil leukocytosis.

Functional neutrophilic leukocytosis is observed for a short time and is not associated with symptoms of the disease (from several minutes to several hours). Eating is followed by stress.

True neutrophilic leukocytosis is an increase in neutrophil leukocytes for a long time (from several hours to several weeks).

True neutrophilic leukocytosis occurs in the following cases:

1. Inflammatory diseases of bacterial etiology.

2. Severe exogenous and endogenous intoxications.

3. Severe hemolysis.

4. Heavy bleeding.

5. Paraneoplastic inflammatory diseases.

There are the following types of neutrophilic leukocytosis:

1. Degenerative neutrophil leukocytosis.

Neutrophils with dystrophic changes with segmented nuclei and rod nuclei increase in the blood.

2. Regenerative neutrophil leukocytosis.

Neutrophils with segmented nuclei and rod nuclei increase in the blood, and myelocytes, metamyelocytes appear (leftward shift of the leukocyte formula).

Eosinophilic leukocytosis.

Eosinophilic leukocytosis (eosinophilia) is an absolute increase in the number of eosinophils in the blood. Eosinophilia occurs in the following cases:

1. In allergic reactions.

2. Worm infestations.

3. Immunopathological diseases (rheumatoid arthritis, Crohn's disease, nonspecific ulcerative colitis, etc.

4. Hemoblastosis and other neoplasias (chronic myeloid leukemia, lymphogranulomatosis, lymphomas, etc.).

5. Lung eosinophilic infiltrates, bronchial asthma.

6. Quincke's angioneurotic tumor.

7. Dermatoses.

8. After vaccination, etc.

Basophilic leukocytosis.

Basophilic leukocytosis (basophilia) is an absolute increase in the number of basophils in the blood. Basophilia occurs in the following cases:

1. In allergic reactions.

2. Worm infestations.

3. Immunopathological diseases (rheumatoid arthritis, Crohn's disease, nonspecific ulcerative colitis, etc.

4. Hemoblastosis and other neoplasias (chronic myeloid leukemia, lymphogranulomatosis, lymphomas, etc.).

5. Autoimmune endocrinopathies (thyroiditis, myxedema).

6. Pregnancy.

Lymphocytic leukocytosis.

Lymphocytic leukocytosis (lymphocytosis) is an absolute increase in the number of lymphocytes in the blood. Lymphocytic leukocytosis occurs in the following cases:

1. Viral infections (influenza, parainfluenza, pertussis, viral hepatitis, infectious mononucleosis, etc.).

2. Special infections (tuberculosis, sarcoidosis, wounds).

Monocytic leukocytosis.

Monocytic leukocytosis (monocytosis) is an increase in the absolute number of monocytes. Monocytosis occurs in the following cases:

1. Chronic infectious and inflammatory diseases (infectious mononucleosis, tuberculosis, brucellosis, wounds, salmonellosis, listeriosis).

2. Simple animal invasion (toxoplasmosis, amebiasis, leishmaniasis).

3. Septic endocarditis, septic condition.

4. Viral infections.

5. Period of recovery from infection.

6. Malaria.

7. Immunopathological diseases (rheumatoid arthritis, nonspecific ulcerative colitis, autoimmune thyroiditis).

8. Neoplastic diseases (acute and chronic leukemias, tumors of poor quality, etc.).

9. Typhoid fever.

10. Heavy intoxications.

Leukemic reactions.

Leukemic reactions are a protective reaction of the body and a pathological process characterized by the release of immature blood cells. Leukemia should be differentiated from leukemic reactions due to the release of immature blood cells.

There are the following types of leukemic reactions:

1. Lymphocyte.

2. Monocytic.

3. Myeloid.

a. Neutrophil.

b. Eosinophil.

c. Basophil.

Myeloid leukemic reaction.

Myeloid leukemia reaction is characterized by:

1. Strong leukocytosis.

2. Appearance of metamyelocytes, myelocytes, promyelocytes in the blood.

3. Bone marrow granulocytic cells - metamyelocyte, myelocyte, promyelocyte increase in the myelogram.

Myeloid leukemia reaction occurs in the following cases:

1. Acute inflammatory diseases of bacterial etiology.

2. Purulent processes.

3. Osteomyelitis.

4. Septic conditions.

5. Severe exogenous and endogenous intoxications (uremia, diabetic ketoacidosis, coma).

6. Rheumatism.

7. Severe hemolysis.

8. Tissue breakdown and necrosis (myocardial infarction).

9. Food toxicoinfections.

10. Use of high doses of steroid hormones, cytostatics, insulin.

11. Heavy bleeding.

12. Neoplastic diseases (poor quality tumors).

Leukemic reactions of the myeloid type are differentially diagnosed with chronic myeloid leukemia (Appendix 3).

