Ministry of education and science of Ukraine
V.N. Karazin Kharkiv National University

MANAGING PATIENTS WITH TUBERCULOSIS AND HIV INFECTION

Methodical recommendations
for self-study for practical classes of students of higher medical education
of the 5th year of study in the discipline "Phthisiology"

Electronic resource

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М 24

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Managing patients with tuberculosis and HIV infection : methodical recommendations
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The methodical recommendations were developed by the team of teachers of the Department of General and Clinical Immunology and Allergology of the Medical Faculty of V.N. Karazin Kharkiv National University. An indicative map of the work of candidates for higher medical education is provided, which clearly defines, consistently and in detail describes the recommendations for preparation at each stage of practical teaching. The list of basic theoretical issues and practical skills, structure and content of the subject, test tasks for control of initial and final level of knowledge, basic and additional literature, the appendices contain links to electronic resources of educational materials of the department.

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INDICATIVE MAP OF THE WORK FOR APPLICANTS OF HIGHER MEDICAL EDUCATION IN PREPARATION FOR PRACTICAL CLASSES

	Preparatory stage:
1.	Know the **interdisciplinary integration** of the topic of practical training with acquired theoretical knowledge and practical skills in basic disciplines (medical biology, medical and biological physics, Latin, human anatomy, normal and pathological physiology, biological and bioorganic chemistry, pathological anatomy, pharmacology, philosophy). To know the terminology (and in Latin transcription).
2.	**Motivational characteristics** and **substantiation of the topic** of practical training for the **formation of clinical thinking**, in particular for the further formation of skills to apply knowledge in diagnosing the main symptoms and syndromes and the possibilities of modern laboratory and instrumental methods of examination in further study and future professional activity.
3.	Get acquainted with the types of educational activities, information on which is provided on the reference stands of the department: **thematic- calendar plans of lectures, practical classes and extracurricular independent work of students** of higher medical education of the 5th year of study, corresponding to the syllabus of the discipline «Phthisiology».
4.	Use of the corresponding basic and additional **educational and methodical literature**: • **textbooks** and **manuals** (printed and electronic versions), the list of which is provided in these guidelines after the theoretical section; • **educational and methodical materials of the department** (methodical recommendations for independent preparation of applicants for higher medical education of the 6th year of study in the discipline "Management of tuberculosis patients in combination with HIV infection" for practical classes and for extracurricular independent work); • attending **lectures** (classroom lecture support of the educational process using multi-media presentations) - according to the thematic-calendar plan. For preparation to use the **printed editions** which can be received in library, and or **electronic** versions of these editions which are placed on the official website of V.N. Karazin KhNU http://www.univer.kharkov.ua/en/departments - see Appendix 1; and in the open interactive database of the electronic archive of resources of the Repository of VNKarazin KhNU http://ekhnuir.univer.kharkov.ua (navigation: Medical faculty / Educational editions. Medical faculty) - see Appendix 2. It is desirable to note the main issues in the form of abstracts.

	Main stage:
1.	To achieve the educational goal of the practical lesson and master the theoretical part of the topic - you need to **STUDY** and **KNOW** the answers to the **main theoretical questions** on the topic of the lesson (see list of basic theoretical questions), which will be checked by the teacher by oral and / or written questioning(correction, clarification, addition of answers) at the main stage of the practical lesson.
2.	**BE ABLE** to solve with explanations theoretical, test (to control the initial and final level of knowledge), situational problems that are proposed for mastering the topic.
3.	**MASTER PRACTICAL SKILLS** on the topic of the class: ● Take an active part in the demonstration by the teacher of the methodology of studying a case patient, and practice practical skills at the patient's bedside under the supervision of the teacher. ● Supervise patients, give interpretation of the obtained laboratory and instrumental research methods, be able to use the necessary devices, instruments, and instruments. ● Establish a syndromic diagnosis, make a differential diagnosis, analyze the principles of treatment, write prescriptions for basic medicines.
4.	**PERFORM** obligatory tasks provided for independent classroom and extracurricular work.
	Final stage:
1.	On the basis of mastering theoretical knowledge and practical skills on the topic to define methods of microbiological diagnostics, etiotropic therapy and prophylactics of the infections caused by pathogenic M.tuberculosis for further training in the medical profession.

The purpose and main tasks of work on the topic of practical training "Managing patients with tuberculosis and HIV infection"

To study the features of diagnosis of co-infection with tuberculosis / HIV, their interaction on the course and prognosis of treatment of both diseases, to teach graduates of higher medical education in the 5th year of training modern tactics of management of patients with co-infection with TB / HIV.

KEY ISSUES:

Applicants for higher medical education in the 5th year of study must KNOW (basic theoretical issues):

1. etiology of tuberculosis and HIV infection, pathogenic factors of pathogens;
2. epidemiology of tuberculosis and HIV infection;
3. pathogenesis of tuberculosis in HIV-infected people;
4. clinical manifestations of tuberculosis and HIV infection;
5. laboratory diagnosis of tuberculosis and HIV infection;
6. the impact of tuberculosis on the course of HIV infection
7. principles of treatment;
8. principles of prevention;
9. tactics in case of emergencies;
10. prognosis of tuberculosis / HIV co-infection;
11. medical examination rules.

Applicants for higher medical education in the 5th year of study must BE ABLE (basic practical skills on the topic of practical training):

1. follow the basic rules of work at the bedside of a patient with co-infection with tuberculosis / HIV;
2. collect a history of the disease with an assessment of epidemiological data;
3. examine the patient and identify the main symptoms and syndromes of tuberculosis / HIV, justify the clinical diagnosis for timely referral to the hospital;
4. conduct a differential diagnosis of tuberculosis and HIV infection;
5. on the basis of clinical examination to timely identify possible complications of co-infection with tuberculosis / HIV, emergencies;
6. draw up medical documentation on the fact of establishing a preliminary diagnosis of “tuberculosis / HIV” (emergency notification to the district epidemiological department);
7. make a plan for laboratory and additional examination of the patient;
8. interpret the results of laboratory tests;
9. analyze the results of specific diagnostic methods depending on the material and duration of the disease;
10. make an individual treatment plan taking into account epidemiological data, stage of the disease, the presence of complications, severity, allergy history, comorbidities; provide emergency care at the pre-hospital stage;
11. make a plan of anti-epidemic and preventive measures in the center of infection

Materials of pre-classroom independent work

Basic knowledge, skills, abilities necessary for studying the topic (interdisciplinary integration)

Discipline	To know	Be able to do
Previous disciplines		
Microbiology	Properties of human Immunodeficiency virus Properties of M. tuberculosis; methods of diagnosing Tuberculosis and HIV infection	Interpret the results of methods of diagnosis of tuberculosis and HIV infection.
Physiology	Parameters of physiological norm of human organs and systems; normal indicators of laboratory examination (general analysis of blood, urine, biochemical analysis of blood, parameters of urine, electrolytes, etc.).	Evaluate laboratory test data
Pathophysiology	The mechanism of dysfunction of organs and systems in the development of TB and HIV	Interpret pathological changes in the results of laboratory examination in disorders of organs and systems of different genesis.
Immunology and allergology	The basic concepts of the subject, the role of the immune system in the infectious process, the impact on the elimination of the pathogen from the human body.	Evaluate immunological data.
Epidemiology	Epidemic process (source, mechanism of infection, routes of transmission) in TB and HIV, the concept of epidemic, pandemic; prevalence of TB and HIV in the world and in Ukraine.	Collect epidemiological history, carry out anti-epidemic and preventive measures in the center of infection; follow the rules of work in a TB and HIV hospital.
Neurology	Clinical and laboratory signs of tuberculosis meningitis.	Timely diagnose, assess the extent of the lesion. Prescribe appropriate examination and treatment.

