МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
ХАРКІВСЬКИЙ НАЦІОНАЛЬНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ

BIOPSY-AUTOPSY COURSE (CLINICAL PATHOLOGY)

Text-book for practical classes in clinical pathology for English medium medical students

Edited by I.V. Sorokina, V.D. Markovskiy

БІОПСІЙНО-СЕКЦІЙНИЙ КУРС (КЛІНІЧНА ПАТОЛОГІЯ)

Навчальний посібник для практичних занять з клінічної патології для англомовних студентів медичних ВНЗ

Під редакцією І.В. Сорокіної, В.Д. Марковського

Kharkiv
2012

УДК 616-091(075.8)
ББК 52.5я7
Б63

Затверджено вченою радою
Харківського національного медичного університету
Протокол № 1 від 19.01.2012

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Б63 Biopsy-autopsy course (Clinical pathology): [text-book for practical classes in clinical pathology for English medium medical students] / [I.V. Sorokina, V.D. Markovskiy, G.I. Gubina-Vakulik and other]; edited by I.V. Sorokina, V.D. Markovskiy. – Kharkiv: **изд-во**, 2012. – **…. p.**

The book contains the main materials in biopsy-autopsy course according to the syllabus approved by Central Methodological Office for Higher Education of The Ministry of Health of Ukraine. Text-book in Clinical Pathology for English medium medical students is published for the first time in Ukraine.

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Б63 Біопсійно-секційний курс (Клінічна патологія): [навчальний посібник для практичних занять з клінічної патології для англомовних студентів медичних ВНЗ] / [І.В. Сорокіна, В.Д. Марковський, Г.І. Губіна-Вакулик та ін.]; під ред. І.В. Сорокіної, В.Д. Марковського. – Харків: **изд-во**, 2012. – **…. с.**

У навчальному посібнику висвітлені основні питання з секційно-біопсійного курсу згідно з програмою, затвердженою Центральним методичним кабінетом з вищої освіти Міністерства охорони здоров'я України. Навчальний посібник з клінічної патології для англомовних студентів вперше видається в Україні.

УДК 616-091(075.8)
ББК 52.5я7

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PREFACE

It is pleasure to write this preface for the text-book in Biopsy-autopsy course for international students studying in Ukraine.

This text-book presents very useful information for every student of medical university about the role of pathoanatomical service and a pathologist; autopsies of corpses in hospitals; pathoanatomical diagnosis; international statistical classification of diseases; form, content and rules for filling the autopsy protocol, medical certificate of death, medical certificate of perinatal death; the role of biopsies in diagnosis of different diseases; significance of clinical-anatomical conference and medical-control commission; iatrogenic reactions and diseases; pathomorphosis etc.

This text-book is intended for English medium students of the faculties of general medicine, preventive medicine, pediatrics and dentistry and correspond the syllabus of biopsy-autopsy course approved by Central Methodological Office for Higher Education of the Ministry of Health of Ukraine.

We hope our students will be able to achieve good results in studying Biopsy-autopsy course and their work will be effective as well as enjoyable.

We are thankful to Irina Korneyko, PhD, Head of foreign language department of Kharkiv National Medical University for giving cooperation and copyread in bringing out this book. We are thankful to our colleagues for giving constant support and assistance.

INTRODUCTION TO PATHOLOGY

Pathology is the foundation of medical practice. Without pathology the practice of medicine would still rely on myths and folklore.

Pathology is the scientific study of disease. It constitutes a large body of scientific knowledge and investigative methods essential for understanding disease and for effective medical practice. Pathology embraces the functional and structural changes in disease from the molecular level to the effects on the individual.

Clinical medicine is based on a longitudinal approach to a patient's illness – the patient's history, the examination and investigation, the diagnosis, treatment. Clinical pathology is more concerned with a cross-section analysis at the level of the disease itself, studied in depth: the cause and mechanisms of the disease and the effects of the disease upon the various organs and systems of the body. These two perspectives are complementary and inseparable: clinical medicine cannot be practiced without an understanding of pathology; pathology is meaningless if it is bereft of clinical implications.

Pathology has its own methods of investigation: autopsy (dissection), biopsy and experiment.

The pathologist is a physician who specializes in the diagnosis and management of human disease by laboratory methods. Fundamental to the discipline of pathology is the need to integrate clinical information with physiological, biochemical and molecular laboratory studies, together with observations of tissue alterations. Pathology has a special appeal to those who enjoy solving disease-related problems, using technologies based upon fundamental sciences ranging from biophysics to molecular genetics, as well as tools from the more traditional disciplines of anatomy, biochemistry, pharmacology, physiology and microbiology.

Pathologists function in three broad areas: as diagnosticians, as teachers and as investigators.

The pathologist in patient care. Pathologists participate in day-to-day care of patients by providing and interpreting laboratory information to help solve diagnostic problems and to monitor the effects of therapy. New tools are used to increase the precision of diagnoses, e.g. those utilizing monoclonal antibodies, molecular biology, image analysis and flow cytometry. Because of the expanding volume of new and highly complex tests, clinicians rely on the pathologist for guidance and direction in use of the clinical laboratory and interpretation of test results. The new field of molecular diagnosis is particularly rewarding, with techniques that permit identification of carriers of genetic disease, diagnosis of viral and bacterial infections, monitoring of cancer therapy, DNA fingerprinting for forensic (medico-legal) analysis and detection of cancer markers that assist in prognosis. For all pathologists, clinical, anatomic, molecular, investigators or researchers, better patient care is the ultimate goal. When unusual or unexpected abnormal results are identified and, particularly, when critical or life-threatening alterations are found, the pathologist communicates directly with the patient's physician.

Whenever tissue is removed from the body, it must be examined to determine the precise cause of the illness that prompted its removal. Microscopic analysis of tissue changes is the focus of anatomic pathology. The pathologist plays a central role in the diagnosis of surgically removed tissues, particularly when tumor is suspected, and works closely with surgeons and other physicians in such cases.

During surgery for suspected cancer, a pathologist is often asked to prepare a frozen section. A piece of tissue is removed during the operation, frozen, thinly sliced and prepared for rapid microscopic examination by the pathologist while the patient is still on the operating table. The preliminary diagnosis based on the frozen section guides the surgeon as to the next steps to take during surgery.

The clinical pathology specialty laboratories include hematology, microbiology, immunology, clinical chemistry (and toxicology), the blood bank (transfusion medicine), and laboratory data management. In these areas, the pathologist acts as a consultant to the clinician, defining appropriate tests and interpreting their results. Many of these tests solidify a clinical diagnosis. After diagnosis, many tests are performed repeatedly to assess progress of the disease and response to treatment.

In clinical hematology, for example, pathologists review all abnormal blood smears. They may also obtain bone marrow samples from patients. In examining the smears and microscopic sections from these sources, the pathologist may encounter problems as diverse as the identification of malarial parasites or other blood-borne organisms, investigation of causes of anemia, detection of disorders of coagulation and definitive diagnosis of malignant diseases such as leukemia.

In most hospital settings the pathologist is in charge of the blood bank and functions as an immunohematologist, who is in charge of procurement and processing of blood and blood products. The responsibilities include monitoring the use of blood within the hospital, tracing the causes of transfusion reactions, testing for determinants of tissue compatibility that permit bone marrow and other transplants, and serving as a consultant to plan appropriate therapy for a wide variety of conditions.

In clinical chemistry the pathologist supervises the technical staff in performance of tests to determine the concentration of organic and inorganic substances and medications in body fluids. For example, the level of glucose (sugar) in blood or urine is needed to diagnose diabetes and to monitor the daily insulin dosage. Toxicology is often a part of the clinical chemistry service, involving the pathologist in therapeutic drug monitoring and detection of illicit drugs and poisons. In cases of infection the microbiology laboratory identifies the offending organism and tests to discover which antimicrobials are capable of killing or arresting the growth of that particular agent (bacteria, viruses, parasites).

The tools of molecular biology are contributing to the recent rapid growth of new tests with both greater accuracy and precision in many of the above areas of laboratory medicine. Infectious agents can be identified by virtue of unique DNA sequences. Molecular identification of chromosomal rearrangements is used not only in diagnosis, but also in monitoring for the effectiveness of therapy and detection of

residual disease. Genetic alterations underlying heart diseases, iron metabolism defects and congenital abnormalities to name a few are appreciated to be far more common than was previously recognized. Prenatal screening is now available to detect hemoglobin disorders and many metabolic diseases. Genetic susceptibility to inherited cancer is another dynamic new testing area. For example, the advent of new treatments for certain breast cancers depends on identification of a gene that is amplified and over-expressed in those cancers; the gene amplification can be identified by molecular testing. The metabolism of many important medications can also be predicted by molecular techniques.

The pathologist as a consultant. The pathologist has long been considered the "doctor's doctor" consulted for interpretation of laboratory results, selection of diagnostic tests, monitoring the accuracy of surgical judgments and introduction of new diagnostic modalities. They serve on many committees important in hospital and medical management, continuing medical education and quality assessment. More recently, because of the range and complexity of diagnostic services, a role for the pathologist in explaining tests and their results directly to the patient has evolved. Pathologists have considerable experience with laboratory and hospital management. They are accustomed to thinking diagnostically across a broad spectrum of human disease. Their familiarity with issues of quality control and quality assurance also provides expertise in assessment of appropriate utilization of testing for the individual patient.

The pathologist as a teacher. Pathologists teach at the bedside, in the laboratory, over the microscope, in the lecture hall, in the classroom, in workshops and in seminars. They instruct medical students, residents in pathology and other clinical training programs, graduate students in basic science departments and students in related medical disciplines. They are also important in the continuing medical education of practicing physicians in both academic and community settings. The community-based pathologist has a unique perspective on patients from the viewpoint of each individual's cumulative laboratory data. This perspective is necessary for consultation on individual patients as well as for guidance on the applicability, interpretation and usefulness of both standard and specialized often newly available tests. In the academic setting, the pathologist may be the developer of new testing approaches, responding to perceived patient diagnostic or therapeutic problems. In all these environments, pathologists contribute substantially to teaching on the clinical services.

To teach well, one must continue to learn. Pathologists are committed to their own educational growth and regularly attend and contribute to programs at local, regional, national and international meetings, where new basic science findings, diagnostic applications and technology are presented.

The pathologist in research. The pathologist-investigator seeks new understanding of the basic nature of disease as a first step toward devising better ways to identify, control and prevent it. In many cases, the normal must be understood in order to define the abnormal. Pathologists have a unique advantage in biomedical

research because of their close ties to clinical medicine, their familiarity with laboratory technology and their recognition of and insight into the significance of diseased tissue changes. Pathologists engaged in research use the sophisticated technologies of modern molecular biology, biochemistry, immunology, cell biology and tissue pathology. These tools and methods include cell culture, biochemical analysis, electron microscopy, immunological and molecular genetic techniques, computer modeling and use of animal models. Understanding at the molecular level is particularly critical in defining normal biological mechanisms, so that the defects that lead to disease can be recognized.

Pathologists are uniquely prepared to investigate the causes and mechanisms of disease because of their experience in recognition of disease manifestations. Some examples of the range of problems under study have included tracing a newly recognized disease to its origin, or improving diagnostic approaches to well-known diseases, or identifying the genetic basis for response (or failure of response) to treatment.

The pathologist plays a key role in improving diagnoses through identifying new pathogenic bacteria, discovery of new infectious agents such as Hanta virus, and better application of modern methods of diagnosis. Pathologists have recognized new diseases produced by medications used to treat various illnesses.

Pathologists who used their understanding of pathologic processes to make significant contributions to medicine have garnered Nobel Prizes. For example, Nobel Laureate pathologists in the US have included Karl Landsteiner, (1930) the discoverer of the A, B, O blood groups, George Whipple, (1934) who, with Minot and Murphy, recognized that liver contained a substance necessary to prevent pernicious anemia, Thomas Weller, (1954) who developed methods for the growth of polio virus in tissue culture, Peyton Rous, (1966) the discoverer of tumor-inducing viruses, Baruj Benacerraf, (1980) who identified genetically determined structures on the cell surface that regulate immunological reactions, and J. Robin Warren, (2005) who with Barry J. Marshall, recognized that gastritis and gastric cancer are caused by infections with Helicobacter pylori.

In Ukraine ***pathoanatomical service*** is an integral part of preventive, diagnostic and therapeutic measures which are taken in health care institutions. Its further development is reflected in the order of the Ministry of Health of Ukraine No. 81 dated 12.05.1992 “On development and improvement of pathoanatomical service in Ukraine”.

Main objectives of pathoanatomical service of Ukraine:

1. Conducting with physician clinical anatomical analysis of autopsy results for the effective control of medical diagnostic work.