Lymphocytic leukemic reactions.

There are the following types of lymphocytic leukemic reactions:

1. Infectious lymphocytosis:

- Viral infections (influenza, parainfluenza, pertussis, viral hepatitis, infectious mononucleosis, etc.).

- Special infections (tuberculosis, sarcoidosis, wounds).

- Bacterial infections (whooping cough, tuberculosis, etc.).

- Simple animal invasion (toxoplasmosis, malaria).

2. Acute lymphocytosis:

- Cardiovascular failure (acute heart failure, myocardial infarction, septic shock).

- Drug-induced lymphocytosis.

- Allergic reactions.

- After major surgery.

- After an epileptic seizure.

- Severe injuries.

3. Chronic lymphocytosis:

- Systemic connective tissue diseases (rheumatoid arthritis).

- Tumors.

- Chronic inflammatory diseases.

- Smoking.

Differential diagnosis of chronic lymphocytic leukemia with a lymphocytic myeloid reaction is carried out (Appendix 4).

Eosinophilic leukemic reaction.

Eosinophilic leukemic reaction is characterized by an increase in the amount of eosinophils in the blood by more than 20% and the appearance of eosinophilic metamyelocytes, myelocytes, and promyelocytes.

Eosinophilic leukemic reaction occurs in the following pathologies:

1. In allergic reactions.

2. Worm infestations.

3. Immunopathological diseases (rheumatoid arthritis, Crohn's disease, nonspecific ulcerative colitis, etc.).

4. Hemoblastosis and other neoplasias (chronic myeloid leukemia, lymphogranulomatosis, lymphomas, etc.).

5. Lung eosinophilic infiltrates, bronchial asthma.

6. Quincke's angioneurotic tumor.

7. Dermatoses.

8. After vaccination, etc.

Eosinophilic leukemic reaction is differentially diagnosed with chronic myeloid leukemia. For this, 100 eosinophilic cells are counted. If eosinophils with rod and segment nuclei predominate in the eosinophilogram, an eosinophilic leukemic reaction is considered. Eosinophilic metamyelocytes, myelocytes, and promyelocytes predominate in the eosinophilogram in chronic myeloid leukemia.

Monocytic leukemic reaction.

The etiological factors of monocytic leukemic reaction and monocytosis are the same. Monocytic leukemic reaction is differentially diagnosed with chronic monocytic leukemia (Appendix 5).

Secondary erythrocytosis.

Secondary erythrocytosis is an increase in the absolute number of erythrocytes.

Secondary erythrocytosis develops in the following cases:

1. Increased erythropoietin in kidney diseases.

2. Pulmonary purulent inflammatory diseases.

3. Pulmonary heart failure.

4. Congenital heart defects.

5. Randy-Osler syndrome.

6. Vascular and liver tumor diseases.

Secondary erythrocytosis should be differentially diagnosed with erythremia (true polycythemia) (Appendix 6).

Reactive thrombocytosis.

Reactive thrombocytosis is an absolute increase in the number of platelets.

Reactive thrombocytosis is observed in the following cases:

1. Chronic inflammatory diseases.

2. Hemolytic anemias.

3. After splenectomy.

4. In oncopathology.

5. When heavy bleeding.

6. After burning.

7. After the operation.

8. When treated with corticosteroids.

9. Immunopathological diseases (rheumatoid arthritis, Crohn's disease, nonspecific ulcerative colitis, etc.).

Reactive thrombocytosis should be differentially compared with essential thrombocythemia (Appendix 7).

Review Questions:

1. Neutrophil leukocytosis.

2. Eosinophilic leukocytosis.

3. Basophilic leukocytosis.

4. Lymphocytic leukocytosis.

5. Monocytic leukocytosis.

6. Leukemoid reaction of myeloid type.

7. Lymphocytic type leukemoid reaction.

8. Leukemic reaction of eosinophilic type.

9. Leukemoid reaction of monocytic type.

10. Secondary erythrocytosis and reactive thrombocytosis.

CHAPTER 4. ANALYTICAL PART

4.1. TESTS

1. CYTOLOGY BU

1) tissue science

2) the science that studies the cell

3) a science that studies a person

4) department of anatomy

2. TEST MATERIALS FOR CYTOLOGY

1) Urine

2) Sputum

3) puncture material

4) all are correct

3. INCLUDES TUMOR SCREENING

1) mass examination to clarify the diagnosis

2) checking people who are not at risk

3) survey of a small population group

4) check family members

4. NECESSARY WHEN WORKING WITH STRONG ODOR MATERIALS

1) to chemically neutralize them

2) burn gas fuel

3) use of safety glasses, gloves and apron

4) open the window

5. MAIN OBJECTIVE OF CYTOLOGICAL EXAMINATION

1) to determine the inflammatory process

2) detection of atrophic changes

3) detection of low-quality tumors

4) all answers are correct

6. CYTOLOGICAL LABORATORY SUPPLY

1) microscope

2) hematological analyzer

3) flow cytofluorimeter

4) biochemical analyzer

7. STRUCTURAL AND FUNCTIONAL UNITY OF LIFE

1) cell

2) tissue

3) DNA

4) protein

8. AUTHORS OF CELL THEORY

1) Watson and Sreek

2) Schleiden and Schwann

3) Sharko and Leyden

4) There is no correct answer

9. FORM THE CELL SURFACE

1) cytoplasm

2) plasmolemma

3) cytoskeleton

4) ribosomes

10. PROGRAMMED CELL DEATH

1) necrosis

2) dystrophy

3) apoptosis

4) atrophy

11. ENTERS THE INFLAMMATION STAGE

1) alteration

2) transudation

3) differentiation

4) dystrophy

12. ENTERS THE EPITHELIUM OF THE BLADDER WALL

1) transitional epithelium

2) multilayered squamous epithelium

3) multilayered squamous epithelium

4) single-layered squamous epithelium

13. EPITHELIUM COVERING TRACHEA AND BRONCHUS

1) passing

2) cubical

3) swinging cylindrical

4) multilayered squamous epithelium

14. DANGER SIGN IN CYTOLOGICAL PREPARATION

1) cellular and tissue polymorphism

2) symmetrical arrangement of cells

3) the color of the drug should be pale

4) few elements in the preparation

15. DISORDER OF DIFFERENTIATION IN PRE-CANCER

1) dystrophy

2) atrophy

3) hypertrophy

4) dysplasia

16. MUST HAVE QUALITY LUBRICANT

1) thick

2) as thin as possible

3) accumulated

4) wavy

17. THE BEST FIXATOR

1) ethyl alcohol

2) acetone

3) diethyl ether

4) methyl alcohol

18. CUTTING OF PATIENT TISSUE FOR DIAGNOSTIC PURPOSES

1) shredding

2) biopsy

3) exfoliation

4) puncture with a thin needle

19. TYPE OF BIOPSY OF MATERIAL REMOVAL

1) aspiration biopsy

2) scarification biopsy

3) operative biopsy

4) puncture biopsy

20. MOST USED FOR STAINING HEMATOLOGICAL PREPARATIONS

1) Papanicolaou

2) Romanovsky-Gimza

3) Leishman

4) May-Grunwald

21. ENDOCERVIX MUCOUS FLOOR COVERED

1) single-layered squamous epithelium

2) cuboidal epithelium

3) cylindrical epithelium

4) multilayered squamous epithelium

22. EXOTCERVIX IS COVERED BY THE MUCOUS FLOOR

1) single-layered squamous epithelium

2) cuboidal epithelium

3) cylindrical epithelium

4) multilayered squamous epithelium

23. OBSERVED IN THE BONE Marrow AS A RESULT OF RADIATION

1) rich cellular content

2) strong cellular polymorphism

3) low number of cells

4) abundance of reticular tissue

24. INCLUDES AGRANULOCYTES

1) basophils

2) neutrophils

3) monocytes

4) eosinophils

25. T-LYMPHOCYTES UNDERGO DIFFERENTIATION DEPENDING ON ANTIGEN

1) divorce

2) red bone marrow

3) thymus

4) Peyer's nodes

26. CHARACTERISTIC OF LEUKEMIC DISEASE

1) acute leukemia

2) chronic leukemia

3) leukopenia

4) leukocytosis

4.2. SITUATION ISSUES

Situational issue #1

Parameters	Results	Unity
Hemoglobin	70	г/л
Erythrocyte	2,7	$x10^{12}$/л
Color indicator	0,77	
Platelet	186	$x10^{9}$/л
Leukocyte	6,8	$x10^{9}$/л
Neutrophil with a rod nucleus	4	%

Neutrophil with a segmented nucleus	69	%
	Eosinophil 2	%
	Basophil 1	%
	Monocyte 4	%
Lymphocyte	20	mm/hour
Erythrocyte sedimentation rate	20	
Morphology of erythrocytes	microcytosis++, hypochromia++, poikilocytosis+	

Questions: 1. Are there changes in the analysis?