Surgery	Clinical and laboratory signs of hemoptysis, pulmonary hemorrhage, spontaneous pneumothorax, emergency care tactics.	Diagnose these complications in a timely manner, prescribe appropriate examination, and provide emergency care.
Propaedeutics of internal diseases.	Methods and main stages of clinical examination of the patient.	Collect anamnesis, conduct a clinical examination of the patient, identify pathological symptoms and syndromes. Analyze the obtained data
Clinical pharmacology	Pharmacokinetics and pharmacodynamics, side effects of antituberculosis and antiretroviral drugs	Prescribe treatment depending on the categorical classification, individual characteristics, age of the patient, choose the optimal method, speed and volume of drug administration.
Resuscitation and intensive care	Emergencies: • spontaneous pneumothorax • pulmonary hemorrhage • hemoptysis • atelectasis • acute pulmonary failure	Timely diagnose and provide emergency care in emergencies: •spontaneous pneumothorax • pulmonary hemorrhage • hemoptysis • atelectasis • acute pulmonary failure
Intra-subject integration		
Infectious diseases	Features of infectious diseases. Principles of diagnosis, treatment, prevention of infectious diseases. Pathogenesis, epidemiology, clinical manifestations, laboratory diagnosis, possible complications of TB and HIV co-infection. Features of clinical manifestations of TB/HIV. Principles of prevention and treatment.	Carry out differential diagnosis of TB with other infectious diseases. Recognize TB, its complications, interpret laboratory test data. Prescribe treatment. Provide emergency care at the prehospital stage.

Test tasks to control the INITIAL LEVEL OF KNOWLEDGE:

1. What is the most important diagnostic sign of joining tuberculosis in an AIDS patient?

A. Positive tuberculin sensitivity after Mantoux test.
B. Detection of the MTB in sputum.
C. The presence of symptoms of tuberculosis intoxication.
D. Information on past tuberculosis.
E. The presence of focal shadows on the X-ray.

2. What is the sensitivity to tuberculin after the Mantoux test with 2 TO PPD-L for characteristic of patients with HIV / AIDS?

A. Mostly negative.
B. Doubtful.
C. Weakly positive.
D. High or hyperergic.
E. Vesiculo-necrotic.

3. The appearance of which symptoms (complaints) may indicate a complication of AIDS by tuberculosis?

A. Intoxication.
B. Weight loss.
C. Cough.
D. Chest pain.
E. All of these symptoms accompany AIDS / TB.

4. What disease can contribute to the development of tuberculosis?

A. Hypertensive disease.
B. Infectious mononucleosis.
C. HIV infection.
D. All these diseases.
E. None of the above.

5. Diagnosis of HIV / AIDS-associated tuberculosis is based on:

A. detection of HIV antibodies, anemia, leukopenia, lymphopenia, thrombocytopenia
B. a decrease in the number of CD4 lymphocytes less than 500 cells / ці of blood
C. decrease in the ratio of SD4 / SD8 less than 1
D. negative reaction to tuberculin at MBT + in sputum
E. all these criteria

6. Patients with which diseases belong to the risk group for tuberculosis:

A. HIV-infected;
B. patients with diabetes mellitus;
C. patients with occupational lung diseases;
D. patients who are constantly taking corticosteroids, radiation therapy;
E. all of the above

7. Which of the following is characteristic of the tuberculosis process in the late stages of HIV infection?

A. prolonged intoxication with a negative reaction to the Mantoux test is expressed;
B. diffuse infiltrates with localization in both the upper and middle and lower lungs;
C. mainly extrapulmonary lesions, enlargement of intrathoracic lymph nodes, generalized lymphadenopathy;
D. in half of patients - lack of MBT in sputum;
E. all of the above is characteristic.

8. In an AIDS patient, X-ray examination revealed massive focal-infiltrative shadows in the lower lobes of both lungs. The reaction to the Mantoux test with 2 TO PPD-L is negative. What diagnosis is most likely in the patient?

A. bilateral lower lobe pneumonia;
B. miliary tuberculosis;
C. carcinomatosis;
D. bronchiectasis;
E. mycobacteriosis.

9. At the level of which population of lymphocytes is assessed the state of the immune system in HIV / AIDS infection?

A. CD 6
B. CD 4
C. CD 2
D. CD 8
E. CD 3

10. The patient is 38 years old, extrapulmonary tuberculosis, candidiasis of the esophagus, trachea and bronchi, cachexia. HIV-positive for 8 years. Subsequently, on the left leg there were cherry-colored spots with a cyanotic tinge, painless, dense to the touch. The development of any AIDS-associated disease should be considered:

A. skin vasculitis
B. skin lesions caused by herpes simplex viruses
C. Kaposi's sarcoma
D. hair leukoplakia
E. erysipelas

Standards of answers: 1 - B. 2 - A. 3 - E. 4 - C. 5 - E. 6 - E. 7 - E. 8 - E. 9 - B. 10 - C.

STRUCTURE AND CONTENT OF THE TOPIC

Background. Tuberculosis and HIV / AIDS are a global problem in the public health system. Tuberculosis is the leading cause of death for people living with HIV / AIDS, and HIV is the most important factor in the development of the TB epidemic in countries with high HIV prevalence. The WHO estimates that about 20 million people have died in the 25 years since the HIV pandemic. Today, more than 50 million people, or more than 1% of the world's adult population, are infected with HIV. In the period 1987-2007, 122,314 cases of HIV infection were officially registered in Ukraine, including 22,424 cases of AIDS and 12,490 deaths from AIDS-related diseases. In Ukraine, the rapid spread of HIV infection has been registered since 1997 (8913 cases), which is due to the introduction of HIV among injecting drug users.