2. Developing new methods of intravital morphological diagnosis of pathological processes and diseases through investigation of biopsy and postoperative materials.

3. Improvement of physician’s skill in the process of discussion of autopsy results.

4. Diagnosis of dangerous infections.

5. Investigation of different problems of human pathology.

6. Control of treatment and diagnosis with the purpose of reducing the errors in diagnosis and treatment.

7. Organization of the clinical-anatomical conferences and participation in them.

The basis of pathoanatomical service are pathoanatomical department of a hospital, pathoanatomical bureau, department of pathology of higher medical educational institutions, specialized laboratories and departments of research institutes.

PATHOLOGICAL ANATOMY DIAGNOSIS

Diagnosis is medical conclusion regarding pathologic state of health of the person under examination, presence of disease (trauma) or the cause of death expressed in terms, provided by International Classification of Diseases (ICD), Traumas and Causes of Death. Making diagnosis is the final stage of the history taking, investigation of the clinical manifestations, laboratory investigations, macro- and microscopic morphology examination results analysis.

Morphological and clinical principles of making the diagnosis are similar. The diagnosis of the disease includes only a nosological form mentioned in the ICD. Pathological anatomy diagnosis consists of 4 compulsory components (parts): 1) basic (main) disease, 2) complication, 3) accompanying disease, 4) cause of death.

Basic (main) disease is disease or its complications causing the death of the patient. Only nosological form mentioned in the ICD must be present in clinical diagnosis as well as pathological anatomy one. It is impossible to use the names of symptoms and syndromes instead of clinical diagnosis, it is also impossible to name morphological signs of the disease instead of pathological anatomy diagnosis.

In the section of the main disease the stage of the disease, activity of the pathological process, clinical-anatomical form of the disease, location of the pathological process, histological variant of main pathological process, etiology of disease based on the results of bacteriological and virological investigations should be pointed out.

If a new acute disease develops within the period when the patient is in hospital, this disease is the main disease (e.g. acute appendicitis, acute pneumonia, acute myocardial infarction) and the previous diseases is regarded accompanying one.

Combined main disease. Frequently, there are two or more diseases simultaneously, which develop independently from each other or they are in the complicated pathogenic interrelation. Among these diseases it is impossible to choose only one main disease. These diseases may be concurrent, associative, background.

Concurrent diseases are two diseases diagnosed simultaneously, each disease may cause death.

Every of ***associative diseases*** is not deadly, but simultaneous development of these diseases is deadly.

Background disease is the disease which takes an important place in the pathogenesis of the main disease or it precondition severity of the main disease. In the ICD, combined main diseases are only in the section of IHD (Ischemic heart diseases) and nosological forms of vascular injury of the brain in hypertension disease. The physician should chose only one disease from several combined diseases in other cases.

Complications are pathological processes which are pathogenically connected with the main disease. Rarely, the etiology of these pathological processes differs from those of main disease (e.g. thromboembolism of pulmonary artery in thrombophlebitis).

Accompanying diseases are those not connected pathogenically with the main disease and not influencing the course of the main disease, e.g. chronic cholecystitis in

myocardial infarction, chronic and acute gastric ulcer in cerebral hemorrhage, etc.

Immediate causes of death are pathomorphological changes which result in unfavorable functional changes causing death (e.g. myocardial infarction, cerebral hemorrhage, cancer of stomach, etc.). Immediate cause of death differs from the mechanism of death. There are a lot of immediate causes of death, but there are only several mechanisms of death: cardiac, pulmonary and cerebral. Sometimes the mechanisms of death may be immediate causes of death (e.g. cardiac insufficiency in myocardial infarction). As a rule, immediate cause of death is a result of clinical-anatomical analysis. It bases on the clinical information about the patient (complaints, character of symptoms, technical and laboratory analysis, etc.) and pathological anatomy information (macroscopic, microscopic, etc.).

Clinical-anatomical analysis allows drawing a clinical-anatomical conclusion.

Comparison of clinical and pathological anatomy diagnoses is performed for improvement of professional skills of attending physicians and for gaining reliable statistical information.

The variants of comparison of clinical and pathological anatomy diagnosis are as follows:

1. Coincidence of main clinical and pathological anatomy diagnosis.
2. Difference of main clinical and pathological anatomy diagnosis. It may be:

a) in the nosological form (e.g. cirrhosis of liver instead of cancer of liver);

b) in the etiology (e.g. tuberculosis pneumonia instead of staphylococcus one);

c) in the location (e.g. cancer of intestine instead of cancer of stomach).

3. Difference of clinical and pathological anatomy diagnosis in complications, which changed the course of the disease or cause of death.
4. Difference of clinical and pathological anatomy diagnosis in important accompanying diseases.

All cases of differences of clinical and pathological anatomy diagnoses are divided into three categories.

Category 1. The disease was not recognized at the previous stages of treatment, and in the hospital, where the patient died, it was impossible to establish the correct diagnosis due to the severity of the condition of the patient, the prevalence of the process, short presence of patient in the hospital. This category includes patients with inoperable malignant tumors or widely spread metastases; patients with complex, difficult for diagnostics diseases in the terminal stage of the process (rheumatic diseases, nephrosclerosis and others).

Category 2. The disease was not recognized in the hospital, however the wrong diagnosis did not influence upon the mortal outcomes, whereas, patient has entered in the hospital in incurable condition (patient with several severe diseases with torpid course; patient in the terminal phase of chronic heart failure, hepatic insufficiency).

Category 3. The correct diagnosis was not made in the hospital and this affected the course of the disease, treatment and fatal outcome. In this category all urgent cases, requiting immediate radical medical help, are included: acute destructive appendicitis, pancreonecrosis, perforative gastric ulcer, incarcerated hernia, acute myocardial

infarction, insult of the brain, croupous pneumonia and other acute infections).

Causes of incorrect clinical diagnoses are divided in two groups: objective and subjective.

Objective causes:

– absence of the necessary information (case history);
– difficulties of the contact with the patient;
– short term of observation especially in neglected patients;
– severe illness with difficulties in diagnosis;
– impossibility of consultations;
– uncommon diseases with difficulties in diagnosis;
– atypical diseases with pronounced pathomorphosis.

Subjective causes:

– unskilled attending physician;
– absence of consultations although they were possible;
– making diagnosis using the results of instrumental and laboratory investigations;
– making diagnosis based on the opinion of the consultant.

Significance of incorrect clinical diagnosis:

1. Incorrect clinical diagnosis has no practical significance.
2. Practical significance is not considerable, it slightly burdens the patient's condition.
3. Practical significance of medium degree it prolongs the disease and burdens the patient's condition.
4. Practical significance of the highest degree it shortens the patient's life.

Difference of clinical and pathological anatomy diagnosis should not be considered in the following cases:

1. Background disease is not determined.
2. Hyperdiagnosis of concurrent, associative, background diseases, without damage to the patient due to treatment.
3. False diagnosis of location of the pathological processes in the nonspecialized departments of the hospital (e.g. myocardial infarction of the anterior part of the left ventricular wall instead of posterior one).

INTERNATIONAL STATISTICAL CLASSIFICATION OF DISEASES

The International Classification of Diseases (ICD) is an alphanumeric disease coding system developed by the World Health Organization (WHO) in 1993 year. The full name of the ICD-10 publication is the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision. ICD is the system of sections with definite nosological forms.

The purpose of ICD is establishment of preconditions for classified registration, analysis, interpretation, and comparison of information about disease incidence and death-rate obtained in different countries at different time.

ICD is international standard diagnostic classification for epidemiologic purpose and those connected with the management of health organization. ICD may be used for classification of diseases and other related health problems encountered in different documents devoted to the problems of health and natural movement of population.

The core of the ICD is a three-digit code used for compulsory coding of information about death as well as for performance of bases international comparison.

The importance and benefits of coding:

1. The quality and integrity of data is increasingly becoming important in the health care industry as health information management evolves from record management to data management. Worldwide coding systems form an essential part of the health information system.

2. Coding allows for easy storage and retrieval of information for patient care, research, planning, facility management etc.

3. Coding enables fair reimbursement for health care services and communicates in a predictable, consistent and reproducible manner.

4. Benefits provided by medical schemes can be appropriately managed with access to sound diagnostic data.

The structure of ICD has developed out of that proposed by William Farr in the early days of international discussions on classification structure. His scheme was that, for all practical, epidemiological purposes, statistical data on diseases should be grouped in the following way: epidemic diseases; constitutional or general diseases; local diseases classified according to the anatomical location; developmental diseases; injuries. This structure is seen in the classes of ICD.

ICD-10 consists of 3 volumes:

1. The most part of the first volume is devoted to the basic classification with the list of three-digit sections and four-digit subheadings. Besides, there are “Morphology of neoplasms”, “Special lists for cumulated statistical development” (4 special lists for cumulated statistical development are in the ICD: 1 and 2 lists are for general mortality, 3 and 4 are for infantile and baby mortality).There are definitions in this volume. They are used for simplification of international comparison.

2. Volume two provides guidance to users of the ICD.

3. Volume three is the alphabetical index as a guide to the classification (contained in volume 1) and has three main sections:

a) section one – an alphabetical index to diseases and nature of injury;

b) section two – the index of external causes of injury. These are not diagnoses but descriptions of the circumstances in which the violence occurred e.g. fire, assault, collision.

c) section three – the index of drugs and other substances. The introduction gives instructions on how to use it. These instructions should be read carefully before starting to code. The introduction to the index of volume 3 also provides important information about its relationship with volume 1.

ICD-10 has 22 classes, each of which is identified by a Roman numeral. Classes XIX (Injury, poisoning and certain other consequences of external causes) and XXI (Factors influencing health status and contact with health services) are not used for coding the underlying cause of death.

A letter is a first sign in the ICD. Each letter corresponds to certain classes. Letters D and H are exceptions from this rule. Letter D is used for class II "Neoplasms" and class III "Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism". Letter H is used in class VII "Diseases of the eye and adnexa" and class VIII "Diseases of the ear and mastoid process". Four classes (I, II, XIX, XX) more than one letter is used.

There is sufficient amount of three-digit codes for included material in each class. All codes of each section are not used for further revision of ICD and more deep specification.

There are following classes in the ICD:

Chapter	Title	Range of codes in whole chapters
I	Certain infectious and parasitic diseases	A00–B99
II	Neoplasms	C00–D48
III	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	D50–D89
IV	Endocrine, nutritional and metabolic diseases	E00–E90
V	Mental and behavioural disorders	F00–F99
VI	Diseases of the nervous system	G00–G99
VII	Diseases of the eye and adnexa	H00–H59
VIII	Diseases of the ear and mastoid process	H60–H95
IX	Diseases of the circulatory system	I00–I99
X	Diseases of the respiratory system	J00–J99
XI	Diseases of the digestive system	K00–K93
XII	Diseases of the skin and subcutaneous tissue	L00–L99
XIII	Diseases of the musculoskeletal system and connective tissue	M00–M99
XIV	Diseases of the genitourinary system	N00–N99
XV	Pregnancy, childbirth and the puerperium	O00–O99
XVI	Certain conditions originating in the perinatal period	P00–P96
XVII	Congenital malformations, deformations and chromosomal abnormalities	Q00–Q99
XVIII	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	R00–R99
XIX	Injury, poisoning and certain other consequences of external causes	S00–T99
XX	External causes of morbidity and mortality	V01–Y98
XXI	Factors influencing health status and contact with health services	Z00–Z99
XXII	Codes for special purposes	U00–U99*
**Only some categories in this chapter are used in mortality coding*		

The classes are divided into congenerical blocks of three-digit codes. For instance class IX “Diseases of the circulatory system” (I00–I99) contains the following three-digit codes:

I00–I02 Acute rheumatic fever
I05–I09 Chronic rheumatic heart diseases
I10–I15 Hypertensive diseases
I20–I25 Ischemic heart diseases
I26–I28 Pulmonary heart disease and diseases of pulmonary circulation
I30–I52 Other forms of heart disease
I60–I69 Cerebrovascular diseases
I70–I79 Diseases of arteries, arterioles and capillaries
I80–I89 Diseases of veins, lymphatic vessels and lymph nodes, not elsewhere classified
I95–I99 Other and unspecified disorders of the circulatory system

The majority of three-digit sections are divided into four-digit subheadings. For instance in class IX “Diseases of the circulatory system” (I00–I99), three-digit section I21 “Acute myocardial infarction” there are following four-digit subheadings:

I21.0 Acute transmural myocardial infarction of anterior wall
I21.1 Acute transmural myocardial infarction of inferior wall
I21.2 Acute transmural myocardial infarction of other sites
I21.3 Acute transmural myocardial infarction of unspecified site
I21.4 Acute subendocardial myocardial infarction
I21.9 Acute myocardial infarction, unspecified

The four-digit subheadings add more specific detail to that diagnosis, identifying, for example, different varieties of the three-character condition.

