MINISTRY OF HEALTH CARE OF UKRAINE
KHARKIV NATIONAL MEDICAL UNIVERSITY

Department of <u>Phthisiology and Pulmonology</u>
Faculty: <u>II medical</u>

METHODICAL RECOMMENDATION
FOR THE STUDENT'S SELF WORK
DURING THE PREPARATION FOR PRACTIICAL CLASS

Educative discipline <u>Internal medicine with infectional diseases and phthisiology</u>
for students of <u>   6   </u> Course__of _<u>Medical</u>__faculty

"Approved"
Educative-Methodical counsel of
department of <u>Phthisiology and</u>
<u>Pulmonoogy</u>
" <u>   </u> " <u>   </u><u>   </u> 20<u>   </u>y.
**   Protocol №<u>   </u>**
Head of Department
Professor Shevchenko O.S
«<u>   </u>»<u>   </u>2014

Kharkiv – 2014

Topic "Drug-resistant TB. Clinical features, diagnostics. Peculiarities of TB running and treatment of drug-resistant TB patients. Medical care after TB patient, organizing measures. Examination of patient with drug-resistant TB**".**

1. **Quantity of hours** ___6_____

2. **Financial and methodical support of the topic:** tables, results of patients examination and their case histories, X-ray pictures.

3. Currency of the topic.

Drug-resistant tuberculosis especially multidrug-resistant tuberculosis (MDR TB) and extensively-resistant (XDR TB) tuberculosis remains a major threat to global TB control.

Adequate treatment of multidrug-resistant tuberculosis patients by antituberculosis drugs allows receiving encouraging results. Therefore it is important to know specified pathology and methods of its treatment.

4.General goal:

To create for students the conditions which provide opportunity to master of knowledge and skills, allowing distinguishing drug-resistant tuberculosis from other condition, to diagnose and treat patients suffering from drug-resistant tuberculosis.

The concrete aims:

4.1.

1. To sum up the results of examination of patients suffering from drug-resistant tuberculosis.
2. To identify the basic syndromes in the patients suffering from drug-resistant tuberculosis.
3. To diagnose drug-resistant tuberculosis.
4. To treat patients suffering from drug-resistant tuberculosis.

4.2. Practical skills:

1. To be able to examine the patients affected suffering from drug-resistant tuberculosis.

To be able to perform physical examination of the patient, including chest examination: to define the form, to reveal deformations, respiration act lagging of this or that half of the thorax of patients with drug-resistant tuberculosis.

2. To be able to perform the palpation, percussion, and auscultation of patient's chest.
3. To give clinical estimation of the findings in drug-resistant tuberculosis, to understand pathogenesis of revealed symptoms.
4. To be able to sum up the findings.
5. To know the genesis of studied pathological changes.
6. To be able to define concrete syndrome of tuberculosis in patients with drug-resistant tuberculosis.
7. To describe path morphological changes in the body of
8. To classify antituberculosis drugs, to apply optimum performance of chemotherapy in drug-resistant tuberculosis patients.
9. To be able to sum up the findings.
10. To know the genesis of studied pathological changes.
11. To be able to define concrete syndrome of tuberculosis in patients with drug-resistant tuberculosis.
12. To describe path morphological changes in the body of
13. To classify antituberculosis drugs, to apply optimum performance of chemotherapy in drug-resistant tuberculosis patients.

5. Graph- logical structure of the topic.

Multi-drug resistant tuberculosis – tuberculosis, caused by MBT which is resistant at least to isoniazid and rifampicin. Extensively-drug resistant tuberculosis – tuberculosis, caused by MBT which is resistant to isoniazid and rifampicin, to at least one of injectable second line drugs and fluorochinolone. Per WHO guidelines, MDR TB treatment is increasingly being administered in

outpatient settings. Treatment for MDR TB is associated with many side effects and toxicities which can compromise medication adherence and eventual outcomes. MDR TB Regimen: kanamycin, ofloxacin, ethambutol, PZA, ethionamide, and cycloserine (or terizidone).