Another group at high risk of HIV infection in Ukraine are young people in prisons (penitentiaries). Analysis of the structure of secondary (opportunistic) diseases showed that at the beginning of the HIV epidemic (1987-1992), when AIDS patients were still few, the structure of opportunistic diseases was dominated by Kaposi's sarcoma (32%), manifest forms of CMV infection). In recent years, tuberculosis has become the most common opportunistic disease in Ukraine. HIV infection increases the risk of developing active tuberculosis and, conversely, tuberculosis adversely affects HIV-associated tuberculosis. More than 30% of HIV-infected people have tuberculosis and about 30-40% of those who die from tuberculosis. The number of TB patients among HIV-infected patients is constantly growing. Such interaction between the two infections requires healthcare institutions to pay special attention to the fight against tuberculosis among HIV-infected people within the framework of the overall strategy for combating HIV infection.

The impact of HIV infection on the development of tuberculosis. Both HIV infection and tuberculosis affect the immune system, mainly the cells of the lymphatic system and especially the lymph nodes. The difference is that the pathogen of HIV directly affects CD4 - T-lymphocytes. The tuberculous process destroys primarily the lymph node tissue. Tuberculosis has a negative effect on the progression of HIV infection. In vitro studies have shown an increase in the ability of HIV to replicate under the influence of MBT antigens, which is confirmed by an increase in the number of copies of RNA virus in the peripheral blood.

Most cases of tuberculosis in HIV-infected patients are associated with reactivation of latent tuberculosis infection, a significant number of cases of tuberculosis in HIV-infected adults are associated with endogenous reinfection. When the immune system is affected by HIV infection, the Office, without encountering obstacles to its development, begin to actively multiply in the lymph nodes, followed by the development of specific granulomas and caseosis. Hence the peculiarities of the clinical course of tuberculosis in patients with HIV infection, lymph nodes are involved in the process, tuberculosis infection spreads in the body by lymphogenic and lymphohematogenous routes. Tuberculosis is characterized by severe lymphotropy, the development of exudative

reactions and progressive course.

Absolute and relative decrease in the number of CD4 - T-lymphocytes changes the relationship in the cellular immune system, which is the main course of tuberculosis: the differentiation of macrophages and the formation of specific granulation tissue is disrupted. If in the early stages of HIV infection, the morphology of tuberculous inflammation changes, then in the late period of AIDS specific granulomas do not form.

Influence of tuberculosis on the course of HIV infection. Infections affecting HIV-infected people, their clinical manifestations depend on the stage of HIV infection and the degree of reduced immunity. Highly pathogenic pathogens, such as pneumococci, salmonella (other than typhus and parasites) and M. tuberculosis, can cause the disease at any stage of HIV infection. Tuberculosis is the most virulent infection that occurs earlier than others, including earlier mycobacteriosis, which causes *M.avium* complex. Less pathogenic, including opportunistic pathogens (*Candida spp*, *Cryptococcum neoformans*, *Toxaplasma gondii* and atypical MBT) cause the disease with a more pronounced decrease in immunity. Disseminated infections develop in the late stages of HIV infection with significant immunodeficiency.

In HIV-infected people, the presence of any infection, including tuberculosis, provokes a faster spread of HIV infection. This can manifest itself in its rapid progression and development of AIDS. HIV infection causes the spread of tuberculosis by increasing the risk of developing tuberculosis during primary infection and due to reactivation of endogenous infection. During the year, 5-15% of co-infected with HIV and M. tuberculosis develop tuberculosis.

Signs and criteria for diagnosing the disease. All HIV-infected patients should be screened for or at risk of developing tuberculosis, and all TB patients should be offered counseling and testing for HIV. The main reasons for this assessment are:

- HIV-infected patients are at risk for the presence or development of active tuberculosis as one of the leading causes of death;
- HIV infection affects the course of tuberculosis and the effectiveness of treatment;
- active tuberculosis affects the course of HIV infection and the effectiveness of antiretroviral therapy;
- Tuberculosis can be one of the manifestations of stage III or IV HIV infection, which requires treatment.

Risk assessment and diagnosis of tuberculosis in HIV-infected people. Tuberculosis patients are identified by examining HIV-infected patients who have sought medical help at a regional AIDS center or public health facilities with a network and / or symptoms of tuberculosis; the diagnosis of tuberculosis is confirmed by a tuberculosis specialist; registration of a case of tuberculosis is carried out in the regional anti-tuberculosis dispensary, in accordance with the current legislation. Particular attention should be paid to patients with:

- respiratory symptoms;

- bronchopulmonary symptoms and symptoms of intoxication lasting more than 2 weeks;
- known contact with a patient with active pulmonary tuberculosis at home or in the immediate environment;
- the presence of additional factors of increased risk of infection (injecting drug users, alcohol abuse, imprisonment).

Symptom complexes that require mandatory examination for tuberculosis

Bronchopulmonary symptoms	**Symptoms of intoxication lasting more than 2 weeks**
Cough dry or with sputum for more than 2 weeks	Febrile, subfebrile fever
Chest pain associated with breathing	Weight loss, loss of appetite, night sweats
Hemoptysis, pulmonary hemorrhage	Weakness

In HIV-infected individuals, pulmonary tuberculosis must be differentiated from other pulmonary pathology. A number of diseases can occur in HIV-infected people and were accompanied by a similar course, cough, fever, sometimes chest symptoms and changes in the radiographic picture.

Radiological signs and the most probable etiology of the disease

Focal	*M. tuberculosis*, *Pneumocystis carinii*
Diffuse	M. tuberculosis, P. carinii, cytomegalovirus, fungi, Kaposi's sarcoma, hypoproteinemia
Dissemination	Kaposi's sarcoma (large nodes), *M. tuberculosis* (miliary), fungi
Pneumothorax	P. carinii
Mediastinal lymphadenopathy	*M. tuberculosis*, *M. avium*, *M. intracellulare*, Kaposi's sarcoma, lymphoma, fungi
Pleural effusion	Parapneumonic effusion, *M. tuberculosis*, Kaposi's sarcoma, lymphoma, fungi, cardiomyopathy
Formation of cavities	M. tuberculosis (high level of CD4 +), Pneumocystis Carinii (low level of CD4 +), Pseudomonas Aeruginosa (low level of CD4 +), R.egui, fungi, lymphoma

Depending on the periods of development of HIV infection and histopathological immune reactions in combined forms of tuberculosis and HIV infection in the development of the disease there are 3 stages:

1. Early (granulomatous): formation of specific granulomatous tissue reactions and relatively intact cellular immunity with a decrease in the number of CD4 -T cells from 500 to 250. In the affected areas a significant number of epithelial and giant Langhans cells with accumulation of CD4 -T lymphocytes macrophages with active cytoplasm. The most common clinical form is local pulmonary tuberculosis.