RULES AND INSTRUCTIONS FOR CODING OF MORBIDITY AND MORTALITY. MEDICAL CERTIFICATE OF DEATH. MEDICAL CERTIFICATE OF PERINATAL DEATH

Statistics of mortality is the main source of medical information. The definition of the causes of death was accepted in the 20th session of the World Health Organization (WHO) in 1967. ***The causes of death*** were defined as "all diseases, pathological conditions or injuries which cause the death … as well as circumstance of accidence or outrages and assassinations".

The term ***"initial cause of death"*** is used in the statistical documents. It is defined as "disease or injury caused link of diseased processes caused the death directly" or "circumstance of accidence or outrages and assassinations caused lethal injury".

The form of medical certificate of death recommended by the WHO is signed by the attending physician on the basis of hospital or outpatient observation or it is signed by a pathologist or forensic expert on the basis of autopsy.

Death certification serves a number of functions. A medical certificate of death enables the deceased's family to register the death. This provides a permanent legal record of the fact of death and enables the family to arrange disposal of the body, and to settle the deceased's estate.

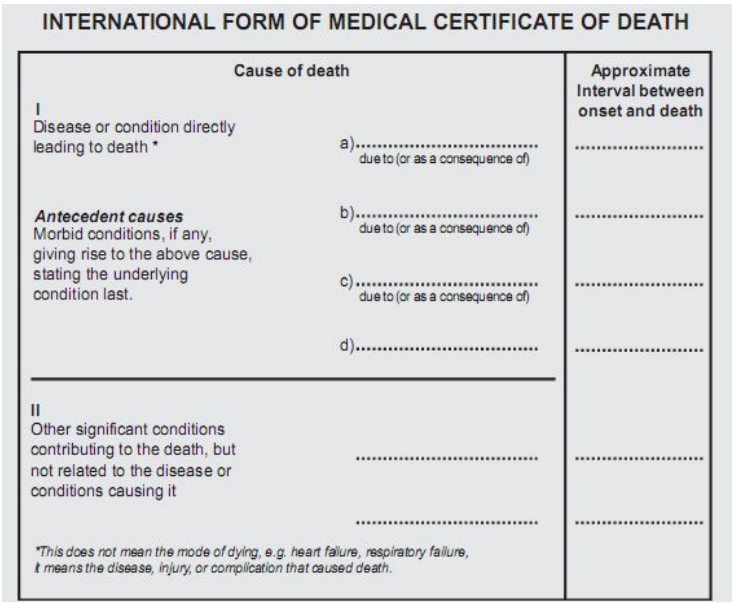
Information from death certificates is used to measure the relative contributions of different diseases to mortality. Statistical information on deaths by underlying cause is important for monitoring the health of the population, designing and evaluating public health interventions, recognizing priorities for medical research and health services, planning health services, and assessing the effectiveness of those services. Death certificate data are extensively used in research into the health effects of exposure to a wide range of risk factors through the environment, work, medical and surgical care, and other sources.

After registering the death, the family gets the Medical certificate of death, which includes an exact information about the cause of death that doctor gives. This provides them with an explanation of how and why their relative died. It also gives them a permanent record of information about their family medical history, which may be important for their own health and that of future generations. For all of these reasons it is extremely important that doctor provides clear, accurate and complete information about the diseases or conditions that caused the death of the patient.

Especial attention should be paid to the item "Cause of death" of Medical certificate of death, which is filled in according to the WHO recommendation published in the ICD-10.

Medical certificate of death consists of two parts. The first one is for noting the related diseases caused death of the patient. The second part is for noting another important pathology caused death of patient but unrelated with main disease and its complications.

The first part of the Medical certificate of death consists of 4 headings (a, b, c, d). If several pathological processes caused death, we fill in d – main disease, after that we fill in intermediate links (complications) – b and c and at least we fill in a – immediate cause the death.



INTERNATIONAL FORM OF MEDICAL CERTIFICATE OF DEATH

Cause of death		Approximate Interval between onset and death
I Disease or condition directly leading to death *	a) ..... due to (or as a consequence of)	.....
Antecedent causes Morbid conditions, if any, giving rise to the above cause, stating the underlying condition last.	b) ..... due to (or as a consequence of)	.....
	c) ..... due to (or as a consequence of)	.....
	d)	.....
II Other significant conditions contributing to the death, but not related to the disease or conditions causing it	.....	.....
	.....	.....

**This does not mean the mode of dying, e.g. heart failure, respiratory failure, it means the disease, injury, or complication that caused death.*

For instance:

I

a) Embolus in pulmonary artery

b) Pathological fracture

c) Secondary carcinoma of femoral bone

d) Carcinoma of breast

Accompanying diseases are noted in the second part of the Medical certificate of death.

For instance:

II

Hypertension disease

Denotation of approximate period of time between the onset of the disease and death can help to recognize the link of events caused death by physician filling in a form of Medical certificate of death.

The first part of the Medical certificate of death may only consist of 3 headings (a, b, d).

For instance:

I

a) Urosepsis

b) Ascending cystourethropyelonephritis

c) –

d) Adenoma of prostate

II

Diabetes mellitus

A part from that first part of the Medical certificate of death may only consist of 2 headings (a, d).

For instance:

I
a) Intoxication
b) –
c) –
d) Caseous pneumonia
II –

Besides the first part of the Medical certificate of death may only consist of main disease (d), if it caused the death of the patient.

For instance:

I
a) –
b) –
c) –
d) Acute leukemia
II –

Main disease should be marked exactly and circumstantially, e.g. you should write "small-focal or abscess pneumonia" instead of "pneumonia". If it is possible you should name its etiology.

In case of death of tuberculosis, you should mark its form, location, e.g. "fibrocavernous tuberculosis of the lung". In the death of tumor you should mark the type of tumor, its location, e.g. "esophageal carcinoma".

Medical certificate of perinatal death

The perinatal periods commences at 22 completed weeks (154 days) of gestation (the time when birth weight is normally 500.0 g) and ends seven completed days after birth. The perinatal period and the respective pathology and mortality is divided into antenatal (before the delivery), intranatal (during the delivery) and postnatal, or neonatal. The neonatal period commences at birth and ends 28 completed days after birth. Neonatal period may be subdivided into early neonatal period, occurring during the first seven days of life, and late neonatal period, occurring after the seventh day before 28 completed days of life.

Fetal death is death prior to the complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of pregnancy; the death is indicated by the fact that after such separation the fetus does not breathe or show any other evidence of life, such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles.

As a rule perinatal mortality depends on the maternal pathology. That is why the Medical certificate of perinatal death should indicate diseases of newborn or fetus as well as diseases, complications of pregnancy and other pathological processes of the mother. Maternal pathology is the main (initial) cause of fetal (newborn's) death.

The Medical certificate of perinatal death is filled for each fetus or newborn.

In the Medical certificate of perinatal death the causes of death have the following order:

a) main disease or pathological state of the fetus or newborn;
b) other diseases or pathological states of fetus or newborn;
c) main maternal disease or pathological state affecting the fetus or newborn;
d) other maternal disease or pathological states affecting the fetus or newborn;
e) other circumstances which cause to death.

Sections (a) and (b)

Enter diseases of the fetus or infant, with the most important one of these in section (a) and the remainder, if any, in section (b). By "the most important" is meant that pathological condition which in the opinion of the certifier made the greatest contribution to the death of the infant or fetus.

Sections (c) and (d)

Enter all diseases or conditions affecting the mother which in your opinion had some adverse effect on the infant or fetus. Again, the most important one of these should be entered in section (c) and the others, if any, in section (d).

Sections (e)

This is provided for the reporting of any other circumstances which the certifier considers to have a bearing on the death but which cannot be described as a disease or condition of the infant or the mother.

Personal information (first and second names), dates of birth and death, live-birth or dead-born, as well as autopsy results should be marked in the Medical certificate of perinatal death.

Besides maternal information is important.

Mother ……..
Date of birth……
Quantity (amount) of preceding pregnancies ……
Delivery with alive fetus….., dead-fetus……, abortion …..
Date and outcome the last preceding pregnancy: delivery with alive or dead fetus ……. abortion……..
Present pregnancy:

- first day after menses
- antenatal medical examination
- delivery: normal, premature, hard / etc.

Infant
Weight at delivery (g)
Sex: male / female
One fetus / twins: first from twins, second from twins etc.

In the case of dead-fetus the following should be marked: antenatal / intranatal / postnatal death. Besides the Medical certificate of perinatal death may include some information about persons assisting delivery (physician, midwife, etc.).

For instance:

The female was hospitalized on the 24th week of pregnancy with the diagnosis of premature delivery. The newborn weighing 700.0 g died during the first day of life. The autopsy demonstrated hypoplasia of lungs as main pathological process. It is known that preceding pregnancies (2) ended with spontaneous abortions at the term of 12 and 18 weeks.

Causes of perinatal death:

a) Hypoplasia of lungs

b) –

c) Premature delivery

d) Regular abortion

e) –

CERTIFICATE OF CAUSE OF PERINATAL DEATH

To be completed for stillbirth and liveborn infants dying within 168 hours (1 week) from birth

Identifying particulars

☐ This child was born live on ____ at ____ hours
and died on ____ at ____ hours

☐ This child was stillborn on ____ at ____ hours
and died before labour □ during labour □ not known □

Mother

Date of birth ☐☐☐ 1st day of last
or, if unknown, age (years) ☐ menstrual period ☐☐☐

Number of previous pregnancies

or, if unknown, estimated duration of pregnancy (completed weeks) ☐

Live births ☐

Stillbirths ☐

Abortions ☐

Antenatal care, two or more visits

□ Yes
□ No
□ Not known

Outcome of last previous pregnancy:

□ Live births

□ Stillbirths

□ Abortions

Delivery:

□ Normal spontaneous vertex

Other (specify)
.....

Date ☐☐☐

Child

Birthweigth.....grams

Sex:
□ Boy □ Girl □ Indeterminate

□ Single birth □ First twin

□ Second twin □ Other multiple

Attendant at birth

□ Physician □ Trained midwife

Other trained person (specify)
.....

Other (specify)
.....

Causes of death

a. Main disease or condition in fetus or infant

b. Other diseases or condition in fetus or infant

c. Main maternal disease or condition affecting fetus or infant

d. Other maternal diseases or conditions affecting fetus or infant

e. Other relevant circumstances

□ The certified cause of death has been confirmed by autopsy

□ Autopsy information may be available later

□ Autopsy not being held

I certify .....
.....
.....

Signature and qualification

BIOPSY

Biopsy is rather complicated and responsible part of the clinical pathologist work (investigation of a surgical and diagnostic material). The responsibility of the pathologist is the quality of his work, and the results of his research, whether it is diagnostic or surgical material. It depends not only on the choice of methods of treatment, but also destiny of the patient. Mistakes are possible at any stage beginning from the taking of the material and to reading the pathologist conclusion.

Biopsy is diagnostic measure which characterize by microscopic investigation of removed tissue material which is taken from a living organism. This term was introduced in 1879 by E. Besnier.

The first biopsy report on the use of needles for therapeutic purposes can be found in Arab medicine, in the writings of Albucasis or Abu al-Qasim Khalaf ibn al-Abbas Al-Zahrawi as it was his Arab name (936–1013 A.D), court physician to the caliph of the Andalusia, Al-Hakim II. In his famous treatise, Kitab al-Tasrif (The Method of Medicine), the most influential book of Arab Medieval Medicine, Albucasis described for the first time therapeutic punctures of the thyroid gland, using instruments resembling modern aspiration needles. Albucasis' description resembles a modern fine-needle aspiration (FNA) of the thyroid gland.

The 10th-century text contains figures of numerous surgical instruments and even medical needles. Some of the needles are clearly hollow, representing the first documented needles in the history of Medicine. The work by Albucasis was so influential that his book was translated into Latin by Gerard of Cremona (1114–1187 A.D.), a famous translator of Arab scientific works. The French surgeon and "Restorer of Surgery," Guy de Chauliac (1300–1368 A.D.), in his famous book "Inventarium Sive Chirurgia Magna" quoted the work of Albucasis more than 200 times.

Biopsy is used especially popular after 1830th in Europe and USA. Baron Dupuytren reports the diagnosis of echinococcus cyst by puncture biopsy in 1833 almost simultaneously with Stanley. Kün published his paper "A new instrument for the diagnosis of tumor", reporting the use of biopsy for cancer in 1846. Among important first European biopsy investigation which was done in 1864 by Dushen de Boulogne for diagnosis of pseudohypertrophic mastopathy.