Pathogenesis of Drug Resistance and Definitions

Although its causes are microbial, clinical, and programmatic, drug-resistant TB is essentially a manmade phenomenon. From a microbiological perspective, resistance is caused by a genetic mutation that makes a medicine ineffective against the mutant bacilli. From a clinical and programmatic perspective, the cause is an inadequate or poorly administered treatment regimen that allows a drug-resistant strain to become the dominant strain in a patient infected with TB. Through random genetic mutation, TB strains may become resistant to any of the anti-TB medicines currently available. During treatment of active disease, at the level of the patient, these resistant strains may be "selected" and propagated through "inadequate" treatment. Inadequate treatment occurs when an insufficient number of anti-TB medicines are used, incorrect medicine dosing is prescribed, interruptions in therapy occur, or therapy of too short duration is given. Once these resistant organisms are selected and multiply, an affected patient will no longer respond to standard TB therapy and becomes an acquired resistance TB case (i.e., someone who has received at least one month of anti-TB therapy). These patients subsequently spread their resistant disease to their contacts that often become sick with the same resistant stain transmitted by the original patient. This type of newly diagnosed case is called a primary resistance TB case. In the prison setting, the propagation of drug-resistant TB is magnified and rapidly becomes a mixture of resistance among new and previously treated patients.

Factors that contribute to the generation of drug resistance can be divided into those related to the health care providers, the medicines used, and the patients undergoing therapy. TB patient can has anti-TB treatment in the past and, due to poor adherence, have a greater chance of contracting drug-resistant TB.

Components of the DOTS Strategy as Applied to MDR-TB

Component	Element
Sustained political commitment	• Addressing the factors leading to the emergence of MDR-TB • Long-term investment of staff and resources • Coordination of efforts between communities, local governments, and international agencies • A well-functioning program
Appropriate case-finding strategy, including quality-assured culture and drug-susceptibility testing (DST)	• Rational triage of patients into DST and the drug-resistant TB control program • Relationship with supranational TB reference laboratory
Appropriate treatment strategies that use second line medications under proper case management conditions	• Rational treatment design • DOT • Monitoring and management of adverse effects • Properly trained human resources
Uninterrupted supply of quality assured second line medications (SLM)	

Recording and reporting system designed for drug-resistant TB control programs that enables performance monitoring and evaluation of treatment outcomes	

Diagnosis of MDR-TB and XDR-TB

An MDR-TB case is defined as a patient who is identified as infected with a strain that is resistant to at least isoniazid and rifampicin. XDR-TB is one that is resistant to isoniazid, rifampicin, plus any fluoroquinolone, and at least one of three injectable SLMs (amikacin, kanamycin, or capreomycin). The only way to confirm MDR-TB and XDR-TB is through DST of first- and second-line medicines, respectively.

In developing countries, DST is mostly done in reference laboratories that are part of the NTP network. DST on solid cultures (egg-based or agar-based) can be performed as direct or indirect tests. The former has the advantage that results are available sooner.

Direct tests are also more representative of the patient's original bacteria. When results are not valid using the direct method due to insufficient or excessive bacterial growth or contamination, however, the test must be performed again with an indirect method (pure culture). WHO recommends three types of methods for DST in Lowenstein-Jensen (solid) media: the indirect proportions method, the resistance ratio method, and the absolute concentration method. The indirect proportions method is most popular. Under program conditions, the total turnaround time is 10 to 12 weeks, from inoculation on culture media to determination of resistance patterns. Other more rapid tests for assessing MDR and XDR-TB, which use solid and liquid media with either automated, semi automated, or non-automated systems, are becoming more widely used. These systems include BACTEC-460 and BACTEC-960 (MGIT-960), microscopic-observation for drug susceptibility (MODS) testing, and colorimetric methods. Other rapid tests include genetic methods such as the line probe assays that identify genes associated with resistant mutation and bacteriophage-based assays (FAST Plaque-TB), which identifies growing *M. tuberculosis* in the presence of isoniazid and rifampicin. In areas where DST is limited due to cost, maintenance, and untrained personnel, only patients suspected of MDR-TB or XDR-TB should be evaluated with culture and DST.

WHO's *Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis* lists the following groups of patients living in resource-poor settings for whom DST should be prioritized due to an increased risk of drug-resistance—

• Patients who have experienced failure of re-treatment regimens; chronic TB
cases
• Individuals who have had exposure to a known MDR-TB case
• Patients who have experienced failure of Category I
• Individuals who have experienced failure of anti-TB treatment in the private
sector
• Patients who remain sputum smear-positive at the second or third month of
short-course chemotherapy
• Patients who have relapsed and returned after default without recent
treatment failure
• Individuals who have had exposure in institutions that have MDR-TB
outbreaks or a high MDR-TB prevalence

Even more important than DST, a meticulous and complete medical history of the patient is extremely valuable when investigating drug resistance. This history should review previous anti-TB treatments taken, results of such treatments, contact with MDR-TB cases, and drug-

susceptibility patterns of those contacts. This information can be retrieved by interviewing the patient and cross-checking his or her medical chart.