2. Tuberculosis, HIV infection with moderate HIV immunosuppression (hyporeactivity): disappearance of giant Langhans cells, reduction of epithelioid cells, CD4 -T-lymphocytes and macrophages with active cytoplasm. In the center of an infection the zone of a necrosis increases and the quantity of KSB increases. Clinical forms: common pulmonary tuberculosis and extrapulmonary tuberculosis.

3. Tuberculosis, HIV infection with severe immunosuppression (miliary process with anergy): no specific granulation tissue reaction of epithelioid and giant Langhans cells and a small number of CD4 -T cells in the affected area. Instead of caseous necrosis, coagulation necrosis and melting with a large number of CSBs are observed, which continue to multiply in bacteriophages. Clinical forms - miliary, generalized tuberculosis with multiorgan lesions, including meningitis with early death.

HIV infection not only causes the spread of tuberculosis, but also changes its clinical picture, which depends on the stage of HIV infection and the degree of immunodeficiency.

Features of tuberculosis at each stage of HIV infection

Stage of HIV infection	Features of tuberculosis
I	Typical course of pulmonary tuberculosis: infiltrates and foci in the upper lobes, cavities, fibrosis, detect AFB and MTB in sputum
II	Typical course of pulmonary tuberculosis: infiltrates and foci in the upper lobes, cavities, fibrosis, detect AFB and MTB in sputum
III	Atypical course of pulmonary tuberculosis: infiltrates in the lower lobes, no cavities, no fibrosis, rarely detect AFB and MTB in sputum. Atypical granuloma and the absence of typical morphological signs of tuberculosis determine the AFB and MTB in the affected organs. Extrapulmonary forms of tuberculosis.
IV	The primary form of tuberculosis has a septic character: the Office is determined in the case of blood seeding (miliary tuberculosis, tuberculous meningoencephalitis).

In the early stages of mild and moderate immunodeficiency, secondary tuberculosis develops due to reactivation or reinfection, which is little different from normal tuberculosis. With a decrease in immunity, pulmonary tuberculosis without bacterial excretion, which resembles primary pulmonary tuberculosis and extrapulmonary tuberculosis, develops more often. The more pronounced the immunodeficiency, the more often miliary tuberculosis occurs, the more difficult it is to diagnose. Due to this, it is easier to diagnose tuberculosis in the early stages of HIV infection: bacterial excretion is more often determined during this period; in the later stages of HIV infection, pulmonary tuberculosis without bacterial excretion and extrapulmonary (including miliary) are more common.

One of the reasons for the delay in the diagnosis of tuberculosis in HIV- infected and AIDS patients is the atypical course of tuberculosis and its clinical features as an associated disease. In the early stages of HIV infection, the course of tuberculosis is not much different from tuberculosis in vilnegative individuals with a predominant lung lesion. In the later stages of HIV infection, tuberculosis in 50-60% of patients has extrapulmonary localization and joins AIDS more often when the number of CD4-T lymphocytes decreases to 200 cells per 1 mm3 or less. Miliary tuberculosis and tuberculous meningitis develop mainly when the number of CD4-T lymphocytes is about 100 in 1 mm3 or less.

The structure of tuberculosis does not differ between HIV-negative and HIVpositive people, except that HIV-infected patients are less likely to find focal forms, more often infiltrative, fibro-cavernous and generalized forms, which is not due to the peculiarities of tuberculosis, but insufficient contingent preventive fluorographic examination of the chest. In AIDS patients, the frequency of infiltrative form of tuberculosis remains the same (51.7%) as in HIV-positive and vilnegative persons, but the frequency of disseminated form increases (41.4%), the frequency of focal (5.2%) and fibrous -cavernous (1.7%) forms of tuberculosis. The proportion of disseminated tuberculosis and tuberculosis of intrathoracic lymph nodes is 50-70%.

Clinical picture of tuberculosis in the early and late stages of HIV infection

Manifestation of pulmonary tuberculosis	Stage of HIV infection	
	early	late
The clinical picture	Often resembles a secondary one	Pulmonary tuberculosis often resembles primary pulmonary tuberculosis
MTB in sputum (bacterioscopically)	Often detected	Rarely detected

Radiological signs	Destruction of a pulmonary parenchyma is often found.	Infiltration without Disintegration is often found.

The main clinical manifestations of tuberculosis in HIV-infected:

- asthenia;
- constant or intermittent fever (more than 1 month);
- sharp sweating;
- weakness;
- prolonged dry or with a small amount of sputum cough (more than 3 weeks);
- hemoptysis;
- chest pain, shortness of breath;
- significant weight loss;
- diarrhea;
- in 1/3 of cases at inspection in 2-4 weeks. from the beginning of the disease lymphadenopathy is detected, enlarged mainly cervical and axillary, intrathoracic, rarely inguinal. Peripheral l / nodes, dense, bumpy, immobile on palpation. (In HIV-negative patients, peripheral lymph nodes are not enlarged).

Clinical symptoms typical of HIV infection in patients with TB

Anamnesis	History of sexually transmitted diseases; Herpez zoster (shingles); recurrent pneumonia; bacteremia (Salmonella thphimurium)
Symptoms	Weight loss (more than 10 kg or 20% of primary weight); diarrhea (more than a month); pain when swallowing (characteristic of oropharyngeal candidiasis); burning pain in the lower extremities (peripheral sensory neuropathy)
Objective signs	Traces of scars from Herpez zoster; papular rash; Kaposi's sarcoma; symmetrical generalized lymphadenopathy; oral candidiasis; oral hair leukoplakia; persistent painful genital ulcers

It was found that HIV-negative people are more likely to have an inflammatory reaction, parenchymal disintegration, bronchial lesions than HIVpositive people. This

means that coughing and hemoptysis are more common in HIV-negative people, while weight loss and fever are more common in HIVpositive people. In general, the symptoms of intoxication (weight loss, fever) and respiratory symptoms (dry cough and sputum, shortness of breath) in HIV- infected and HIV-negative patients differ little, but are more common in AIDS patients. In HIV-infected and AIDS patients, the symptoms of intoxication are determined 2-3 times more often, they occur later and last more than 5 months, and the symptoms of respiratory disorders join earlier and last 1-3 months. until the diagnosis of tuberculosis. HIV-negative people, on the other hand, first develop symptoms of intoxication and last 1-3 months, and symptoms of respiratory disorders last equally often - from 1 month. and more than 5 months. until the diagnosis of tuberculosis.

The peculiarities of the course of tuberculosis, depending on the HIV status, can be the cause of untimely diagnosis and treatment of tuberculosis. In addition to the peculiarities of the course of tuberculosis, the reason for late diagnosis in HIV-infected people may also be an atypical localization of the tuberculosis process in the lungs. HIV-infected people with prolonged fever and other symptoms of intoxication should be screened for tuberculosis. Diagnosis of tuberculosis is extremely necessary in patients with a high risk of developing TB in patients with a small number of CD4 -T-lymphocytes in the blood (less than 100 in 1 mm3).