2. Your presumptive diagnosis?

3. Your inspection plan?

Situational issue #2

Parameters	**Results**	**Unity**
Hemoglobin	95	г/л
Erythrocyte	3,4	$x10^{12}$/л
Color indicator	0,84	
Platelet	235	$x10^{9}$/л
Leukocyte	6	$x10^{9}$/л
Neutrophil with a rod nucleus	3	%
Neutrophil with a segmented nucleus	77	%
Eosinophil	1	%
Basophil	-	%
Monocyte	4	%
Lymphocyte	16	%
Erythrocyte sedimentation rate	10	mm/hour

Morphology of erythrocytes	microcytosis++, hypochromia++, poikilocytosis+

Questions: 1. Are there changes in the analysis?

2. Your presumptive diagnosis?

3. Your inspection plan?

Situational issue #3

Parameters	Results	Unity
Hemoglobin	40	г/л
Erythrocyte	1,8	$x10^{12}$/л
Color indicator	0,66	
Platelet	388	$x10^{9}$/л
Leukocyte	10,5	$x10^{9}$/л
Neutrophil with a rod nucleus	5	%
Neutrophil with a segmented nucleus	68	%
Eosinophil	2	%
Basophil	-	%
Monocyte	4	%
Lymphocyte	21	%
Erythrocyte sedimentation rate		mm/hour
Morphology of erythrocytes	microcytosis++, hypochromia++, poikilocytosis+	

Questions: 1. Are there changes in the analysis?

2. Your presumptive diagnosis?

3. Your inspection plan?

Situational issue #4

Parameters	Results	Unity

Hemoglobin	40	г/л
Erythrocyte		$x10^{12}$/л
1’4		
Color indicator	0’86	
Platelet		$x10^{9}$/л
50		$x10^{9}$/л
Leukocyte	1’8	%
Neutrophil with a rod nucleus	4	%
Neutrophil with a segmented nucleus	10	%
	Eosinophil	%
	_Basophil	%
	-	%
	Monocyte	mm/hour
10	Lymphocyte	
	76	
Erythrocyte sedimentation rate	62	

Questions: 1. Are there changes in the analysis?

2. Your presumptive diagnosis?

3. Your inspection plan?

Situational issue #5

Parameters	**Results**	**Unity**
Hemoglobin	60	г/л
Erythrocyte	2,2	$x10^{12}$/л
Color indicator	0,82	
Platelet	50	$x10^{9}$/л
Leukocyte	2,4	$x10^{9}$/л
Neutrophil with a rod nucleus	2	%
Neutrophil with a segmented nucleus	30	%
Eosinophil	-	

%

	Basophil _Monocyte	% %
	2	%
Lymphocyte	66	
Erythrocyte sedimentation rate	45	mm/hour

Questions: 1. Are there changes in the analysis?

2. Your presumptive diagnosis?

3. Your inspection plan?

Situational issue #6

Parameters	**Results**	**Unity**
Hemoglobin	40	г/л
Erythrocyte	1,3	$x10^{12}$/л
Color indicator	0,92	
Platelet	6	$x10^{9}$/л
Leukocyte	280	$x10^{9}$/л
Neutrophil with a rod nucleus	26	%
Neutrophil with a segmented nucleus	15	%
Eosinophil	14	%
Basophil	22	%
Monocyte	8	%
Lymphocyte	5	%
Erythrocyte sedimentation rate	66	mm/hour

Questions: 1. Are there changes in the analysis?

2. Your presumptive diagnosis?

3. Your inspection plan?

Situational issue #7

Parameters	Results	Unity
Hemoglobin	131	г/л
Erythrocyte	4,3	$x10^{12}$/л
Color indicator	0,91	
Platelet	188	$x10^{9}$/л
Leukocyte	21,9	$x10^{9}$/л
Neutrophil with a rod nucleus	3	%
Neutrophil with a segmented nucleus	8	%
Eosinophil	12	%
Basophil	18	%
Monocyte	30	%
Lymphocyte	2	%
Erythrocyte sedimentation rate	28	mm/hour

Questions: 1. Are there changes in the analysis?