Treatment of MDR-TB

Selection of Medicines Used in MDR-TB (and XDR-TB) Regimens

In the WHO consensus guidelines on drug-resistant TB management, medicine choices are grouped into five distinct categories. In designing a treatment regimen, all first-line anti-TB medicines with preserved potency should be included. An injectable agent with preserved efficacy should also be incorporated. Fluoroquinolones have demonstrated a bactericidal effect against TB and should be included if resistance testing reveals susceptibility to these agents. Susceptibility to fluoroquinolones has been shown to be an independent predictor of cure among MDR-TB patients. Thioacetazone should be avoided in TB patients with HIV given its association with severe skin eruptions, including Stevens-Johnson syndrome in individuals with HIV.

WHO Core Principles for Selecting MDR-TB Treatment Regimens

1. The choice of regimen should be made based on the history of prior medicine exposure.
2. The local prevalence of resistance to anti-TB agents should be taken into consideration.
3. Regimens should include at least four medicines that are almost certain to be effective for the patient's isolate, based on quality-assured drug-susceptibility testing.
4. Medicines should be administered at least six days a week.
5. Medicine dosing should be based on the patient's weight.
6. An injectable agent (e.g., amino- glycoside or capreomycin) should be used for a minimum of six months, with at least four months of continued injectable therapy after culture conversion. Thrice weekly regimens of injectable agents can be considered after the first two to three months.
7. Treatment should be continued for a minimum of 18 months after culture conversion.
8. DOT should be used throughout treatment.
9. Drug-susceptibility testing, where available, should guide regimen design.
10. Pyrazinamide can be used throughout the treatment course.
11. Early detection of MDR-TB and the rapid initiation of effective treatment are key elements to achieve success.
12. When possible, pyrazinamide, ethambutol, and fluoroquinolons should be given once per day because the high peaks attained in once-a-day dosing may be more efficacious. Once-a-day dosing is permitted for other SLMs depending on patient tolerance; however, ethionamide/prothionamide, cycloserine, and P-amino salicylic acid have traditionally been given in split doses during the day to reduce adverse effects.
13. Treatment of adverse medicine effects should be immediate and adequate to minimize the risk of treatment interruptions and prevent increased morbidity and mortality due to serious adverse effects.

Treatment Strategies

Three options or types of treatment schemes are recommended by WHO.
These schemes use information obtained from DST results and drug-resistance surveillance within the local population. The latter can also be obtained from drug resistance surveys. Patients with MR TB, XDR TB and patients with proved cases of chemo-resistant tuberculosis are watched in the Category 4 and need chemotherapy during at least 12 months.
● 4.1. category – cases of multi-drug-resistant tuberculosis, confirmed by the test of drug sensitivity, including
- 4.1.A. - general treatment;
- 4.1.B. - palliative treatment – for patients, whom the chemotherapy is not recommended to (severe adverse reactions, severe concomitant diseases, administration of palliative therapy, proved patient's absence of adherence to treatment at the patient).
● 4.2. category – cases of TB with extensive drug resistance of MTB to antituberculosis drugs according to drug resistance test (XDR TB) including

- 4.2.A. - general treatment;

-4.2.B. - palliative treatment– for patients, whom the chemotherapy is not recommended to (severe adverse reactions, severe concomitant diseases, administration of palliative therapy, proved absence of adherence to treatment at the patient).

● 4.3. category – cases of chemo- resistant TB (registered from categories 1-2 and from chronic case who according to resistant profile demand the treatment longer than 12 months.

- 4.3.A. - general treatment;

- 4.3.b. - palliative treatment – for patients, whom the chemotherapy is not recommended to (severe adverse reactions, severe concomitant diseases, administration of palliative therapy, proved absence of adherence to treatment at the patient).