Pathohistology had acquired the same significance, as well as macroscopic anatomy after acceptance of the theory of cellular pathology by R. Virchow. Pathological anatomy received a reliable assistant. It was the beginning of the development for new direction – research of the organs and tissue removed for diagnostic purposes, i.e. biopsy method. For the first time, biopsy was used by R. Virchow in Germany, H. Schroder attended for this problem, dermatologist J.C. White worked with biopsy in the USA. Thus, pathologist became to accept direct and active participation in destiny of the patient.

A piece of tissue taken from a patient during life to establish a precise diagnosis so that the most appropriate treatment can be initiated. Usually a thin section of the

specimen on a glass slide is examined by a pathologist under a microscope, but if the specimen is small and soft it may be more appropriate to make a smear on the slide. On occasion the biopsy may require to be examined biochemically or immunohistochemically. Biopsies may also be taken, for example, from chorionic villi (the projections of fetal tissue around the early embryo after it is embedded in the womb) for chromosomal analysis when a hereditary disorder is suspected.

The technique of biopsy is vital in all branches of medicine. Various methods are used. The simplest is a scraping from an accessible site such as the skin, or from a mucous membrane, such as in the mouth or the cervix of the womb. One of the commonest is a needle biopsy when a small sample is sucked out into some type of syringe through a needle of a calibre appropriate to the consistency of the tissue. This method is applicable to obtaining tissue from the breast, kidney, liver, brain, or heart.

In other situations a lesion is biopsied by a surgeon either at an operation undertaken just for that purpose, or in the course of an exploratory procedure. Often only part of the lesion being investigated is taken at operation – an incisional biopsy, but if the lesion is small, such as an ulcer, a pigmented spot on the skin, or a lymph node it may be removed in its entirety: an excision biopsy. Procedures of this type involve the use of a scalpel. Other instruments may be appropriate: a curette is used to take scrapings from the inner lining of the womb (the endometrium); small biopsies may be obtained by endoscopy – from the lungs during bronchoscopy, or from the lining of the stomach or colon. Occasionally specially designed instruments are used, in the form of 'punches' or 'brushes'.

One of the commonest reasons for undertaking a biopsy is to establish whether a tumor is malignant or benign. A common example of this is the investigation of a lump in a woman's breast. In such circumstances the pathologist often undertakes an immediate microscopical examination while the patient is still in the operating theatre, the surgeon waiting for the result before deciding how extensive an operation is required. This is also a common procedure during operations for tumors of the brain, or for cancers in other sites when lymph nodes need to be examined to establish whether or not they have been invaded by malignant cells.

Apart from the assessment of malignancy, biopsies are taken to examine organs such as the liver or kidneys for evidence of intrinsic disease, or to look for any signs of rejection of a transplanted organ such as a kidney or a heart.

By the time of performing biopsy it can be divided into:

1. Planned (about 3 days or from 2 to 5 days).
2. Urgent or intraoperative – 20–25 minutes.

Urgent biopsy is necessary for establishment of the nature of disease, determining the volume of operation (usually in malignant tumors).

Fast morphological investigation is realized using frozen biopsy tissue in the cryostat, clear staining of slides and high qualification of pathologist. At urgent biopsy it is sometimes possible to determine only preliminary conclusion, final histological diagnosis is established in 3–5 days.

By the method of tissue taking biopsy is divided into:

Excision biopsy – total dissection of the injured tissue or organ with subsequent study.

Incision biopsy – taking of a part of the injured tissue for studying.

Open (operative) biopsy – taking biopsy after surgical opening of the injured focus.

Needle (aspiration) biopsy – taking of the specimen by drawing it off through a needle or trochar.

Endoscopic biopsy – taking of the specimen by instrument through the endoscope or by needle under endoscopic control.

Puncture biopsy – taking of the small cylindrical specimen through puncture or small incision.

Brush biopsy – taking of the biopsy material with help of the brush catheter with subsequent study of the attached specimen.

Shave biopsy – taking the material with the help of the razor or surgical edge (is used for biopsy of the tissue which is prominent above the skin or upper layers of the derma).

Trepanobiopsy, curettage, smear, smear-imprint, forceps biopsy, biopsy by wash-out of operative wound and ulcerative defect, casual biopsy are also used.

Today a pathologist spends about 3/4 of his working day to study the operational and diagnostic biopsy material. The boundaries of such separation are indistinct, as quite often ordinary operational material (i.e. organs removed with the medical purpose with "beforehand known" diagnosis), opens new facts updating or even changing the diagnosis. As a matter of fact this material appears diagnostic. And, on the contrary, the excision of tissues conducted with the diagnostic purpose, appears sufficient for medical effect. Therefore it is more correct to call biopsy any research of the tissue from alive organism, all measures beginning from excision of the tissue and finishing their histologic investigation and answer by the pathologist.

Importance of biopsy:

1. Early diagnosis of the tumor.
2. Verification of the tumor.
3. Ascertainment of the histogenesis and anaplasia degree for tumors.
4. Determination of efficacy for operative procedures and prognosis for tumor.
5. Determination of characteristics of non-neoplastic processes.

Characteristic of the most widespread techniques for obtaining tissue samples by biopsy

Method	Description	Size of sample	Demerit	Application
Needle biopsy	Uses cutting needle to sample tissue (tumor)	Sample is a core of tissue 1–2 mm wide and 2 cm long	Small size can make histological interpretation difficult	Can be applied to any lesion, including those in brain
Endoscopic biopsy	Uses small forceps to sample lesions seen at endoscopy	Samples are fragments 2–3 mm in size	Small size can make histological interpretation difficult	Applied to lesions in GI, respiratory, genital and urinary tracts
Incision biopsy	Scalpel is used to remove a sample of the lesion	Sample is of variable size depending on nature of lesion	Applied to surgically accessible lesions only	Applied to surgically accessible lesions only
Excision biopsy	Whole abnormal lesion is removed surgically	Sample is of variable size depending on nature of lesion	Applied to surgically accessible lesions only	Applied to surgically accessible lesions only

Students and young physicians readily forget that the pathologist assumes an important role in prevention and treatment of diseases. Clinically this role becomes obvious through the examination of biopsy specimens, where the pathologic diagnosis may make the difference between life and death for the patient. By observing a few simple and essentially technical guidelines, the clinician can contribute materially to the establishment of an accurate histological diagnosis.

General motivation of biopsy:

1. Identification of pathological process:
a) tumors;
b) specific or non-specific inflammation;
c) enzymopathy;
d) reactive processes in lymphoid tissue and bone marrow;
e) dysfunctional metrorrhagia.
2. Control of medical and diagnostic aid.

Biopsied sites

Location	Description
Bone marrow biopsy	Since blood cells are formed in the bone marrow, a bone marrow biopsy is employed in the diagnosis of abnormalities of blood cells when the diagnosis cannot be made from the peripheral blood alone. In malignancies of blood cells (leukemia and lymphoma) a bone marrow biopsy is used in staging the disease. The procedure involves taking a core of trabecular bone using a trephine, and then aspirating material.
Gastrointestinal tract	Flexible endoscopy enables access to the upper and lower gastrointestinal tract, such that biopsy of the esophagus, stomach and duodenum via the mouth and the rectum, colon and terminal ileum are commonplace. A variety of biopsy instruments may be introduced through the endoscope and the visualized site biopsied. Until recently, the majority of the small intestine could not be visualized for biopsy. The double-balloon "push-pull" technique allows visualization and biopsy of the entire gastrointestinal tract. Needle core biopsies or aspirates of the pancreas may be made through the duodenum or stomach.
Lung biopsy	Biopsies of the lung can be performed in a variety of ways depending on the location.
Liver biopsy	In hepatitis, most biopsies are not used for diagnosis, which can be made by other means. Rather, it is used to determine response to therapy which can be assessed by reduction of inflammation and progression of disease by the degree of fibrosis or, ultimately, cirrhosis. In Wilson's disease, the biopsy is used to determine the quantitative copper level.
Prostate biopsy	Forms include transrectal biopsy and transurethral biopsy.
Nervous system biopsy	Forms include brain biopsy, nerve biopsy and meningeal biopsy.
Urogenital biopsies	Forms include renal biopsy, endometrial biopsy and cervical conization.
Other	Other sites include breast biopsy, lymph node biopsy, muscle biopsy and skin biopsy.

Technological chain in biopsy investigation at the department of clinical pathology

The biopsy process represents a long technological chain of manipulations consisting of many links. It begins with taking of the material, its transportation to histologic laboratory, macroscopic description of the delivered material, fixing, placement in media, preparation and staining of microspecimens, their microscopic

study and it is completed by description of histologic picture and diagnosis, sending the conclusion to clinical department.

Each link of this long chain requires scrupulousness in performance. The violation even in one link can cause distortion of all histologic picture, and consequently can lead to the incorrect conclusion, which the surgeon, gynecologist, therapeutist or other specialist will receive. Such conclusion will result in incorrect choice of the method of treatment and can be cause a iatrogenic disease.

Taking material

The list of diagnostic manipulations contains biopsies which were taken with the help of an operational endoscope, including laparoscopes, puncture by a thick needle, etc. The amount of such biopsies already comes nearer to the amount of the incision biopsies, and in some clinical departments considerably exceeds it. The decision about using of the biopsy method proceeds from clinical specialist but pathologist can also give some advises.

As the biopsy is preliminary planned in most cases and is preliminary discussed, it is necessary to know what clinical specialist can take from the injured organ for the most detailed answer after histological research. The pathologist is invited in inconvenient cases for such purpose. He can be engaged in the operation to ensure the correct choice of the place for taking material, it volume and appropriate fixing. The obtained material should be sufficient in volume for histological processing. It is desirable, but sometimes and it is necessary, not to limit by taking of only one slice. The operating doctor should take whenever possible some specimen from the lesion: from central and peripheral parts, that is especially important, for example, for pathological formations detected in the stomach, intestine. Moreover, background picture can be interesting for the physician and some specimens adjacent to the pathological formation are necessary. The puncture biopsy of solid formations at compact organs in their diffuse changes should be performed under ultrasonic or X-ray monitoring.

It is desirable to make smear-print on the glass for cytological research from the immediately obtained material, which is a good help for histological investigation. The small specimens taken by endoscope method can not be the subject for urgent (express) investigation, the material can be lost and distortion of the histological picture with its incorrect interpretation can occur. It is necessary to offer the repeated taking of the material for deriving rather informative picture in case of any doubt.

The physician needs pathologist's advise more often in case of the incision biopsy, about the volume of the material. The fundamental rule is: if there is a possibility to remove the formation completely within the visually healthy tissue, it is necessary to make enucleation of all this formation, instead of to limit only by its fragments. In this case it will be not only a diagnostic procedure, but also medical one for benign formation, but it is necessary to pay attention also about cosmetic outcome not only technical and surgical possibilities.

The traumatism should be excluded in excision of the tissue. Special attention should be given to possible mechanical or thermal damage of the excised tissue. These

effects damage the tissue especially hardly, sometimes with histological impossibility to determine even tissue origin. The excised tissue should not be rumpled by the instrument and fingers. All manipulations should be limited by enclosing fat in excision of a lymphatic node. It is necessary to research such lymphatic nodes which are less changed due to contact of the person and environment. The lymphatic nodes of lower extremities (especially inguinal), upper extremities (especially cubital and axillary) are most "inconvenient" for diagnosis. There are always unspecific changes in these nodes sometimes completely varying node structure. The cervical and other superficial lymph nodes are more appropriate for biopsy.

The interpretation of the morphologic appearance of the specimen depends to a considerable degree on the clinical findings, the site of the biopsy, and the patient's age and sex. These data may be crucial for the pathologic diagnosis. For this reason, careful completion of the pathology request form that accompanies the biopsy specimen is extremely important. It is equally important to fix the sample correctly (10% formalin solution; the ratio of the volume of the tissue to the volume of the formalin solution should be at least 1:20; the thickness of the specimen should be no more than 1cm). A fundamental principle in taking the biopsy is that normal and suspected tissue should be excised together so that their relationship can be evaluated in the histological preparation. It is particularly important for polyps and papillomas that the base of the new growth be included in the specimen in sufficient depth so that the presence or absence of invasive growth may be determined.

Surgical material

The surgeon determines the volume of surgical invasion and possibility of the organ or tissue removal personally. Sometimes, there is a necessity in urgent (express) intraoperative histological research in case of organ resection. It most often concerns oncologic cases. The pathologist can make a rapid intraoperative diagnosis by using frozen sections that can be prepared and stained within a few minutes. In this way the surgeon can immediately proceed to the appropriate procedure, e.g., axillary node dissection in the case of breast cancer. The accuracy of frozen-section diagnosis is almost as good as with permanent sections. The surgeon needs to know precisely the nature of the formation, degree of malignancy, the boundary of propagation of the pathological focus that determines the zone and volume of the resection. Modern surgery is directed to preserving for the organism a maximum of which belongs to it. Such direction is correct and progressive without doubt. But express-biopsy has some drawbacks and most important of them is a poor quality of the microspecimen due to fast fixing, insufficient dehydration, accelerated staining. Studying of such microspecimen can lead to tragic mistakes for the patient. The lack of time does not improve precision of diagnosis.