2. Your presumptive diagnosis?

3. Your inspection plan?

Situational issue #8

Parameters	Results	Unity
Hemoglobin	122	г/л
Erythrocyte	4,0	$x10^{12}$/л
Color indicator	0,91	
Platelet	187	$x10^{9}$/л
Leukocyte	42,3	$x10^{9}$/л
Neutrophil with a rod nucleus	2	%
Neutrophil with a segmented nucleus	16	%

Eosinophil	60	%
Basophil		%
8		%
Monocyte	2	%
Lymphocyte		mm/hour
12		
Erythrocyte sedimentation rate	35	

Questions: 1. Are there changes in the analysis?

2. Your presumptive diagnosis?

3. Your inspection plan?

Situational issue #9

Parameters	**Results**	**Unity**
Hemoglobin	114	г/л
Erythrocyte	3,8	$x10^{12}$/л
Color indicator	0,9	
Platelet	234	$x10^{9}$/л
Leukocyte	30	$x10^{9}$/л
Neutrophil with a rod nucleus	1	%
Neutrophil with a segmented nucleus	14	%
Eosinophil	1	%
Basophil	-	%
Monocyte	2	%
Lymphocyte	82	%
Erythrocyte sedimentation rate	36	mm/hour

Questions: 1. Are there changes in the analysis?

2. Your presumptive diagnosis?

3. Your inspection plan?

Situational issue #10

Parameters	Results	Unity
Hemoglobin	76	г/л
Erythrocyte	2,4	$x10^{12}$/л
Color indicator	0,95	
Platelet	35	$x10^{9}$/л
Leukocyte	48	$x10^{9}$/л
Neutrophil with a rod nucleus	69	%
Neutrophil with a segmented nucleus	1	%
Eosinophil	14	%
Basophil	-	%
Monocyte	-	%
Lymphocyte	1	%
Erythrocyte sedimentation rate	75	mm/hour

Questions: 1. Are there changes in the analysis?

2. Your presumptive diagnosis?

3. Your inspection plan?

4.3. APPLICATIONS

Appendix 1

Cytological classification of cervical pathology

US BETESDA terminology Russian Russian terminology	US BETESDA terminology terminology
Normal cytogram Normal cytogram	Normal cytogram Normal cytogram
Reactive Changes: - intrauterine spiral - infections - atrophy radiation	Epithelial degenerative, reparative changes, inflammatory atypia, squamous cell metaplasia, hyperkeratosis, parakeratosis, atrophy, - etc.
Epithelial pathological changes ASCUS (atypical squamous cells of undetermined significance) is a suspicious change of flat epithelium that cannot be differentiated from reactive or precancerous processes.	Detection of superficial and interstitial cells with dyskaryotic, enlarged, hyperchromic nuclei - superficial and intermediate cells with slight dyskaryosis
LSIL (low-grade squamous intraepitelial lesion) – slow intraepithelial changes associated ith apil oma v r s ama e w p l i u d g	with the ability of cell differentiation is preserved - koilocytic, condylomatous atypia - atypical basal cells occupy 2/3 of the epithelial layer
HSIL (High -grade squamous intraepitelial lesion) severe intraepithelial changes	- cell differentiation ability is impaired - atypical surface, intermediate and parabasal cells are identified - almost all epithelial layers consist of atypical cells
Pак in situ (CIS – carsinoma in situ)	- the integrity of the basement membrane is preserved - the ability of cells to differentiate is almost lost - strongly dyskaryotic cells - changed cells are located as plastids, syncytium. - strong polymorphism of cells
Invasive cancer: - Squamous cell cancer - Adenocarcinoma **Poor quality cancer metastases**	- the integrity of the basement membrane is broken - syncytial bundles of cells with rough chromatin

Appendix 2

Cytological differentiation of anemias

Types of animias deficiency	Iron deficiency anemia	Vitamin V12 deficiency anemia	Acute posthemorrhagic anemia	Hemolytic anemia	Aplastic anemia
Size of red blood cells	Microcytosis	macrocytosis, megalocytosis	normocytosis	normocytosis, microspherocytosis	normocytosis
Erythrocyte form	Poikilocytosis	poikilocytosis	normocytosis	Microspherocytosis, ovalocytosis, acanthocytosis, stomatocytosis, sickle cell, kodocytosis	normocytosis
Erythrocyte staining	Hypochromic	hyperchrome, polychromophile	normochromic	normochromic, hypochromic in thalassemia, hyperchromic in microspherocytosis	normochromic
Reticulocyte	decreases	decreases, increases severely	It will increase after 4-5 days	increases	decreases
Leukocyte	normally	hypersegmentation of myelocytes and metamyelocytes, neutrophils	normally	in a hemolytic crisis, leukocytes increase, myelocytes and metamyelocytes appear	decreases