Examination methods for suspected TB on the background of HIV infection:

Mandatory examinations	***Additional examinations (in level 3 medical institutions)***
Collection of complaints and medical history	Computer tomography of the chest
3-times done analysis of sputum or other biological material by Ziel- Nielsen microscopy	Fibrobronchoscopy with BAL for microscopic and bacteriological examination and biopsy of the affected areas
Chest Xray. Tomography of the affected parts of the lungs	Transthoracic or transbronchial or open puncture lung biopsy; biopsy of enlarged lymph nodes with sampling for microscopic and bacteriological examination
3-time analysis of sputum or other biological material by culturing	Thoracoscopy with pleural biopsy with sampling for microscopic and bacteriological examination
	Pathohistological examination of biopsy material (in case of suspected extrapulmonary TB)

	Fibroscopic methods of research at defeat of concrete bodies and systems (gastro-; colonolaparoscopy)
	Ultrasound of the abdominal cavity
	Accelerated bacteriological methods of MTB detection: BACTEC
	Molecular genetic laboratory methods: nucleic acid amplification tests (PCR)
	Trial antimycobacterial therapy
	Tuberculin diagnostics (Mantoux test)

Features of the reaction to tuberculin depending on the stage of HIV infection

I-II stages of HIV infection:

- reaction and tuberculin are typical;
- positive or hyperergic tests are detected during infection or active disease.

Negative tests - in the absence of infection with *M. tuberculosis* or severe common forms of tuberculosis.

Late stages (III-IV) of HIV infection:

- reaction to tuberculin is atypical;
- in 70% of patients negative tuberculin tests can be determined regardless of M. tuberculosis infection, the presence of active disease. Some patients (30%) respond positively to tuberculin when infected with M. tuberculosis or the presence of active tuberculosis.

Diagnosis of HIV infection

Clinical examination of patients with tuberculosis with a positive HIV test is carried out by tuberculosis specialists together with specialists from the regional AIDS center in the following order:

- assessment of the clinical condition and personal characteristics of the patient, which could influence the choice of therapy (history of tuberculosis, contraceptive methods, liver and kidney condition);
- physical examination;
- blood test to determine the formula;
- determining the number of CD4 cells;
- determination of viral load;
- pregnancy test in women;
- serological tests to determine markers of hepatitis B and C, especially in patients with tuberculosis who are injecting drug users;
- determination of the level of alanine aminotransferase (ALT) in the blood and bilirubin (the level of ALT, which exceeds the control values by more than 3 times will

affect the choice of antimycobacterial and antiretroviral drugs);

- other examinations depending on the patient's condition;
- consultations of specialists.

For screening studies: determination of antibodies to HIV (ELISA: enzyme- linked immunosorbent assay). In the case of a positive analysis in the laboratory is performed twice (with the same serum). Upon receipt of at least one positive analysis, the serum is sent for test confirmation. In this case, the confirmatory laboratory test is the method of immune blotting (IB), which detects antibodies to individual proteins of the virus.

Bacterial excretion is less common in HIV-infected patients with pulmonary tuberculosis and AIDS than in HIV-negative patients. AIDS patients have a higher level of multi- and polyresistance than HIV-negative patients.

The sensitivity of the skin tuberculin test in HIV-infected people is inversely proportional to the degree of immunosuppression, ie the number of CD4 -T lymphocytes in the blood. A negative tuberculin test does not rule out a diagnosis of tuberculosis because more than 50% of HIV-infected people with active tuberculosis have a negative reaction to tuberculin.

The course of pleurisy in HIV-infected patients is more severe (more often with exudation) than in non-HIV-infected patients, they die more often before the end of treatment and they are more likely to have MBT in the pleural fluid.

The development of meningitis is especially characteristic of HIV-infected patients. The most rapid course of tuberculous meningitis is characteristic of HIV-positive young people (18-24 years), in whom, along with CT, changes in the brain are observed.

HIV-infected people and AIDS patients are characterized by both typical and medium- and lower-partial localization of tuberculous infiltrates in contrast to HIV-negative patients, in whom the upper-partial typical localization predominates. Lower partial localization of tuberculous infiltrate in HIV-infected and AIDS patients may be the cause of low diagnosis of tuberculosis and overdiagnosis of community-acquired pneumonia.

Radiological features of clinical forms of tuberculosis in HIV-positive individuals

Form of tuberculosis	***Characteristics of the radiological picture***
Disseminated	Small and medium foci without a tendency to fusion and caseous necrosis with a low frequency of destruction of lung tissue and involvement in the pathological process of intrathoracic lymph nodes.

Focal	Atypical mid-lobe and lower lobe localization, often bilateral lesions.
Infiltrative	As in patients with AIDS, mid-lobe, low-lobe localization with a low frequency of destructive forms, mainly hematogenous dissemination and involvement in the pathological process of intrathoracic lymph nodes.

Small-focal and medium-focal dissemination predominates in the lungs of *AIDS patients*. In HIV-infected patients, the extent of dissemination in the lungs is the same as in HIV-negative individuals.

Atypical localization, prevalence of lesions, propensity to disseminate with multiple extrapulmonary localizations are considered to be the main distinguishing features in HIV-infected and AIDS patients. Detection of them should raise suspicions of severely reduced immunity, even if the reactions to HIV are negative.

Detection of extrapulmonary tuberculosis is performed in patients with intoxication syndrome, enlarged peripheral lymph nodes, pleurisy, meningitis, bone and joint damage, pathological changes in the urine, diarrheal syndrome, enlarged mesenteric l / nodes, etc.

- Biopsy of enlarged peripheral lymph nodes with histological examination and culture of the material;
- Thoracoscopy with pleural biopsy and exudate culture for the presence of MBT in patients with exudative pleurisy;
- CT of the chest in patients with prolonged fever of unknown origin;
- Ultrasound of the abdominal cavity in persons with prolonged fever of unknown origin with examination of l / nodes of the abdominal cavity or CT of this area;
- Five urine cultures for the presence of MBT in the case of persistent pathological changes in the urine in the absence of growth of non-specific flora and a positive response to broad-spectrum antibiotics;
- Cerebrospinal fluid culture for the presence of MBT in meningoencephalitis, regardless of the isolated pathogen, as the course of tuberculous meningitis can be combined with cryptococcal.

Typical signs of tuberculosis in the terminal stage of AIDS are:

1. Prolonged persistent increase in body temperature to 39-40 ° C on the background of active anti-TB treatment;
2. Significant weight loss of almost 10 kg for 2-3 months;
3. Liquid, light, up to 400 ml foamy sputum, which "easily pours out of the lungs" during coughing;
4. Increased ESR (> 45 mm / h), leukocytosis up to 20 x 10^9 / l;
5. X-rays in the lungs on the background of localization of the tuberculous process in the upper lobe reveal diffuse infiltrates, mainly in the lower middle lobes, which quickly (up to 3 months) turn into multiple cavities (with a picture of "destroyed lungs"). anti-tuberculosis therapy, even with the preserved sensitivity to these drugs;
6. In all patients determine candidiasis of the oral cavity;

7. Tuberculin test loses its informativeness;
8. Complications of the late stage of AIDS with pneumocystis pneumonia (8085%).
9. 15 days before the lethal end of the HIV test is negative.