The use of the express-investigation should be strictly limited and the frozen section technique should be limited to certain specific indications and should not be extended beyond them (for example, nonmetastatic involvement of the lymph nodes is especially difficult to determine by this technique).

Firstly, it is not necessary to make urgent research if its outcomes will not

influence the course of operation.

Secondly, express-biopsy method is not allowed when taking the material not connected with large operation: skin biopsy, majority of endoscope biopsies, biopsies of the rectum, sigmoid colon, gastro- and enterobiopsies, endolaryngeal and endotracheobronchial biopsies, i.e. biopsies with relatively easy access. It is not allowed to use express-biopsy method for research of the lymph nodes because of the same reason and character of the material. The research of the latter is very difficult with excellent microspecimen and is almost impossible with urgent.

Thirdly, physician ought not wait for correct answer from express research of such epithelial tumors as ovarian cyst, especially large, multicystic and papillary. The investigation of such tumors needs studying of numerous pieces and urgent microspecimens prepared urgently on freezing microtome do not allow to determine the character of the tumor. The possibility of mistake is very high at any stage.

Fourthly, urgent research of boundary tissues or peripheral lymph nodes in cavitary operations with excision of tumors also has limited value. Only positive result indicating availability of the malignant growth in the delivered specimen can be used by the surgeon. The negative result does not suggest a definite answer.

So, express-biopsy method should be provided in the most necessary cases after consultation of the surgeon and pathologist because of all these reasons. The express research is most informative and helpful for osteal, thyroid and mammary pathology.

The majority of emergency biopsies are planned as well as operation. Therefore the surgeon should notify the pathologist about the time of the operation with emergency biopsy and to receive the agreement about the biopsy research. The laboratory should be ready for express biopsy. If nevertheless necessity in emergency biopsy arises during of the operation, the surgeon or his assistant must discuss the situation with the pathologist by telephone for updating all necessary clinical details and operational findings simultaneously with acceptance of the material.

It is the physician's concern that every specimen is examined histologically. This procedure should never be omitted regardless of how convincing the gross specimen may be.

If physicians follow these simple rules, they will help not only their patients but also themselves. Unfortunately, physicians suffer from unwarranted confidence in their diagnostic skills. In fact, only 40 percent of clinical diagnoses are correct in fatal diseases. In additional 40%, the correct diagnosis is one of a group of differential diagnoses. In 20% the diagnosis is incomplete or incorrect. Excisional or needle biopsies can substantially improve this batting average.

Direction and transportation of the biopsy material

The forms of the direction for biopsy research are filled in duplicate. The doctor fills all columns of the direction by readable handwriting or typewriting, signs the forms of the direction, checks up the correspondence with the directed material including passport and brief clinical data of the patient, precise localization of the formations and preliminary diagnosis. The result of the previous histological research and their terms of realization should be indicated. The nurse prepares jars with the

sticker for dispatching the removed material with the indication of the patient' name, department and character of the material.

If there is no possibility to transmit the native material to Pathology laboratory (remoteness, time, etc.), the material should be fixed in 10% solution of neutral formalin as the most universal fixative. The main enemy is drying of the material that should be avoided by all methods. The smaller the pieces, the greater the danger of drying is.

The material is delivered together with the forms by the ward attendant of the clinical department to Pathology laboratory at fixed time where it is examined by the laboratory assistant in the biopsy reception room.

First of all, the laboratory assistant reads the form of the direction, checks up if all the columns of this form are filled, and then verifies the delivered material with the data indicated on the form. If something is not clear for the laboratory assistant, he will call the doctor-in-charge and together with him will recognize the material. If there is any discordance, the material should be returned to clinical department.

Cutting out the biopsy

The doctor-in-charge cuts out the pieces from the taken material for consequent histological processing together with two laboratory assistants. Cutting out is started from reading data of the form-direction, including demographic, clinical information and character of the material. The doctor should compare all these data with the information indicated on the sticker of the jar containing the material. Then he describes material: its appearance, consistence, sizes (volume and mass in grams), the amount of fragments and their character, and then cuts the pieces or distributes the material on blocks. The laboratory assistant fills in the appropriate columns of the form-direction at doctor's dictation. The doctor specifies the amount of the taken slices, method of their fixing and type of the media, methods of staining and appropriates them serial numbers. The other laboratory assistant immerses the dissected pieces in small jars with fresh fixing solution for their further processing. The serial number is written on hard paper and it is put together with the pieces to the jars. The laboratory assistant ties up the remaining material in gauze dressing for "the wet archive" and places them into an archival tank.

Investigation of microspecimens

The processing of the material in laboratory is carried out according to the instructions of the doctor marked on the form. The ready microspecimens are studied by the doctor and the conclusion is made. Most interesting and complicated biopsies, the rare pathological processes are represented for survey to all doctors of Pathology department.

It is very important not to hurry with the opinion. It is better to discuss the microspecimens several times, to make additional shears or to apply other staining, to consult other experts and to produce the uniform judgement. The old Russian rule "measure seven times – cut off once" should be strictly observed in clinical and pathologianatomical practice. Especially it concerns the biopsies of the larynx, rectum, extremities, stomach as positive answers are always followed by difficult and

dangerous operations.

The issue of the microspecimens for investigation in other establishments is carried out only after the request from these establishments or as exception after the request of the treating doctor of the patient with notification about the place of consultation. The microspecimens for consultation are issued only by the pathologist (the most qualitative and informative glasses). The microspecimens can be given to the relatives of the patient or patient.

If there is a necessity of comparison of the microspecimens with the microspecimens of the previous investigations done in other medical establishments, the pathologist enjoys the right to request them officially.

Storage of the forms of the answers, "wet archive" in Pathology department

The forms of the biopsy answers are stored in department eternally. The histological microspecimens with tumors, infectious processes and suspicion on their availability, and also rare cases are stored constantly. The remaining microspecimens are destroyed after a year of storage. "The wet archive" of the tumors, infectious and parasitical processes is stored for a month; the remaining material is destroyed in 3 months.

Finally, histological examination ***of all tissues and cadavers is essential*** for medical quality assurance. Anyone who discards excised organs, e.g., tonsils, gallbladders, or appendices with the comment, "Everybody can see that this is normal" does not contribute to quality assurance. The increasing number of malpractice suits should serve as a warning.

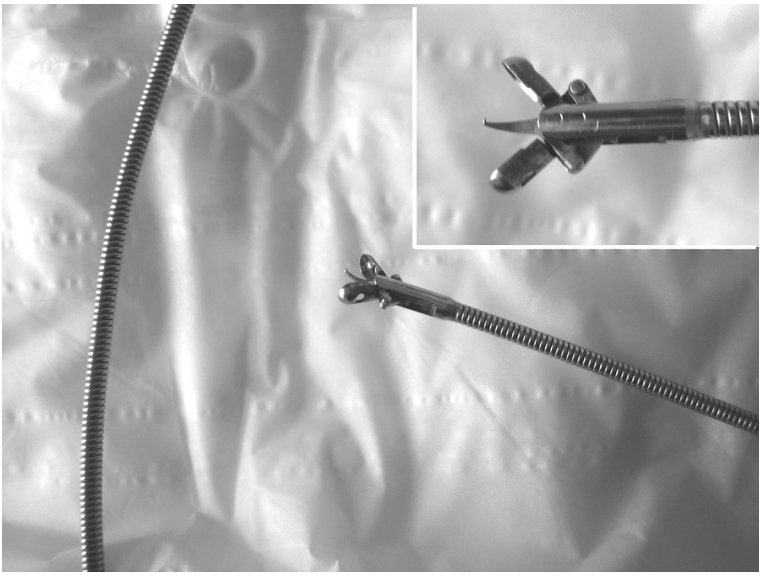


Figure 1. *Endoscopic edge for taking tissue.*

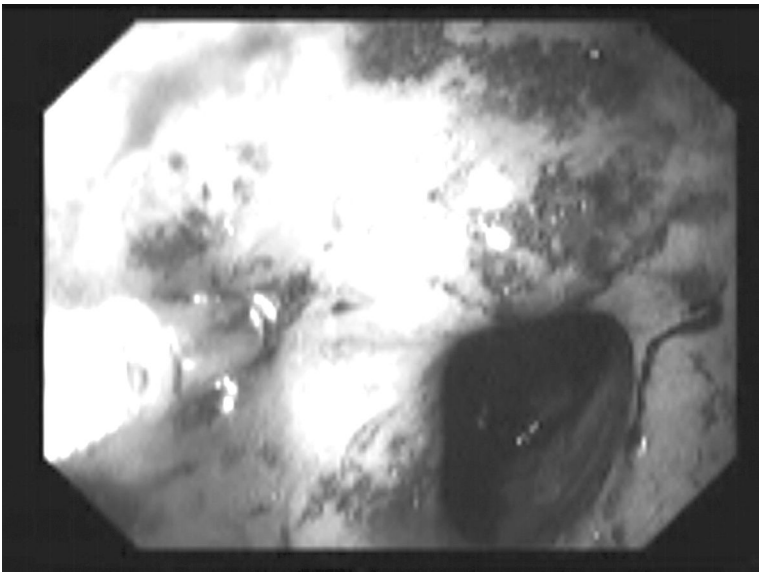


Figure 2. *Endoscopic biopsy of gastric mucosa with intestinal metaplasia.*

Figure 3. *Hospital system for pneumotransportation of materials between different units; transport of urgent biopsy to Pathology Department.*

Figure 4. *Registration of urgent biopsy.*

Figure 5. *Automatic biopsy processing.*

Figure 6. *Exhaust hood cupboard for work with toxic substances in biopsy processing.*

Figure 7. *Processing of the material in laboratory; manual passing on paraffin embedding.*

Figure 8. *"Wet archive" in archival tank.*

Figure 9. *Discussion of biopsy results of pathologists and therapeutists.*

AUTOPSY. AUTOPSY PROTOCOL. SCHEME OF AN AUTOPSY PROTOCOL. EXAMPLE OF AN AUTOPSY PROTOCOL. EXAMPLE OF AN AUTOPSY PROTOCOL IN UKRAINE

Autopsy, a surgical procedure performed on a recently deceased patient, is the last and most completely diagnostic procedure. The autopsy answers the final question: Why did life pass from a specific human body? It is a question we have all asked when a loved one, friends, coworker or even a public figure dies. The more untimely the death, the more tragic it seems, so many more questions arise. The autopsy serves to answer these and many other questions. Carefully performed by a thoughtful, interested and experienced individual, it should reveal much of the truth about the health of the deceased patient and the mechanism of death.

The term "autopsy" derives from the Ancient Greek *autopsia*, "to see for oneself", derived from *αυτος* (autos, "oneself") and *όψις* (opsis, "eye"). Around 3000 ago ancient Egyptians were one of the first civilizations to practice the removal and examination of the internal organs of humans in the religious practice of mummification. Autopsies that opened the body to determine the cause of death are attested at least in the early third millennium BC, although they were opposed in many ancient societies where it was believed that the outward disfigurement of dead persons prevented them from entering the afterlife (as with the Egyptians, who removed the organs through tiny slits in the body). Notable Greek autopsists were Erasistratus and Herophilus of Chalcedon, who lived in the 3rd century BC in Alexandria, but in general, autopsies were rare in ancient Greece. In 44 BC, Julius Caesar was the subject of an official autopsy after his murder by rival senators, the physician's report noting that the second stab wound Caesar received was the fatal one. By around 150 BC, ancient Roman legal practice had established clear parameters for autopsies. The dissection of human remains for medical reasons continued to be practiced irregularly after the Romans, for instance by the Arab physicians Avenzoar and Ibn Al-Nafis, but the modern autopsy process derives from the anatomists of the Renaissance. Giovanni Morgagni (1682–1771), celebrated as the father of anatomical pathology, wrote the first exhaustive work on pathology "De Sedibus et Causis Morborum per Anatomen Indagatis" ("The Seats and Causes of Diseases Investigated by Anatomy", 1769). The great 19th century medical researcher Rudolf Virchow, in response to a lack of standardization of autopsy procedures, established and published specific autopsy protocols (one such protocol still bears his name).