Platelet	normally	decreases, macroplastins	normally	normally	decreases
Specific symptoms		Formation of Jolly bodies, Cabot rings, megaloblast	After 4-5 days, the appearance of nucleated erythrocytes -normocytes	formation of nucleated erythrocytes - normocytes	relative lymphocytosis
Myelogram	erythroid row hyperplasia	megaloblast type blood formation	the norm	erythroid row hyperplasia	all cell lines are drastically reduced

Appendix 3

Myeloid leukemoid reaction and chronic myeloid leukemia cytological differentiation

Cytological index	**Myeloid-type leukemic reaction**	**Chronic myeloid leukemia**
Myelocytosis is the obvious cause	Available	Not available
Metamyelocyte, myelocyte and promyelocyte in blood	Available	Available
Normochromic anemia	Not available	Available
Platelets	Normally	Thrombocytosis in 40%, thrombocytopenia in 30%
Leukocytes	Leukocytosis	Hyperleukocytosis

Blasters	10-100x109/l	50-1000x109/l
Neutrophils with rod nuclei	Not available	Available
Neutrophils with segmented nuclei	Increased	Increased
Eosinophil-basophil association	Increased	Decreased
Toxogenic granulation	No	There is
Cell atypia	There is	No
Bone marrow myeloid hyperplasia	Undetectable	To be determined
Philadelphia chromosome in blood cells	Undetectable	To be determined
Against the background of antibacterial therapy	Undetectable	To be determined

Appendix 4

Lymphoid leukemic reaction and chronic lymphocytic leukemia cytological differentiation

Cytological index	**Leukemic reaction of the lymphoid type**	**Chronic lymphocytic leukemia**
Lymphocytosis is the obvious cause	Available	Not available

Absolute lymphocytosis	Available	Available
Normochromic anemia	Not available	Available
Platelets	Normally	Thrombocytopenia
Leukocytes	Leukocytosis	Hyperleukocytosis
Blasters	10-100x109/l	50-600x109/l
The appearance of prolymphocytes in the blood	Not available	Available
Neutrophils with rod and segment nuclei	There is	There is
Riedel cells	Decreased	Decreased
Botkin-Gumprecht shades	Undetectable	To be determined
Cell atypia	Undetectable	To be determined
Bone marrow lymphocytic hyperplasia	Undetectable	To be determined
In the background of the treatment of the underlying disease	Undetectable	To be determined

Appendix 5

Monocytic leukemic reaction and chronic monocytic leukemia cytological differentiation

Cytological index	Monocytic leukemic reaction	Chronic monocytic leukemia
The obvious cause of monocytosis	Available	Not available
Absolute monocytosis	Available	Available
Normochromic anemia	Not available	Available
Platelets	Normally	Thrombocytopenia
Leukocytes	Leukocytosis	Hyperleukocytosis
Blasters	10-100x109/l	50-600x109/l
Appearance of promonocytes in the blood	Not available	Available
Neutrophils with rod and segment nuclei	There is	There is
Cell atypia	Decreased	Decreased
Bone marrow monocytic hyperplasia	Undetectable	To be determined
In the background of background disease therapy	Undetectable	To be determined

Appendix 6

Secondary erythrocytosis and true polycythemia cytological differentiation

Cytological index	Secondary erythrocytosis	Polycythemia vera
Erythrocytosis is the exact cause	Available	Not available
Absolute erythrocytosis	Available	Available
Hematocrit	Available above 52%	above 52%

Platelets	Normally	Thrombocytosis
Leukocytes	Normally	Leukocytosis
Myelocytes, metamyelocytes and promyelocytes in blood	Not available	10-100x109/l
Blasters	Not available	Available
Three-cell hyperplasia of the bone marrow	Undetectable	Available
Erythrocyte sedimentation rate	Increased	To be determined
Blood viscosity	Normally	Decreased to 5.0-10 mm/h
Background disease therapy	Changes in the blood completely disappear	increased 5-6 times

Reactive thrombocytosis and essential thrombocythemia

cytological differentiation

Cytological index	**Reactive thrombocytosis**	**Essential thrombocythemia**
Thrombocytosis is the obvious cause	Available	Not available
Absolute thrombocytosis	Available	Available
Leukocytes	Normally	Leukocytosis
Bone marrow megakaryocytic hyperplasia	Undetectable	10-50x109/l
In the background of background disease therapy	Changes in the blood completely disappear	To be determined

REFERENCES

1. Архипова Т.В., Коничев В.С., Стволинская Н.С. Руководство к практическим занятиям по цитологии: методическое пособие. – М.:Прометей, 2014. – 56 с.