The course of HIV infection in the form of a mixed infection (frequent combination with pneumocystis pneumonia or CMV infection, etc.) also affects the radiographic picture. In this case, typical signs of tuberculosis are rarely detected (infiltrates in typical places, usually at the apex); more often define diffuse changes with signs of basal, paratracheal or mediastinal lymphadenopathy. If possible, it is advisable to perform a CT scan, especially if there is a suspicion of extrapulmonary process.

Algorithm for assessing the risk of TB in HIV-infected people

Atypical course, frequency of extrapulmonary localization, combination with other opportunistic diseases complicate, and sometimes make impossible, timely diagnosis of tuberculosis in HIV-infected patients, which affects the conduct of adequate therapy, as well as the quality and duration of life.

Treatment of HIV-infected patients with tuberculosis

Currently, there are no means by which to cure AIDS, but there are only those that can slow the progression of the disease, prolong the life of the patient. When HIV is not detected during treatment, it is due to a decrease in the level of HIV in the blood below the threshold concentration that can be detected by methods available to the doctor, or the virus is contained in cells in the form of provirus, remaining inaccessible to drugs. As there is currently no possibility of complete elimination of HIV from the human body, the goal of therapy is to prolong the life of infected people and maintain its quality for a long time.

The following approaches are followed in the organization of treatment of patients with a combination of tuberculosis and HIV infection (TB / HIV coinfection):

- Treatment for active tuberculosis is clinically and epidemiologically more important than treatment for HIV infection, so treatment of patients with coinfection begins mainly with the appointment of anti-tuberculosis therapy;
- Treatment of tuberculosis in HIV-infected patients is carried out according to the same regimens and duration as in non-HIV-infected patients;
- If the patient is already receiving ART, it is continued, and if necessary, adjust the treatment to take into account the compatibility of ARV drugs and antimycobacterial therapy (AMBT);
- After completion of the main course of AMBT antirelapse prophylactic treatment is not used;
- Prophylactic treatment with cotrimazole prevents death from other infections in co-infected patients.

Treatment of patients with TB / HIV co-infection is carried out:

- In the case of pulmonary tuberculosis with bacterial excretion - in antituberculosis

institutions;

• In case of detection of tuberculosis of different localization without bacterial excretion:

• for the period of intensive treatment in the conditions of a tuberculosis hospital, dispensary / office (outpatient) or in regional AIDS centers, depending on the course and severity of the disease;

• for the period of the main course of supportive chemotherapy - in health care facilities of the general network or in regional AIDS centers under the direct supervision of medical workers (DOTS) under the condition of supervising the process of treatment by the district TB doctor.

Standard regimens of the main course of chemotherapy depend on the dispensary group of patients with tuberculosis. The main course of chemotherapy is a long continuous combination treatment with AMB drugs in a full daily dose for 1 dose. The standard course of AMBT is carried out using 4-5 antituberculosis drugs of the I series (isoniazid, rifampicin, streptomycin, pyrazinamide, ethambutol), which includes an intensive stage (2 months and longer to prevent the emergence of multidrug-resistant strains of MBT, duration - depending on the clinic sensitivity of the Office to drugs) and the maintenance phase (prescribe isoniazid and rifampicin for at least 4 months, depending on the effect obtained).At decrease in cellular immunity it is inexpedient to apply pyrazinamide (as its action extends to intracellularly located MBT). The choice of the appropriate AMBT regimen depends on the results of the bacterioscopic examination before treatment, the previous course of AMBT and the severity of the disease.

If the MTB is resistant, at least 2 main drugs active to the MTB should be prescribed, and reserve - ciprofloxacin (750 mg 2 times a day) or ofloxacin (400 mg 2 times a day).

Standard treatment regimens for patients with tuberculosis

Case of the disease	Initial phase (daily)	Continuation phase (daily)
New case**	2 HRZE	4 HR
Previously treated patients*	2 HRZE	4 HR

Notes:

* - before starting OKHT in previously treated patients with TB it is necessary to conduct cultural studies (preferably on a liquid medium) and DST MTB (at least for sensitivity to H and R, if possible, by molecular genetic methods) ** - except for patients with TB of the nervous system, bones and joints

Treatment of HIV patients

Highly active antiretroviral therapy (HAART) involves the use of a combination of three antiretroviral drugs (ARVs) and makes it possible to suppress the replication of HIV, to restore the function of the immune system. HAART is an integral part of providing comprehensive health care to people living with HIV.

The appointment of ARV drugs in patients with pulmonary tuberculosis, in which

the number of CD4 + lymphocytes> 200 in 1 mm3 should be postponed until the end of treatment for tuberculosis. In patients at high risk of progressive HIV infection (in case of extrapulmonary tuberculosis or if the number of CD4 + lymphocytes <200 per 1 mm3 of ART should be performed in parallel with treatment for tuberculosis). However, traditional treatment of patients with pulmonary tuberculosis in the terminal stage of AIDS is ineffective - the prognosis remains unfavorable, as patients die from various infectious complications of AIDS (more often from pneumocystis pneumonia).

Adverse reactions to antimycobacterial drugs and their management

Adverse reactions to anti-TB drugs in HIV-positive people develop more often than in HIV-negative people. Some side effects can be prevented. For example, peripheral neuropathy may occur with isoniazid, especially during pregnancy, alcohol abuse, diabetes, chronic liver disease, and malnutrition. The risk of drug intolerance increases with increasing immunosuppression. Most side effects occur in the first 2 months of treatment. The most common manifestation of an adverse reaction is each reaction. Fever often precedes and accompanies a skin rash. Most often, skin reactions occur to thioacetozone (WHO does not recommend its use due to the risk of severe intoxication with dermatological complications with a fatal outcome in 12-20%), as well as to streptomycin and rifampicin. Among other reactions, the most common are gastrointestinal disorders and hepatitis. The development of rifampicin-associated shock and thrombocytopenia is possible. Patients are prescribed pyridoxine 20-40 mg per day, along with antimycobacterial drugs.