All dead bodies of dying in hospitals, as a rule, are subject to autopsy. Head physician of the hospital may abolish the autopsy in the cases if he has permission from the patient's relatives, which may refuse on religious or other grounds; if there is no suspicion of violent death; if there is documented desire of the deceased. Abolition of the autopsy is not settled in the case of death of patients which stayed in the hospital less than a day; in the cases of requiring medical legal investigation; in the case of death from the quarantines or extrahazardous infectious diseases, suspicion of them; in all cases of not clearing diagnosis regardless of term of stay in permanent establishment; in cases of death during or after diagnostic instrumental investigations performed in the patient.

Dead body stays in the ward for two hours after the fact of natural death has been established by hospital's physician. The surname, name, father's name, date and time of death, department are to be written on the hip with brilliant green. Usually rubber-coated label on which above mentioned passport data are written is fixed to the arm. The latter method is better to use in those medical and preventive treatment facilities in which sporadic death cases occur. The medical document is delivered in the pathomorphological department together with the dead body and in the case of death in the second half of the previous day until 9–10 a.m.

Under body lift and its further examination it is necessary to keep all moral-ethical and professional requirements. Ethical requirements include medical secrecy keeping regarding everything revealed at autopsy. It is should also be born in mind that dead body serving for science has relatives and family. For example, professor V. Gruberg required from his students and those working in autopsy room to take off hats, as "hats wearing does not correspond the credit of the room". It is advised to warn junior health professionals of the fact that cadaveric hypostasis can disfeature the face in case the body stays the back upward. It should be kept in mind that after the fact of natural death has been established, it is necessary to close eyes, fasten up lower jaw, to cover the body with a clean linen, etc. Simultaneously with diseased body completely filled-in medical records should be submitted to the mortuary.

The clinical autopsy is performed by the pathologist. Prior to deceased body autopsy the pathologist studies all the data regarding the patient's life, disease and death which can be found in the medical record of hospital patient, asks the attending doctor missing facts relating to course of disease and the death. Sometimes it is useful to clarify some data from relatives, especially in case patient's short terms stay in the hospital. The following should be carefully investigated: laboratory, instrumental and other methods of investigations, methods of treatment, drugs taken by patient, diagnosis written on the title page of medical records as well as all working diagnosis written in log books. All this circumstances study pursues one more important aim – to exclude or to find out medical legal aspects.

It is desirable that the pathologist examining all necessary data independently formulated diagnosis which can differ from that of the attending doctor. Doing this, as P. Kalitiyevskiy mentions, the pathologist in a certain manner puts her / himself in the position of the attending doctor, which is really important for mutual understanding between the pathologist and clinician.

***There is certain algorithm in autopsy fulfillment**:*

1. The autopsy should be conducted in the postmortem room and when there is an official order of the head physician in the medical records. The autopsy should be carried out at day lights as artificial lighting changes the color. Physicians should be present at the autopsy.

2. A gown and rubberized apron and oversleeves should be put on. It is advisable to use anatomical gloves. This will ensure contagious diseases prevention, as well as cadaveric alkaloid penetration through possible defects of the skin.

3. Autopsy should not be restricted to only those areas which are the place of obvious alteration, but should include all the organs of the body, for the normality of certain viscera is often as significant as the disease of others and organs that appear normal macroscopically are frequently abnormal microscopically. The occasional request to omit examination of the brain (usually made by relatives) should be denied, if possible, as should the frequent request by neurologists to limit the autopsy to the brain. A partial autopsy is likely to raise more questions than it answers.

4. External examination of diseased body. The following should be established: sex, body-type, nutrition, state of integument, presence of death signs, eruptions, hematomas, wounds, ulcerations, edema, etc. It is desirable that the attending doctor confirmed demographic data of the diseased.

5. Main incision. It is necessary to watch to prevent it coming through the surgical sections, cicatrix and other defects.

6. Detailed examination of the cavities establishing the position and interlocation of organs, presence of joints, exudates, transudate, foreign objects, etc.

7. Organ withdrawal from the cavities and their investigations (size, weight, color, consistency, shape, etc.) with simultaneous necropsy taking and, depending on tasks set for the pathologist, material for bacteriologic, serologic, biochemical and virology investigations. Sometimes X-ray examination of the bones is done.

8. Short summary incorporating paragnosis, the cause of death, possible discrepancies between the clinical diagnosis and paragnosis, accessory matters clarification which are of interest for clinicians.

First autopsy methods were described in details by R. Virchow. Later on it was improved by Kiary, L'Etule, A. Abrikosov, G. Shore. The methods of the two latter ones are the most widely used in pathological practice.

A. Abrikosov offers to investigate the organs by cavities. First organs of the neck and thoracic cavity are removed in totality. Then separately intestinal tract, liver, stomach and duodenum in one set, urinary tract and genital organs in totality.

G. Shore suggested organs full evisceration method, which means removal of the neck, thoracic cavity, abdominal cavity and small pelvis as a single total complex. This method is rather convenient to be used under investigation of those deceased bodies who died of after surgery complications. In these cases it is reasonable to search for details in the operation area, namely state of surgical sutures, vessels, character of exudates, correctness of surgery fulfillment.

The clinicians are now less interested in autopsy because better antemortem diagnosis is made possible by modern clinical and surgical procedures; in many cases the autopsy findings can be predicted; shortage of time, pressure of work and the demands of living patients make it difficult for clinicians to spare the time to visit the autopsy room; the autopsy is restricted changes such as early myocardial infarction or biochemical and metabolic alterations cannot easily be demonstrated; the postmortem room is cold and uninviting and the atmosphere of blood and guts may even be offensive; autopsy have lost the prestige they used to have, perhaps they are not even carried out as well as before: many senior pathologists, more interested in the

application of newer techniques, join senior clinicians in their waning interest; some clinicians may be unwilling to have their possible errors in diagnosis or treatment exposed by pathologists who are not always tactful; experimental operative procedures are now more often practiced upon experimental animals than on cadavers. Similarly, practice in surgical technique may be obtained easily and realistically by animal surgery.

Bearing these facts in mind, let us consider those circumstances in which the autopsy may have value.

1. Quality control

This is a feature of medical practice much emphasized today. As a method of assessing the accuracy and completeness of clinical diagnosis the autopsy is of great value. In one series more than 40% of antermortem diagnoses were not entirely correct and 7% were totally incorrect. Bauer and Robbins studied 2734 cancer patients. In 40% serious clinical errors were made. In 12% of cases fatal, clinically undiagnosed cancer was found.

During 1973 in the Johannesburg White hospitals, there were 304 autopsies and 1043 hospitals deaths – an autopsy rate of 29%. Postmortem examination is usually requesting in difficult cases or in patients who have only been hospitalized for a short while. A sample of 130 consecutive cases showed that in 53% the clinical and pathological diagnoses were in complete agreement, in 32% there were significant additional pathological findings and in 15% pathological examination refuted the clinical diagnosis – 3% of these patients died of cancer which was not diagnosed during life.

The autopsy may also be of value in revealing the effects of therapy. Thus the assessment of the treatment of cancer, the evaluation of surgical technique, the study of opportunistic infection and the exposure of iatrogenic disease in various forms, e.g. drug reactions are all ways in which information of clinical importance may be gained.

2. Teaching

As a teaching method for undergraduate students the autopsy remains unsurpassed. Generally it precedes or accompanies the introduction to clinical medicine and plays an important part in the transition from systematic study to case studies. A short clinical presentation with the description of the physical findings, relevant laboratory data and X-ray findings, followed by a traditional autopsy demonstration in the mortality would seem to be the best approach. The freshly removed organs are at their most life-like and some of the students may have the opportunity to handle and inspect the organs. If frozen sections have been done, histological correlation can also be achieved. Unfortunately, student numbers nowadays are so large that attendance at such demonstrations has to be limited. However, good photographic records and adequate documentation allow material from autopsy to be used as the basis of clinical-anatomical conferences at a later stage.

For postgraduate students and practitioners the autopsy provides the most comprehensive and integrated case study when it is correlated with previous illness, clinical and laboratory findings and the course of the patient's disease, as well as the

effects of the therapy. Superspecialized pathologists in branches such as cardiology, nephrology, etc., may function as part of the team and make the results of their study of organ pathology from postmortem material available to their clinical colleagues.

Trainee pathologists must learn autopsy technique and the interpretation of the gross and microscopic pathological findings. The autopsy provides adequate material for the basis introduction to histopathology, which is necessary for the better interpretation of the minute biopsy specimen which may be involved in surgical pathology. Interesting specimens obtained at autopsy can be preserved for museums.

3. Research

Epidemiology. From the previous discussion it is obvious that postmortem examination can considerably improve the accuracy and validity of death certification. Mortality figures are used as the basis from which the relative importance of various disease processes are studied and by which problem areas can be outlined.

Applied research. The autopsy provides an opportunity for the recognition of new diseases. It also permits the definition of new diseases and the assessment of their effect on the body as a whole.

Research into postmortem techniques has evolved methods which make the autopsy a more effective diagnostic research tool. New methods are now available for recognizing early myocardial infarction only a few hours after the onset of ischemia. Furthermore, the introduction of the immediate autopsy has made possible the use of newer and more refined techniques of tissue culture, electron microscopy, immunofluorescence and enzyme histochemistry in some cases.

Quality control, teaching at all levels and researches are the main functions of the autopsy and their effectiveness is dependent upon good clinical-anatomical correlation. With all of their widely acknowledged benefits, autopsies would seem to have a central role in current health care programs.

AUTOPSY PROTOCOL

The autopsy protocol is a systematic objective description of the postmortem pathologic findings, which are interpreted and correlated with the clinical findings. It should be concise, and diagnostic terms should be avoided in the gross description. Clarity should be the aim. In general, avoid cliches and unusual descriptive terms. The protocol should be prepared during or shortly after the autopsy.

The protocol is composed of several parts, which are described in the following order:

Passport part of protocol includes such information as full name, sex, his / her age, home address, the number of medical record, occupation, the date of entering to the hospital and date of death, clinical diagnosis.

In the same part of the pathologic autopsy protocol pathologist's full name and that of the physician present during the autopsy, the short clinical data, laboratory tests and methods of treatment should be written.

Autopsy findings

External inspection. This part of the protocol must be prepared very carefully, since it cannot usually be reconstructed later. External description must include general findings, e.g., height, weight, state of nutrition, general build (bone structure), color of the skin (jaundiced or cyanotic), color and appearance of the conjunctivae and cornea, hair distribution, and description of scars, wounds, and body orifices. As a part of this inspection (the cadaver should be prone), the signs of death should be determined.

Body cavities. After opening the body cavities (skull, chest, and abdomen) and before removing the organs, the wall of the cavity and the contents must be examined for the condition of the meninges, extracerebral blood vessels, the bony skull, sinuses, thoracic and abdominal wall, pleura, pericardium, and peritoneum. In addition, exudates (amount and composition), the position of organs, and other pathologic conditions must be assessed, since these may be disturbed by removal.

Organ systems. As already mentioned, organ packages are removed in toto, with consideration being given to their topographic relationships. Then, the individual organs are described. The data should be as objective as possible and include size, weight, and comparison of paired organs.

The description should be done by systems of organs: nervous system, respiratory, digestive, cardiovascular, genitourinary, endocrine, hematopoietic and musculoskeletal systems.

The protocol should contain only the description of pathologic changes without any attempt at a diagnosis. A carefully prepared protocol should enable the reader, even years later, to arrive at the correct diagnosis. The interpretation of the clinical picture may change radically over the years, but the pathologic description never loses its validity. Negative findings are also important; they indicate that the pathologist was purposefully looking for certain changes. If negative findings are important for the interpretation of the clinical picture, they should be stated specifically.

Pathologic autopsy diagnosis. After the autopsy pathologist synthesizes all identified changes in the form of pathoanatomical diagnosis which is a very important part of the autopsy.

Clinical-anatomical conclusion (epicrisis). Conclusive summary of definite autopsy case including clinical as well as morphological findings is defined as clinical-anatomical conclusion. The concluding remarks of an autopsy report should present a dialogue between the attending physician and pathologist. This dialogue is presented in the form of a summary statement that incorporates clinical and pathological findings and diagnoses. The conclusion must be short. There are several obligatory parts in the conclusion. They are:

a) comparison of clinical and pathological anatomy diagnosis;
b) final medical certificate of death;
c) defects of diagnosis and treatment.

A consensus must be achieved on several questions: Was the clinical diagnosis correct? What were the causes for an erroneous conclusion? How can such an error be avoided in the future?

Should emphasize a causes of nonconcurrence of clinical and pathological anatomy diagnosis with they analysis and recommendation for making right clinical diagnosis in the cases of nonconcurrence of clinical and pathological anatomy diagnosis. Should give an opinion about role of nonconcurrence of clinical and pathological anatomy diagnosis in the lethal outcome of the patient.