2. Банин В.В. Цитология. Функциональная ультраструктура клетки: учебное пособие. – «ГЭОТАР-Медиа», 2016. – 264 с.

3. Бойчук Н.В., Быков В., Юшканцева С. Гистология. Эмбриология. Цитология. Атлас: атлас. "ГЭОТАР-Медиа", 2015. – 296 с.

4. Борхунова Е. Цитология и общая гистология. Методика изучения препаратов: учебно-методическое пособие. – «Лань Спб», 2017. – 144 с.

5. Гилл Г. Клиническая цитология. Теория и практика цитотехнологии: учебное пособие. «Практическая Медицина», 2015. – 408 с.

6. Загороднева Е. А., Вахания К. П. и др. Введение в цитологическую диагностику: учебно-методическое пособие. Волгоград: Изд-во ВолгГМУ, 2014. – 204 с.

7. Иноятова Ф.Х., Бабаджанова Ш.А., Курбанова Н.Н., Курбанова З.Ч. Гемостаз: основные принципы функционирования, методы оценки, патофизиологические аспекты: методическое пособие. –Ташкент, 2014. –46с.

8. Курбонова З.Ч., Бабаджанова Ш.А. Цитологик ташхисга кириш: ўқув қўлланма. Тошкент, 2022. 137 б.

9. Курбонова З.Ч., Бабаджанова Ш.А. Диагностика и лечение приобретенной тромбоцитопатии: методические рекомендации. – Ташкент, 2018. – 21 с.

10. Курбонова З.Ч., Бабаджанова Ш.А. Цитологик ташхисга кириш: электрон ўқув қўлланма. 2022, 146 б.

11. Курбонова З.Ч., Бабаджанова Ш.А. Лаборатория иши: ўқув қўлланма. 2023, 150 б.

12. Курбонова З.Ч., Бабаджанова Ш.А. Лаборатория иши: электрон ўқув қўлланма. 2023, 150 б.

13. Курбонова З.Ч., Сайфутдинова З.А. Лаборатор текширувлар учун материал олиш коидалари: ўқув қўлланма. Тошкент, 2023.

14. Курбонова З.Ч., Сайфутдинова З.А. Лаборатор текширувлар учун материал олиш коидалари: электрон ўқув қўлланма. Тошкент, 2023

15. Курбонова З.Ч., Сайфутдинова З.А. Клиник лаборатор таҳлиллар учун биологик материал олиш қоидалари: ўқув - услубий қўлланма. Тошкент, 2023.

16. Луговская С.А., Почтарь М.Е. Гематологический атлас. 4 издание, дополненное: атлас. - Москва-Тверь: ООО «Издательство «Триада». 2016. - 434 с. 1993 ил.

17. Меньшикова М.В., Долгих О.В., Агафонов Ю.В., Зашихин А.Л. Цитология: учебное пособие к практическим занятиям. Архангельск: Изд. Северного государственного медицинского университета, 2016.–136 с.

18. Найяр Р., Уилбур Д. Цервикальная цитология по системе Бетесда. Терминология, критерии и пояснения: учебное пособие. «Практическая медицина», 2017. – 304 с.

19. Николаева О.В., Кучерявченко М.А., Шутова Н.А. и др. Патофизиология системы крови. Часть 2. Нарушения в системе лейкоцитов: учебное пособие. Харьков: «Типография Мадрид», 2016. – 128 с.

20. Полонская Н.Ю. Цитологическое исследование цервикальных мазков. Пап-тест: учебное пособие. «ГЭОТАР-Медиа», 2016. – 168 с.

21. Полонская Н.Ю.и др. Профилактические осмотры и цитологический скрининг шейки матки: учебное пособие. М.: Издательский центр «Академия», 2008. – 80 с. цв. ил.

22. Протасова А.Э.и др. Дисплазия шейки матки – этиопатогенез, диагностика, оптимальная тактика лечения: учебное пособие. СПб.: 2014. – 22 с.

23. Стволинская Н.С. Цитология: учебник для бакалавров по направлению подготовки «Педагогическое образование и Биология». Прометей; Москва; 2012.-55 с.

24. Стемпень Т.П., Лелевич С.В. Клиническая лабораторная гематология: учебное пособие. - Гродно : ГрГМУ, 2016 - 232 с.

25. Титмушш Э. Шейка матки. Цитологический атлас: атлас. «Практическая медицина», 2015. – 256 с.