MONITORING OF THE TREATMENT IN PATIENTS OF 4 CATEGORY

Indexes of the monitoring	Frequency of measures needed
Examination at the doctor	One a week at the start of the chemotherapy, then once a month up to treatment ending. Daily - for children – inpatients of the hospital and sanatorium
Interrogatory with health worker, performing DOT about patient's tolerance of the chemotherapy	With every case of in taking of anti-TB drugs.
Microscopy of sputum smear	Once a month
Sputum culture	Once a month (with broth or solid medium during the phase of intensive chemotherapy), then once in 3 months – on solid medium.
Body weight	Once a week at the start of the chemotherapy and then – once a month.
Drug resistant test	Once a month at the start of the chemotherapy and every 3 months if bacilli expelling is still present.
X-ray examination	At the start of the chemotherapy and then every 3-6 months. For children – at the start of the chemotherapy and then every 3-6 months.
Potassium level in blood	Every month during injectable drugs using and with indication.
Thyroid stimulating hormone level in blood	Every 6 months during ethionamide/prothionamide or/and PAS in taking , once a month with signs of hypothyroidism.
Liver function	Periodical monitoring every 1-3 months in patient who intakes pyrazinamide or in patient with the risk of hepatitis developing. For HIV infected persons – monthly monitoring/ For children – once a month.
Testing for HIV	At the start of the chemotherapy, then test is repeated with clinical indications.
Testing for pregnancy	At the start of the chemotherapy in women t fertile age. Test is repeated with clinical indications.
Hemoglobin and white blood account	With exploiting of linezolid once a week at the start of the disease, then once a month on

	the ground of present symptoms. For HIV infected persons who in taking zidavudine – monitoring is made once a month at the start of the chemotherapy, then – depending on the symptoms. For children – once a month.
Lipase in blood	Investigation is done with abdominal pain to exclude pancreatitis in patients in taking linezolid, stavudin, didanozin.
Lactate acid in blood	Test is done with lactate acidosis in patients who in taking linezolid or WAART.
Glucose in blood	Monitoring once a month once a month in patients in taking gatiphluorokinolone.
Ophthalmologist's consulting	At the start of the chemotherapy and every 3 months with in taking of ethambutol/ For children – once a month.
Audiogram	At the start of the chemotherapy and every 3 months with in taking of injectable drugs
Glomerular filtration	At the start of the chemotherapy and once a month with in taking of injectable drugs I patients with renal insufficiency or hepatitis. For children – once a month.

MONITORING OF TREATMENT RESPONSE

Patients should be monitored closely for signs of treatment failure. Clinically, the most important way to monitor response to treatment is through regular history-taking and physical examination. The classic symptoms of TB—cough; sputum production, fever, and weight loss—generally improve within the first few months of treatment and should be monitored frequently by health care providers. The recurrence of TB symptoms after sputum conversion, for example, may be the first sign of treatment failure. Monthly smear and culture monitoring should be preformed until conversion, with *conversion* defined as two consecutive negative smears and cultures taken 30 days apart. After conversion, the minimum periods recommended for bacteriological monitoring is monthly for smears and quarterly for cultures. Usually culture conversion occurs within the first two to three months of therapy. If smears or cultures continue to be positive after three months of treatment, the regimen should be reassessed, DOT questioned, and DST performed. After conversion and until the end of treatment, smear and cultures should be done every two months. Response to therapy can also be evaluated by improvement of symptoms and signs (e.g., weight loss, cough, malaise, fever).

The result of treatment	Definition	Management
Recovery	A patient who finishes the treatment in Category 4 and has: -as minimum 5 consecutive negative results of culture investigation of the sputum which are made with an interval no less than 30 days during last 12 months of treatment. Example 9m | -m | -m | -m | 20m	To transfer to Category 5.1.

K-	K-	K-	K-	K-

-if only one culture investigation is positive during total period and clinical signs of progression of the disease are absent, patient may be considered as recovered if after positive results there are as minimum three consecutive negative results, taken with the interval no less than 30 days.

Example 1

9m	-m	-m	-m	20m
K-	K+	K-	K-	K-

Example 2

9m	-m	-m	-m	20m
K+	K-	K-	K-	K-

Treatment is over	A patient who finished the course of treatment in Category 4, but does not answer the criterion "recovered" due to absence of the results of bacteriological investigation (for example less than 5 culture investigations were made during 12 months of treatment).	To transfer to Category 5.1

Example 1

9m	-m	-m	-m	20m
K-	K-	K0	K-	K-

Example 2

9m	-m	-m	-m	20m
K-	K0	K-	K-	K-

Treatment failure	Treatment failure is registered: -if 2 or more positive culture results among 5 ones which are made during last 12 months of treatment.	A patient must be discussed at CDCC to make the decision about new course of the treatment or transfer the patient to palliative treatment. If a new scheme of chemotherapy is prescribed, the patient must be reregistered in category 4 as "treatment after failure" with new register number. If a patient is transferred to palliative treatment

Example 1

9m	-m	-m	-m	20m
K-	K+	K+	K-	K-

Example 2

9m	-m	-m	-m	20m
K+	K-	K+	K-	K-

-if the result 1 among 3 lust culture investigations is positive.