Frequently, no morphological equivalent can be found for clinical symptom or even for death. Electromechanical dissociation of the heart, diabetic coma and hypoglycemic shock are examples of diagnoses for which there is no morphological equivalent and for which the diagnosis is a purely pathophysiologic one.

Coding. It is performed according to the ICD-10.

SCHEME OF AUTOPSY PROTOCOL

1. General examination of the body and the location of internal organs

Weight and height of the dead body, frame, nutritional state, color of integuments and their integrity, cadaveric changes, their degree, condition of mucous membranes are described. Abdominal cavity is investigated for contents: exsudate, transudate, solderings; location of the intestine and organs of the abdominal cavity. Pleural cavities for contents, presence or absence of solderings. Condition of the heart sac for contents, presence or absence of solderings.

2. Central nervous system and sense organs

The bones of the skull, their condition; dura mater, blood supply, degree of tension, sinuses of the dura mater; pia mater, color, shine, blood supply, gyri and sulci of the brain are investigated. Substance of the brain on incision, focal changes, weight of the brain are determined. The ventricles of the brain and their contents are investigated. The cavity of the middle ear and its contents on both sides are examined.

3. Respiratory system

The mucous membrane of the entrance to the larynx, condition of vocal cords, mucous membrane of larynx, trachea and bronchi, color; contents of bronchi, blood supply, condition of bronchi and vessels on incision; lungs, color, consistency, character of contents under the pressure are investigated.

4. Cardiovascular system

It is necessary to study the content of the heart sac, condition and shine of the epicardium; size, weight, thickness of the muscle, contents of cavities of the heart; width of apertures, thickness of walls, condition of valves; condition of the coronary arteries; condition of the aorta, presence or absence of atherosclerotic plaques, elasticity of the aorta, condition of vessels of other areas.

5. Digestive system

Teeth, oral cavity, pharynx, tonsils, tongue from the surface and on incision; esophagus, color of the mucous membrane and condition of folds; permeability of the biliary tract, content of the gallbladder, character of the mucous membrane; a consistency, condition of the capsule of the liver, size and weight, tissue of the liver on incision; a consistency of the pancreas, macroscopical features on incision; condition of the mucous membrane of small and large intestine should be assessed.

6. Urinogenital system

It is necessary to investigate the condition of fatty and fibrous capsules of kidneys, size, weight, macroscopical features of surface of the kidneys; condition of the cortex and medulla of kidneys; macroscopical features of the mucous membrane of pelvis, ureter and urinary bladder, condition of sex organs (uterus, ovaries, prostate gland, testicles).

7. Organs of hematopoiesis

Lymph nodes of the bifurcation of the trachea, bronchi, mesentery, paraaortic and others, consistency, size and macroscopical features on incision; spleen (size, weight, consistency, condition of the capsule, tissue on incision); condition of the bone marrow of the sternum and femur are assessed.

8. Endocrine system

Hypophysis, epiphysis, thymus, thyroid gland (their size, consistency, macroscopical features on incision) are described. Adrenal glands, condition of the cortex and medulla layer are examined.

9. Musculoskeletal system

The condition of bones of the skull, extremities, macroscopical features of muscles on incision should be investigated.

EXAMPLE OF THE AUTOPSY PROTOCOL

1. ***General information***

Pathoanatomical examination with the purpose of establishing the course of death of Mr. Sh. F. M. born in 1919 was carried out by pathologist S in the premises of the Pathology Department of Kharkov Hospital No. 1.

Male, aged 80, place of death: at hospital.

2. ***Clinical data***

Primary diagnosis. IHD: Acute myocardial infarction.
Secondary diagnosis. IHD: Acute myocardial infarction. Atherosclerosis of aorta and coronary arteries. Cardiogenic shock. Cardiosclerosis.
Date of death: 08.01.2010
Date of autopsy: 08.01.2010
Beginning of the examination 08.01.2010
End of the examination 08.01.2010

3. Autopsy findings

3.1. External inspection

The corpse of a male, aged 80, the length of the body – 172 cm, body mass – 73 kg, of right stature, satisfactory nutrition. Rigor mortis is well pronounced in all groups of the muscles. The integuments are grey. Cadaveric livores are violet, seen on the posterior surface of the body, they become pale on pressure and restore their initial color after 15 seconds. There are injection marks on the skin of the right and left ulnar croocks caused by injections of drugs in hospital. No putrefactive changes has been noted. Visual examination and palpation of the scalp have not revealed any injuries. The skin of the face is pale-cyanotic. The eyes are closed, the corneas are dimmed, the

pupils are evenly dilated up to 0.4 cm, the conjunctivas are grey. The nasal bones and cartilages are intact on palpation. The nasal and ear ducts are free. The mouth is closed, the labial mucosa are cyanotic. The teeth are artificial. The tongue is in the oral cavity. There are no injuries on the neck. The chest is symmetrical. The abdomen is on the level of costal arches. The development of the outer genitals is regular. The anus is closed, the skin around it is clean. The lower and upper extremities are regularly developed, their bones are intact on palpation.

3.2–3.3. Internal inspection

On autopsy of the abdominal cavity, no unusual odor is felt. The layer of the subcutaneous fatty tissue in the chest region is 2.0 cm thick, and in the abdominal area it is 2.5 cm. The omentum covers intestinal loops. The stomach and intestinal loops are moderately distended. The abdominal cavity contains about 250.0 ml of transparent yellow fluid. The peritoneum is smooth, shining. The diaphragm is intact. The lungs fill the pleural cavities. The pleural cavities contain about 400.0 ml of transparent yellow fluid. The pleura is thin and shining. The pericardium is intact. The pericardial cavity contains about 400.0 ml of blood and blood clots. Some dark liquid blood is discharged from the heart cavity and large vessels.

The heart is drop shaped, measures 12×10×9 cm. The epicardium contains moderate quantity of fatty tissue. The surface of the heart is without hemorrhages. The heart cavities contain dark liquid blood. The myocardium on sections is cyanotic-grey, dimmed and flabby with numerous whitish layers. In the anterior middle and low third part of the left ventricular wall the myocardium is flabby and pale yellow with a rupture, measuring 2.5×0.3 cm. The thickness of the left ventricular muscle is 1.7 cm, that of the right one is 0.3 cm. The tricuspid and mitral valves are elastic. The endocardium is whitish and smooth. The width of the aorta on its section above the valves is 7.5 cm. The inner surface of the aorta is yellow with ulcerative atherosclerotic plaques. The width of the pulmonary artery on its section above the valves is 8.5 cm. The inner surface of the pulmonary artery is yellow, smooth. The lumen of coronary arteries of the heart is narrowed by 80% with atherosclerotic plaques.

The pharynx, larynx and trachea are free, their mucosa is cyanotic-pink. The lungs are paste-like on touch, their tissue on section is pink-red, with profuse foamy and blood-containing discharge. There are no hemorrhages on the surface of the lungs.

The spleen measures 10×5×3.5 cm; its capsule is smooth and its consistence is elastic; the tissue on section is red, with small blood-containing scraping.

The liver measures 20×17×13–10 cm; its capsule is smooth; the liver consistency is elastic; the tissue on section is brown, plethoric, nutmeg. The gallbladder contains about 70 ml of dark bile; its mucosa is net-like.

The gastric cavity contains up to 450.0 ml brown fluid without any specific odor. The gastric mucosa is pink-grey, folded. The pancreas is plethoric, yellow-grey, lobular, measuring 21×2.5×2 cm. The contents of the intestine correspond to its portions; its mucosa is grey without ulceration.

The kidneys measure 11.5×6×4 cm. The fatty capsule is moderately developed. The fibrous capsule is easily removed and thin. The surface of the kidneys is smooth. The tissue on section is plethoric. The border between layers is well-defined. The renal pelvis are free, their mucosa is whitish.

The thyroid gland measures 4.5×2.5×1.5 cm, its surface is granular. The tissue is thick elastic and cyanotic. The adrenal glands are leaf-like, measuring 4.5×4×3–0.5 cm. The border between layers is well-defined. The bladder contains about 250.0 ml of transparent yellow urine, its mucosa is yellow, folded.

The soft integument of the head from the side of its inner surface is pink all over. The bones in the vault of the skull are intact, the dura mater is intact, shining, without any adherence to the bones in the skull vault. There is liquid blood in the superior longitudinal sinus and those of the basis of the skull. The pia mater is transparent, edematous. Its vessels and those in the base of the brain are plethoric. The gyri and sulci are smoothed. The brain tissue on section is plethoric; drops of blood are discharged easily. The brain substance does not produce any unusual odor. The ventricles of the brain contain transparent colorless fluid. The tissue of cerebellum, pons Varolii and medulla oblongata is edematous, moderately plethoric. The bones in the cranial basic are intact.

4. Final medical certificate of death

I
a) hemopericardium
b) rupture of the heart
c) –
d) acute myocardial infarction
II –

5. Clinical-anatomical conclusion.

Mr. Sh. F. M., aged 80. It is known from the history that the man suffered from pain localized behind the sternum and radiating to the left arm during a long period. Severe pain appeared behind the sternum and weakness developed on 08.01.2010. The patient was brought to the cardiology department of the hospital. Arterial blood pressure was 90/0 mm Hg. Transmural myocardial infarction was revealed by electrocardiography. The patient died of cardiogenic shock in 3 hours.

Clinical diagnosis: Acute myocardial infarction. Atherosclerosis of aorta and coronary arteries. Cardiogenic shock. Cardiosclerosis.

Autopsy findings: Pronounced atherosclerosis of aorta and coronary arteries, myocardial infarction with hemopericardium: in the anterior middle and low third part of the left ventricular wall the myocardium on sections is flabby and pale yellow with rupture, measuring 2.5×0.3 cm, the pericardial cavity contains about 400.0 ml of blood and blood clots, cardiosclerosis: the myocardium on sections is cyanotic-grey, dimmed and flabby with numerous whitish layers. Immediate cause of death: hemopericardium.

Comparison of clinical and pathological anatomy diagnosis: coincidence of basic clinical and pathological anatomy diagnosis.

6. Cording I 21.0

Pathologist: Signature

EXAMPLE OF THE AUTOPSY PROTOCOL IN UKRAINE

Ministry of Health of Ukraine The name of hospital	The medical documentation **FORM 013/0** Confirm by the order of MHU 26.07.1999. No. 184

THE PROTOCOL
of pathological investigation No. ___
dated «___» _____ _____

Address of hospital which has filled in the protocol _____

Region _____ district (town) _____

Hospital _____ department _____

Hospital record _____

1. Full name _____

2. Sex: male, female (underline). 3. Age _____

4. Home address_____

5. Occupation (until retirement) _____

6. The patient is taken to the hospital _____ hours (days) after the beginning of disease.

7. Spent _____bed-days. 8. Date of death _____ (number, month, year, time) Date of entering _____ (number, month, year, time)

9. Date of autopsy_____ (number, month, year) 10. Attending physician _____

11. Physician present during the autopsy _____

12. The diagnosis of establishment which referred the patient: _____

13. The diagnosis on entering: _____

14. The clinical diagnosis in the hospital and the date of its establishment: _____

15. The final clinical diagnosis in the hospital and the date of its establishment (main disease, complications of the main disease, accompanying diseases):
a) main disease _____
b) complications of the main disease _____
c) accompanying diseases _____

16. Results of clinical and laboratory investigations:

17. The pathoanatomical diagnosis (main disease, complications of the main disease, accompanying diseases):

18. Errors of clinical diagnostics (underline, enter)
Divergence of diagnoses: on the main disease, on the complications of the main disease, on the accompanying diseases.
Late diagnosis: the main disease, the deadly complication.
The cause of divergence of diagnoses (underline): objective difficulties in diagnosis-1, short-term stay in hospital-2, incomplete examination of the patient -3, revaluation of the data of observation -4, rare disease -5, incorrect registration of the diagnosis -6.

19. The cause of death (in the medical certificate of death No. __)
The code according to ICD-10
_____I. a)
_____ b)
_____ c)
_____ d)
II.

20. Clinical-pathoanatomical conclusion:

Pathologist _____ signature _____
The head of the department_____ signature _____

Continuation of the protocol of pathoanatomical investigation No. ____ dated «____» _____

Results of pathological investigation:

height	body weight	Weight of organs									
		brain	heart	lungs		liver	spleen	kidneys		pancreas	prostate
				left	right			left	right		

The text of the protocol

Microscopic investigation

Pathologist _____

Signature _____

DEATH, SIGNS OF DEATH

Death is the permanent termination of the biological functions that sustain a living organism.

Depending on the causes the following types of death are recognized: natural (physiologic) death from age and organism depreciation, violent death from trauma or other negative influence on organism which ends with death, and of diseases.