26. Шабалова И.П., Полонская Н.Ю. Основы клинической цитологической диагностики: учеб. пособие. М. : ГЭОТАР - Медиа, 2010. – 144 с.: ил.

27. Цаценко Л. Цитология: учебное пособие /. – «Феникс», 2009. – 185 с.

28. Habbard J.D. A conSISe reviyew of clinical laboratory sciyence. 2nd ed. “Wolters Kluwer”, 2010. –408 p.

29. Babadjanova Sh.A., Курбонова З.Ч. Qon kasalliklari: o'quv qo'llanma. 2023, 156 b.

30. Kurbonova Z.Ch., Babadjanova Sh.A. Laboratoriya ishi: o‘quv qo‘llanma. Toshkent, 2022. 140 b.

31. Kurbonova Z.Ch., Babadjanova Sh.A. Laboratoriya ishi: elektron o‘quv qo‘llanma. Toshkent, 2022. 176 b.

32. Kurbonova Z.Ch., Babadjanova S.A. Sitologik tashxisga kirish: o‘quv qo‘llanma. Toshkent, “Hilol nashr”, 2021. 152 b.

33. Kurbonova Z.Ch., Nuriddinova N.F. Najas klinik laborator tahlili, gelmintozlar: o‘quv – uslubiy qo‘llanma. Toshkent, 2022. 34 b.

34. Kurbonova Z.Ch., Babadjanova Sh.A. Sitologik tashxis asoslari: o‘quv – uslubiy qo‘llanma. Toshkent, 2022. 47 b.

35. Kurbonova Z.Ch., Babadjanova Sh.A. Sitologik diagnostika asoslari: o‘quv – uslubiy qo‘llanma. Toshkent, 2022. 47 b.

36. Kurbonova Z.Ch., Sayfutdinova Z.A. Klinik laborator diagnostika fanidan testlar to‘plami: o‘quv – uslubiy qo‘llanma. Toshkent, 2022. 86 b.

37. Kurbonova Z.Ch., Babadjanova Sh.A., Saidov A.B. Gematologik kasalliklar sitologik diagnostikasi: o‘quv uslubiy qo‘llanma. Toshkent, 2021. – 56 b.

38. Kurbonova Z.Ch. Rak oldi xolatlari, yaxshi va yomon sifatli o'smalar sitologik diagnostikasi: o‘quv-uslubiy qo‘llanma. Toshkent, 2021. 50 b.

39. Kurbonova Z.Ch., Babadjanova Sh.A.“Sitologik tashxisga kirish” DGU 2022, Патент № 16152. Талабнома № 2022 1896.

40. Kurbonova Z.Ch., Sayfutdinova Z.A. Laborator tekshirish uchun material olish qoidalari: o‘quv qo‘llanma. Toshkent, 2023.

41. Kurbonova Z.Ch., Sayfutdinova Z.A. Laborator tekshirish uchun material olish qoidalari: elektron o‘quv qo‘llanma. Toshkent, 2023.

42. Kurbonova Z.Ch., Babadjanova Sh.A., Sayfutdinova Z.A. Laboratory work: study guide. Tashkent, 2023.

43. Kurbonova Z.Ch., Babadjanova Sh.A., Sayfutdinova Z.A. Laboratory work: electronic study guides. Tashkent, 2023.

44. Kurbonova Z.Ch., Babadjanova Sh.A., Sayfutdinova Z.A. Introduction to cytological diagnostics: study guide. Tashkent, 2023.

45. Kurbonova Z.Ch., Sayfutdinova Z.A. Klinik laborator tahlillar uchun biologik material olish qoidalari: o‘quv - uslubiy qo‘llanma. Toshkent, 2023.

46. Kurbonova Z.Ch., Sayfutdinova Z.A. Peshobning klinik laborator tahlili: o‘quv – uslubiy qo‘llanma. Toshkent, 2022. 49 b.

47. Laposata M. Laboratory Medicine: The Diagnosis of Disease in the Clinical Laboratory. 2nd ed. “Lange”, 2014. –513p.Lelevich S.V., Vorobiov V.V., Grynevich T.N. Clinical laboratory diagnostics: handbook. GrGMU, 2013. –100p.

48. Michayel T.S., Naveyena S. Cytopathology: an introduction: tutorial. – “Springer”, 2013. –486 p.

49. Shirlyn B. McKenziye, Lynne Williams. Clinical Laboratory Hematology, 3rd ed. – “Pearson education” (US), 2014. –1040 p.

50. Svante R.O., Gregory F.S. Fine neyedle. Aspiration cytology. 5th ed. “Elseviyer”, 2012. –494 p.