Example 1

9m	-m	-m	-m	20m
K-	K-	K+	K-	K-

	Example 2					re- registration is not made and a patient remains in category 4.
	9m	-m	-m	-m	20m	
	K+	K-	K-	K+	K-	
Died	A patient of category 4 who died due to any cause during the course of treatment of MR TB case. -due to TB; -due to other causes.					
Treatment interruption	A patient who interrupted the treatment for 2 consecutive months or more by any causes.					
Discharged	A patient who was transferred to other region and the results of his/her treatment are unknown.					

Management of Adverse Events

Although rarely life threatening, the adverse effects of SLMs can be debilitating for patients. Patients experiencing high rates of adverse effects may be at increased risk of non-adherence. Therefore, early and effective management of adverse effects should be part of adherence-promotion strategies in the management of drug-resistant TB. In most cases, management of adverse effects can be accomplished using relatively simple and low-cost interventions without compromising the integrity of the drug-resistant TB treatment regimen.

Nutritional Support

In addition to causing malnutrition, drug-resistant TB can be exacerbated by poor nutritional status. Without nutritional support, patients, especially those already suffering from baseline hunger, can become enmeshed in a vicious cycle of malnutrition and disease. The SLMs can also further decrease appetite, making adequate nutrition a greater challenge. Vitamin B6 (pyridoxine) should also be given to all patients receiving cycloserine or terizidone to prevent neurological adverse effects. Vitamin (especially vitamin A) and mineral supplements can be given in areas where a high proportion of patients have these deficiencies. If minerals are given (e.g., zinc, iron, calcium), they should be dosed apart from the fluoroquinolones because they can interfere with the absorption of these medicines.

Role of Surgery in Treatment of MDR-TB

Surgical therapy, with resection of involved lung tissue, is considered as adjunctive therapy for those with MDR-TB. Surgery may be particularly useful for those with localized disease who are refractory to pharmaceutical therapy. Surgical intervention for MDR-TB has been shown to be associated with improved outcomes and effective with low complication rates when performed at a center with expertise in this area. Effective anti-TB pharmaceutical therapy remains a critical component, however, and in general should be given for at least two months before surgical intervention and for at least 12 to 24 months afterward.

6. Orientation card for student' work:

a) To enumerate of clinical symptoms and results of objective investigations which are typical for co-infection TB/HIV;

b) To make a choice of most informative tests, laboratory and instrumental investigation, which help to make a correct diagnosis.

c) Perform the differential diagnosis with two concurrent diseases;

d) To prescribe the treatment;

e) To prescribe of pathogenesis treatment;

f) To prescribe the measures for patient adherence to TB treatment, to prevent interruption of treatment;

g) To prescribe the measures for secondary prophylaxis of TB relapse;

All listed above tasks student have to answer according to individual practical task. This is takes into consideration before assessing of mastering level of practical classes.

7. Materials for self-student's work during the preparation for the class
7.1 The list of terms

1. MDR TB	Multi-drug resistant tuberculosis – tuberculosis, caused by MBT which is resistant at least to isoniazid and rifampicin.
2. XDR TB	Extensively-drug resistant tuberculosis – tuberculosis, caused by MBT which is resistant to isoniazid and rifampicin, to at least one of injectable second line drugs and fluorochinolone.
3. SLMs	Second line medications
4. DST	Drug-susceptibility testing
5. NTP	National tuberculosis treatment

7.2. Material for self-control.

1. To give the definition of multi-drug resistant tuberculosis.
2. To give the definition of extensively-drug resistant tuberculosis.
3. To enumerate second-line drugs.

7.3 Practical work (tasks) which have to be done within the class. Task №1. To interpret the interrogatory with a patient with drug-resistant tuberculosis;

to analyze the peculiarities of the disease running, clinical features of the disease, necessity of treatment.

Task №2. To put questions, which are supposed to be discussed at examination of patients: to analyze the complaints of a patient with drug-resistant tuberculosis.

Task №3. To perform physical examination of a patient with drug-resistant tuberculosis and to schedule the survey design.