Test tasks to control the FINAL LEVEL OF KNOWLEDGE:

1. What is active detection of HIV / AIDS-associated tuberculosis?

A. diagnosis of tuberculosis in patients with HIV / AIDS at registration of a new case of HIV infection at the annual preventive examination of patients of this contingent
B. Diagnosis of tuberculosis in patients with HIV / AIDS when visiting a medical institution with symptoms similar to tuberculosis

2. What is passive detection of HIV / AIDS-associated tuberculosis?

A. diagnosis of tuberculosis in patients with HIV / AIDS at registration of a new case of HIV infection at the annual preventive examination of patients of this contingent
B. Diagnosis of tuberculosis in patients with HIV / AIDS when visiting a medical institution with symptoms similar to tuberculosis

3. How many times should a sputum test be performed on the MTB if tuberculosis is suspected in a patient with HIV / AIDS?

A. one
B. two
C. three
D. five
E. does not need to be conducted

4. A patient registered in the AIDS Prevention and Control Center has a wet cough for two months. Is it necessary to perform an X-ray examination of the chest, if this examination was performed 4 months ago?

A. no
B. yes
C. not required

5. Are HIV / AIDS complaints mandatory?

A. required
B. optional, the presence of complaints depends on the form, phase of the tuberculosis process, the presence of complications

6. In a patient with HIV infection, a round shadow was found in the lungs by fluorographic examination. What diseases should be considered in the first place and what additional tests should be done to determine the origin of the target?

A. tuberculosis, to conduct an X-ray examination of the chest
B. pneumocystis pneumonia, to conduct X-ray examination of chest
C. benign lung tumor, conduct an X-ray examination of chest

7. A patient with HIV infection has bronchopulmonary syndrome. No pathological changes were detected on the OGK radiograph. Is it necessary to perform sputum research?

A. no
B. yes
C. not required

8. A patient with HIV infection has bronchopulmonary syndrom. No pathological changes were detected on the chest Xray, MTB (-) three times. What should be the doctor's tactics in this case?

A. conduct a survey in a year
B. prescribe chemoprophylaxis for tuberculosis if the patient is infected with the MTB
C. prescribe broad-spectrum antibacterial drugs

9. What method is used to detect antibodies to HIV?

A. enzyme-linked immunosorbent assay
B. polymerase chain reaction
C. radioallergosorbent test
D. immunoblotting

10. What investigation should be performed on an AIDS patient with suspected pulmonary tuberculosis?

A. Xray scopy
B. fluorography
C. chest Xray
D. tomography
E. bronchography

Standarts of answers: 1. A. 2. B. 3. C. 4. B. 5. B. 6. A. 7. B. 8. C. 9. A. 10. C.

INDEPENDENT CLASSROOM WORK
of applicants for higher medical education of the 5th year of study
on the topic of the practical lesson

- Master the method of examination of a patient with TB / HIV
- Supervise a TB / HIV patient
- Carry out differential diagnosis of TB / HIV
- Make a plan for a laboratory test
- Interpret the results of a specific examination of a TB / HIV patient
- Recognize complications of TB / HIV
- Make a treatment plan for a TB / HIV patient.
- Determine medical tactics in case of emergencies.
- Draw up medical documentation upon diagnosis of TB / HIV.

Recommended literature:

Obligatory literature

1. Ministry of Health of Ukraine. Tuberculosis. Evidence-based clinical guideline. 2023. https://www.dec.gov.ua/wp-content/uploads/2023/01/klinichna-nastanova-tuberkuloz-sichen-2023.pdf
2. Evidence-based clinical practice guideline "HIV infection", https://www.dec.gov.ua/wp-content/uploads/2022/11/2022_2092_kn_vil_1.pdf.
3. Order of the Ministry of Health of Ukraine of November 16, 2022, No. 2092 "On Approval of the Standards of Medical Care "HIV Infection"
4. Boyko MG Phthisiology: a textbook for students of medical and pediatric faculties of higher medical educational institutions of the IV level of accreditation / M.G. Boyko, A.G. Yareshko, A.K. Vorodyukhina, MV Kulish - Poltava: Techservice Company Ltd., 2015. - 276 p.
5. Feshchenko YI, Melnik VM Organization of anti-tuberculosis care for the population - K .: Health, 2006. - 654 p.
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7. Phthisiology. / B.I. Petrenko, LD Todoriko, L.A. Grishchuk et al .; - K .: BCB «Medicina», 2015. - 472 c.
8. Phthisiology. Textbook. Edited by VI Petrenko. - Vinnytsia: New book, 2006. - 504 p.
9. Tsyganenko AY, Zaitseva SI Tuberculosis. The textbook for university students.
10. Kharkiv: Fakt, 2004. - 390 p

Additional literature:

1. Boyko MG Practical skills in the study of tuberculosis: textbook for interns / MG Boyko, A.G. Yareshko, M.B. Kulish [etc.]. - Poltava: Techservice Company Ltd., 2015. - 258 p.
2. Zhdan V.M. Tuberculosis: textbook for family doctors / V.M. Zhdan, [etc.]. - Poltava: Techservice Company Ltd., 2015. - 234 p.
3. John Malcolm Dowling, Chin-Fang Yap. Communicable Diseases in Developing Countries Stopping the Global Epidemics of HIV/AIDS, Tuberculosis, Malaria and Diarrhea. ISBN 978-1-349-46999-4 ISBN 978-1-137-35478-5 (eBook), DOI 10.1057/9781137354785, 2014. – 219 c.
4. Irini Sereti, Gregory P. Bisson, Graeme Meintjes. HIV and Tuberculosis: A Formidable Alliance. – Springer International Publishing, 2019. ISBN 9783030291082 – 341 c.