Depending on reversible or irreversible changes in the organism apparent (clinical) death and natural (biological) death are specified. Apparent death is characterized with apnea, blood circulation arrest and lasts for 5–6 minutes until brain cells die. Apparent death is a reversible process of dying. Reversibility depends on the stage of hypoxic changes in the brain. Natural death is manifested with irreversible changes development and autolytic processes in all the organs.

In case the death process is fast, liquid blood in the heart and vessels is observed causing fibrinolysis, postmortem face lividity, ecchymosis in conjunctiva, intensive and wide spread cadaveric lividity, urine, fecal matter discharge as well as red mucus presence in the respiratory tract, considerable venous plethora of internal organs, hemicardia engorgement, punctuate hemorrhages on the heart and lungs surface. In case agony comes prior to death, dense blood clots are observed in the heart and vessels – red in case of short-term agony and yellowish-white or white under long-term agony.

The following basic vital functions of organism termination, signs of natural death gradually develop in organism:

Cooling of dead body (algor mortis) develops due to the termination of production of heat in the body of the deceased and alignment the temperature of the deceased body with the environment (every hour of death gives 1 degree temperature decrease). In some cases (death from tetanus, strychnine poisoning) the temperature of the deceased body may even rise.

Cadaveric rigidity (rigor mortis) is expressed in the hardening of muscles. Cadaveric rigidity is caused by disappearance after death from muscles adenosintriphosphate acids and the accumulation of lactic acid in them. Cadaveric rigidity develops 2–5 hours after death and by the end of the first day involves all muscles.

Cadaveric desiccation is caused by evaporation of moisture from the body surface. Cadaveric desiccation can be local and general (mummification of a corpse). First of all cadaveric desiccation is marked on the skin, eyeballs and mucous membranes. Mucous membranes become dry, dense, brown. Dry, yellow-brown, a pergament-like spots appear on the skin. The clouding of the cornea is noted. The sclera are dry, brownish, with triangular-shaped spots (their basis are turned to the cornea and tops are turned to the corner of the eye) are seen on the dead body.

Redistribution of blood in the corpse is characterized by the overfilling of veins by the blood and the devastation of arteries by the blood. In veins and right heart cavities postmortem clotting is observed. Postmortem blood clots are yellow or red, with a smooth surface, elastic consistency; freely lie in the vessel or in the chamber of the heart that allows to distinguish them from thrombi.

The origin of ***cadaveric spots*** is conditioned by the redistribution of blood in the dead body. ***Cadaveric hypostases*** are formed in 3–6 hours after death. Cadaveric hypostases look like dark purple spots, pale under the pressure. Cadaveric spots do not arise in those parts of the body which are exposed to pressure (area of the sacrum, shoulder blades at position of the corpse on the back). The areas of cadaveric hypostases filter by plasma of the blood. Thus, there are recent cadaveric spots (***cadaveric imbibition***), which have reddish-pink color and not disappear under the pressure.

Cadaveric decomposition is connected with the processes of autolysis and decay of the corpse.

CLINICAL-ANATOMICAL CONFERENCE

Clinical-anatomical conferences are a kind of joint activity of pathologists and physicians. Clinical-anatomical conferences have been held in Ukrainian hospitals since 1930 year due to proposition of professor I.V. Davydovskiy. Clinical-anatomical conferences always take place in hospitals according to the order of the Ministry of Health of Ukraine No. 81 dated 12.05.1992. Clinical-anatomical conferences may be general-hospital, surgical, therapeutic, obstetrical-gynecological and others.

The main tasks of clinical-anatomical conferences are improvement of doctor's qualification, increase of the quality of clinical diagnosis and patient's treatment.

Clinical-anatomical conferences are held in hospitals once a month in the work time. All doctors of the hospital must be present on the clinical-anatomical conference. The agenda of the clinical-anatomical conference is reported to all doctors of the hospital not later then 7 days before the conference. The agenda of the conference should not be overloaded by discussion more than two cases.

Preparation of clinical-anatomical conference is carried out by the deputy head physician and the chief of pathology department. During the preparation for clinical-anatomical conference it is necessary to choose a suitable case, to study the history of the disease, to prepare demonstration material.

The following item are to be discussed on the clinical-anatomical conference:
– cases that have a scientific and practical interest;
– atypically proceeding and rare diseases;
– cases of iatrogenic disease and medical pathomorphosis;
– cases of deaths on the operating table or as a result of medical intervention;
– errors in polyclinic, clinical or pathoanatomical diagnosis;
– shortages of rendering medical aid;
– various cases of divergences of clinical and pathoanatomical diagnoses.

Annual report of the chief of pathoanatomical department with data containing analysis of all autopsy cases must be discussed in one of the clinical-anatomical conferences.

When the case is selected for the clinical-anatomical conference, the agenda is made and sent to departments of the hospital (not later than 7 days before the conference) and speakers are appointed (the doctor, who treated the patient, the pathologist, who made the autopsy, and the reviewer).

The chairman from among the most highly qualified experts, his deputy and the secretary shall be appointed for the conference. At the beginning of the clinical-anatomical conference the chairman announces the agenda. Then he gives the floor for presentation to the doctor, the pathologist, and the reviewer. The presentation format includes medical history (clinical pattern, diagnosis, treatment, severity) presented by the doctor, and gross autopsy findings (macroscopical and microscopical changes) presented by the pathologist. The reviewer assesses the quality of medical documents, diagnostic and medical actions, timeliness and rightness of operations, causes of

diagnostic divergences. Then discussion takes place. Everybody can give his/her own opinion. If there is any divergence between the clinical and pathoanatomical diagnoses, the following aspects must be discussed: category of divergence, causes of divergence, importance of diagnostic divergence for the patient. After this the chairman sums up the discussion.

In order to make clinical-anatomical conference favorable for practical public health service it is necessary to provide their good preparation, interesting holding, high scientific level as well as sufficient activity of doctors and an experienced chairman who can sum up the discussion. The conference room should be comfortable and well equipped.

The atmosphere of criticism, self-criticism and benevolentness should be during the whole clinical-anatomical conference. It is necessary to tell the audience about any mistakes in order to avoid their repetition. The administration of the hospital, using the conclusion of the clinical-anatomical conference, should carry out measures for elimination of defects in the organization of medical aid.

MEDICAL-CONTROL COMMISSION

It is impossible to discuss all shortages of diagnostic and medical activity of the hospital during clinical-anatomical conferences, therefore in medical institutions it is organized by the order of the head physician special medical-control commission.

Tasks of medical-control commission are

– definition of the quality and correctness of the diagnosis and treatment;

– identification of defects in therapeutic and preventive measures at all stages of hospitalization;

– planning the ways of the elimination and prevention of shortages of medical care of patients in the future.

Medical-control commission is headed by the head physician of the hospital or the deputy of the head physician. Medical-control commission consists of 3–5 persons (the chiefs of departments of the hospital).

IATROGENIC REACTIONS AND DISEASES

From the Greek words *iatros* meaning "medical" and *genea* meaning "origin", ***iatrogenic*** means the occurrence of negative effects caused by a medical procedure. According to The ICD-10, ***iatrogenic diseases*** are any undesirable or adverse effects of preventive, diagnostic, therapeutic interventions or procedures which lead to the infringement of functions of the body, limiting of usual activity, disablement or even death; complications of medical interventions which may arise as a result of false and correct actions of doctors.

It is frequently thought that iatrogenic means "error" or "neglect", but iatrogenic effects and medical errors are opposite terms, not synonymous ones. An error is a mistake or the result of ignorance and, thus, opposes the concept of medical attitude, whereas an iatrogenic effect is the consequence of an accurate action based on a correct orders, indication and adequate criteria and can be predicted by the physician. When, in trying to heal, relieve or treat a patient, the physician (like any other health care worker) generates psychological, functional or organic illness that takes the from of pain, disease or disturbance, he is being iatrogenic. The diagnosis may be difficult, delayed or initially missed as iatrogenic illness can be generated directly from the doctor-patient relationship or by means of agents used in the diagnostic search, or as a consequence of a therapeutic, instrumental (technical) or drug-related measure.

Iatrogenic disease is a serious problem with a great social impact. The world literature shows that the incidence of iatrogenic events in the hospitalized population varies widely, ranging from 6 to 65%. It occurs very frequently, is expensive and is potentially responsible for high morbidity and mortality. In the U.S., it is estimated that iatrogenic causes are responsible for 225,000 deaths each year, thus being the third leading cause of death after heart disease and cancer.

Among ***the causes of iatrogenic diseases*** objective and subjective factors are distinguished. ***The objective factors*** are the imperfection of medicine, the incurability of some pathology, the necessity of the realization of invasive procedures for confirmation or refutation of the diagnosis. ***The subjective factors*** of the beginning of iatrogenic diseases are connected with the individual qualities of the medical worker (the insufficiency of professional skills, the inability to collect correctly the information about the disease of the patient, disinterest in the estimation of the condition of the patient).

Iatrogenic reactions and diseases are divided into 4 groups

1. Connected with diagnostic procedures: instrumental damage of organs by endoscopes and other diagnostic appliances, radiation damage of a patient during X-ray and radiological examination, allergic and toxic reactions to contrast substances.

2. Connected with therapeutic actions: drug disease due to drug intoxication; allergic reactions to drugs; radiation damage during radiation therapy; puncture, injection, infusion damages of organs and tissues; operational stress and mechanical damage of organs.

3. Connected with preventive measures: reaction to vaccination; infectious and inflammatory damages due to injections.

4. Information: reaction to words of medical workers; effects of modern literature, medical books, articles; self-treatment under the influence of newspapers, appeals to witch doctors.

The risk factors for the occurrence of iatrogenesis during hospitalization are: age, number of comorbidities, complexity of the diseases, use of multiple drugs, length of hospital stay, severity of illness at admission and functional status.

The role of the pathologist in the investigation of dead bodies is central to the identifying and monitoring of iatrogenic pathology.

PATHOMORPHOSIS

A man in the era of scientific and technical revolution is exposed by powerful, long, various influences of aggressive factors of the environment, that affect on the integration systems of maintenance of the homeostasis, interrelation of the human body with microorganisms and medical products. There are previously unknown features of the course of various diseases, new diseases, new syndromes, thus the phenomena of pathomorphosis develops.

Pathomorphosis (from Greek *pathos* – suffering, disease and *morphe* – kind, shape) – essential and steady changes of character of the disease, causes of death and properties of various diseases under the influence of various factors.

The term ***"pathomorphosis"*** has been used for the first time in the 30 years of the twentieth century in the foreign literature as the amendment to the presentation accepted in the pathology about stability of nosological forms. W. Hellpach meant first of all changes of clinical and morphological forms of syphilis under the influence of active chemotherapy.

In 1956 W. Doerr specified such forms of pathomorphosis, as natural pathomorphosis (spontaneous changes in the course of the disease arising from changes of external and internal causes of the disease) and induced or therapeutic pathomorphosis (changes in the disease caused by therapeutic effects).

In literature the term "pathomorphosis" was introduced by Ya.L. Rapoport only in 1962. Professor Ya.L. Rapoport singled out one important feature – induced pathomorphosis was not fixed genetically, therefore are possible the reversal of the disease, returning to its classical forms and manifestations after removal of the therapeutic factor.

V.V. Serov gave the following definition of "pathomorphosis": pathomorphosis is nosomorphosis as in wide ("panorama" of diseases) and narrow (some disease) sense.

At the present stage scientists identify two ***forms of pathomorphosis***: spontaneous (idiopathic, natural) and induced (therapeutic). Spontaneous pathomorphosis are transformations in the course of nosological forms which are caused by changes of external causes of disease, influence of factors of environment (ecology), action of the internal causes (the constitution, features of the reactivity of the organism), changes of properties of the pathogenic organism. Manifestations of induced pathomorphosis arise in relatively short periods of time under the influence of treatment by new drugs, radiation therapy and other.

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Навчальне видання

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Губіна-Вакулик Галина Іванівна
Гаргін Віталій Віталійович
Мирошниченко Михайло Сергійович
Плітень Оксана Миколаївна

Біопсійно-секційний курс (Клінічна патологія)

Навчальний посібник для практичних занять з клінічної патології для англомовних студентів медичних ВНЗ

Відповідальний за випуск І.В. Сорокіна
Комп'ютерний набір та верстка М.С. Мирошниченко
Редакція англійською мовою І.В. Корнейко

Формат А5. Ризографія. Ум. друк. арк. 6,2.
Тираж 150 прим. Зам. № 11-2822.

Редакційно-видавничий відділ
ХНМУ, пр. Леніна, 4, м. Харків, 61022
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Свідоцтво про внесення суб'єкта видавничої справи до
Державного реєстру видавництв, виготівників і розповсюджувачів видавничої
продукції серії ДК № 3242 від 18.07.2008 р.