Task №4. According to physical examination and results of investigations to diagnose the disease and to define every chapter of diagnosis formulation, including specified type of tuberculosis, site of the disease, the clinical form, presence of destruction, bacilli expelling, drug sensitivity of MBT, results of histological confirmation of the diagnosis, category, cohort, complications.

Test # 1

Drug-susceptibility testing is needed

Probable answers:

A. to match adequate chemotherapy regimen;

B. to provide epidemiological monitoring;

C. to avoid adverse reactions;

D. to perform scientific studies only;

E. to avoid side effects of medications.

Test # 2

Drug resistant tuberculosis means

Probable answers:

A. tuberculosis disease caused by mycobacterium tuberculosis resistant to a single anti-TB drug;

B. tuberculosis disease caused by mycobacterium tuberculosis resistant to several anti-TB drugs;
C. clinical signs of tuberculosis unchangeable at antibacterial therapy;
D. tuberculosis disease caused by drug resistant mycobacterium tuberculosis;
E. all incorrect.

Test # 3.
Primary (initial) drug resistance means
Probable answers:
A. resistance of mycobacterium found in a patient never treated before with antituberculosis drugs;
B. resistance of mycobacterium, revealed in the patient treated with anti-tubercular drugs no more than 4 weeks;

C. infection by mycobacterium tuberculosis resistant to isoniazid;
D. infection by mycobacterium tuberculosis resistant to rifampicin;
E. infection by mycobacterium tuberculosis resistant to isoniazid and rifampicin.

Test # 4.
Acquired (secondary drug resistance means
Probable answers:
A. resistance of mycobacterium found in a patient never treated before with antituberculosis drugs;
B. drug resistance, which is revealed in a patient never taking anti-TB drugs before;
D. infection by resistant mycobacterium tuberculosis;
C. drug resistance of mycobacterium tuberculosis developed during treatment of tuberculosis;
E. infection by mycobacterium tuberculosis resistant to isoniazid and rifampicin.

Test # 5.
Resistance of mycobacterium tuberculosis to anti-TB drugs is formed due to
Probable answers:
A. a genetic mutation that makes a medicine ineffective against the mutant bacilli.
B. an inadequate or poorly administered treatment that allows a drug-resistant strain to become the dominant strain in a patient;
D. resistant strains may be "selected" and propagated through "inadequate" treatment;
C. all incorrect;
E. all correct.

Test # 6.
What are key elements to achieve success in a treatment of MDR TB?
Probable answers:
A. Early detection of drug resistance;
B. Avoiding of adverse reactions;
C. Exploiting of SLDs;
C. all incorrect;
E. all correct.

Test # 7.
What are appropriate treatment strategies for drug resistant TB?
Probable answers:
A. Rational treatment design;
B. DOT;

C. Monitoring and management of adverse effects;
D. Properly trained human resources;
E. All of them correct.

Test # 8.

Surgical therapy, with resection of involved lung tissue, for those with MDR-TB

Probable answers:

A. is considered as adjunctive therapy;
B. is considered as main therapy;
C. is considered as ethological therapy;
D. is considered as pathogenical therapy;
E. A. and D.

Test # 9.
How long anti-TB pharmaceutical therapy must be performed in MDR-TB patients before surgical intervention?
Probable answers:
A. 2 weeks;
B. 2 months;
C. 4 months;
D. 12months;
E. 24 months.

Test # 10.
How long anti-TB pharmaceutical therapy must be performed in MDR-TB patients after surgical intervention?

Probable answers:
A. 2 weeks;
B. 2 months;
C. 4 months;
D. 12months;
E. 4 months.

Test # 11.
What is MDR TB regimen?
Probable answers:
A. streptomycin ofloxacin, ethambutol, PZA;
B. kanamycin, ofloxacin, ethambutol, PZA, ethionamide and cycloserine (or terizidone);
C. PZA, ethionamide and cycloserine (or terizidone);
D. isoniazid, streptomycin, PAS;
E. rifampicin, isoniazid, streptomycin, ethambutol.

The patterns of answers (drug-resistant tuberculosis):

1.A. 2.D. 3.E. 4.C. 5.E. 6.E. 7.E. 8.E. 9.B. 10.D. 11.B.

Recommended reference

<u>**Main literature:**</u>

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Methodical instruction is composed by <u>S.L.Matveyeva</u>

Methodical instruction is discussed and approved at the conference of the department of Phthisiology and Pulmonology with additions (changes) _____

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Head of the Department,
Professor   O.S.Shevchenko