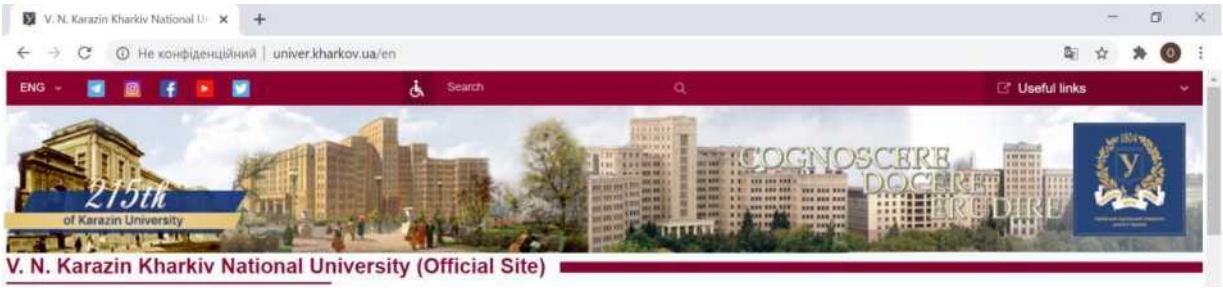
Information resources

1. Website of the Ministry of Health of Ukraine: www.moz.gov.ua.

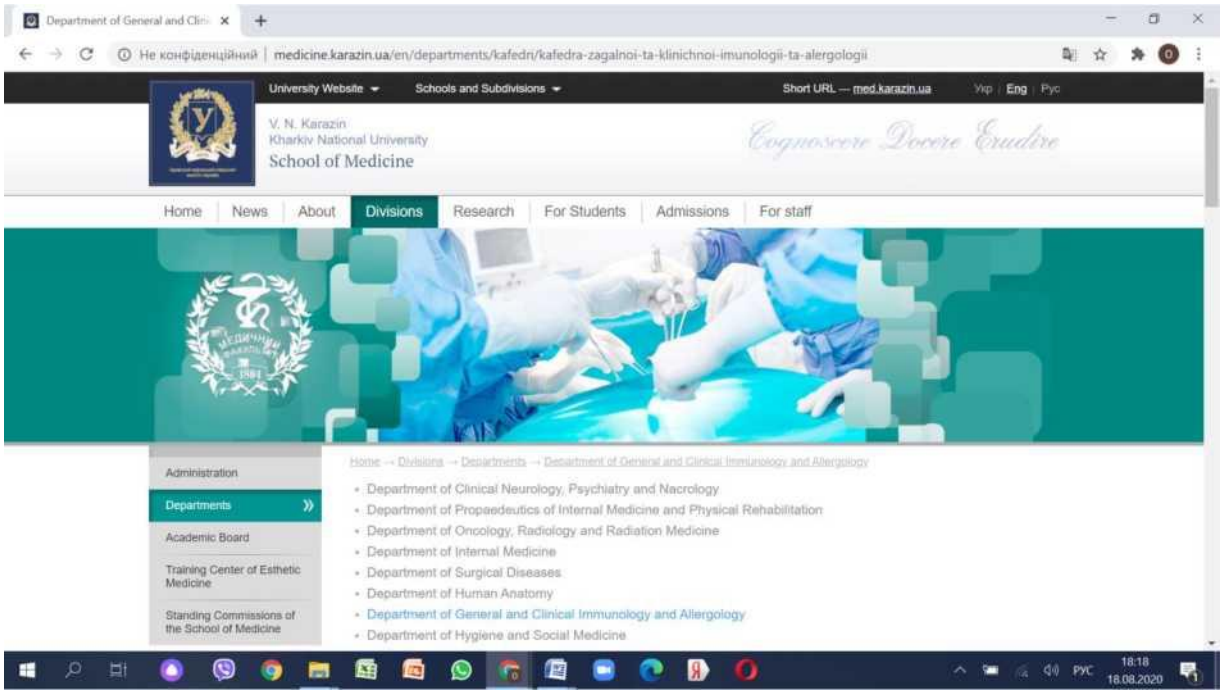
2. Centers for Disease Control and Prevention »http://www.cdc.gov/
3. Ukrainian Center for Control of Socially Dangerous Diseases of the Ministry of Health of Ukraine: online training. - Access mode: http://tb.ucdc.gov.ua/navchannya-onlayn.
4. USAID Project "Strengthening Tuberculosis Control in Ukraine": textbooks, training materials. - Access mode: http://stbcu.com.ua/resources/guidelines/.
5. Stop TB in Ukraine: books and textbooks. - Access mode: http://stoptb.in.ua/uk/tip-publikacii/knigi-ta-pidruchniki.
6. National Tuberculosis Resource Center http://tb.ucdc.gov.ua/
7. Website of the Center for Public Health of the Ministry of Health of Ukraine http://phc.org.ua/
8. Tuberculosis issues on the WHO website http://www.who.int/tb/en/
9. Ukrainian Center for Socially Dangerous Diseases Control of the Ministry of Health of Ukraine: online training - Access mode:http://tb.ucdc.gov.ua/navchannya-onlayn

Appendix 1

The official website http://www.univer.kharkov.ua/ua/departments



Department of Infectious diseases and clinical immunology
http://medicine.karazin.ua/departments/kafedra-zagalnoi-ta-klinichnoi- imunologii-ta-alergologii



Appendix 2

ELECTRONIC REPOSITORY
of V. N. Karazin Kharkiv National University
http://ekhnuir.univer.kharkov.ua/

eKhNUIR

Пошук у бібліотеці
Знайти
Розширений пошук
Пошук за темами
Головна сторінка

Перегляд
Розділи та колекції
За датою випуска
Автори
Назви
Теми
За датою надходження

Зареєстрованим:
Отримувати оновлення по e-mail
Мій архів
зареєстрованим користувачам
Редагувати профіль

Довідка
Про Dspace

eKhNUIR - Electronic Kharkiv National University Institutional Repository

Ласкаво просимо до Електронного архіву Харківського національного університету імені В.Н.Каразіна!

Електронний архів Харківського національного університету імені В.Н. Каразіна наповнюється наступними матеріалами: наукові публікації працівників та студентів Каразінського університету, статті з наукових журналів, монографії, дисертаційні матеріали, навчально-методичні розробки. Наукові публікації студентів розміщуються за умови наявності рецензії наукового керівника.

Репозитарій Харківського національного університету імені В.Н. Каразіна має власний **ISSN 2310-8665**. Тим самим, репозитарій отримав статус повноцінного електронного видання (ресурсу, що постійно оновлюється), в якому можна публікувати результати досліджень як в першоджерелі, нарівні з друкованими періодичними виданнями.

Пошук

Введіть ключові слова для пошуку ресурсів в архіві електронних ресурсів.

Перейти

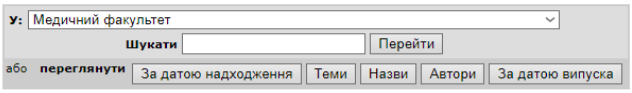
Спільноти

Виберіть спільноту для перегляду її колекцій.

Медичний факультет

Медичний факультет : [1229]

Головна сторінка спільноти



Колекції цієї спільноти

- Із історії харківської медичної школи [281]
- Кваліфікаційні випускні роботи здобувачів вищої освіти. Медичний факультет [0]
- Навчальні видання. Медичний факультет [257]
- Наукові видання. Медичний факультет [62]
- Наукові роботи. Медичний факультет [524]
- Наукові роботи студентів та аспірантів. Медичний факультет [105]

Перегляд статистики

Електронне навчальне видання комбінованого використання
Можна використовувати в локальному та мережному режимі

Потейко Петро Іванович
Грек Іван Ігорович
Константиновська Ольга Сергіївна
Кушнір Василь Борисович
Лядова Тетяна Іванівна
Волобуєва Ольга Вікторівна

ВЕДЕННЯ ХВОРИХ НА ТУБЕРКУЛЬОЗ У ПОЄДНАННІ З ВІЛ-ІНФЕКЦІЄЮ

Методичні рекомендації
для самостійної підготовки до практичних занять здобувачів
вищої медичної освіти 5-го року навчання з дисципліни «Фтизіатрія»

(Англ. мовою)

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