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METHODOLOGICAL RECOMMENDATIONS FOR TEACHERS FOR THE PRACTICAL STUDIES OF PREPARATION FOR PHTHISIOLOGY GENERAL PRACTITIONERS

Academic discipline	Phthisiology
Subject lesson number 12	General principles of treatment of TB patients. Antimycobacterial drugs. Standard treatment regimens for TB patients.
Course	4

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Topic № 12: General principles of treatment of TB patients. Antimycobacterial drugs. Standard treatment regimens for TB patients.

1.Currency of the topic

Positive treatment response of TB patient depends on two factors: an inhibition of mycobacterium colonization by antituberculosis drugs (anti-TB drugs) and regression of TB changes in affected organs with reparation of their structure and function. As tuberculosis is an infectious disease the main method of its treatment is anti-mycobacterium drugs. Treatment response is conditioned by direct bactericidal or bacteriostatic action of anti-TB drugs on Mycobacterium tuberculosis resulting in its elimination. Regression of TB changes in affected organs and reparation of them occur due to anti-TB drugs. Adjacent therapy is also of value. That is why a student has to master of the main methods of TB treatment knowledge and the skills to use it in medical practice.

2. General goal: to master of the knowledge and the skills of the main methods to treat TB patient and to use it in medical practice.

3. The concrete aims:

- To master of the main principle of TB patient treatment;
- To study the questions connected with the performance of specific treatment;
- To define standardized chemotherapy regimens depending on treatment category;
- To master of the combinations of anti-TB drugs;
- To understand the duration of chemotherapy course and multiplicity of administration of anti-TB drugs for every of chemotherapy regimens.
- To diagnose side-effects of anti-TB drugs;
- To master of the methods of prevention of possible adverse reactions, induced by anti-TB drugs and complications which can be appear during the treatment; to be able to delete side effects of anti-TB rugs in case of their appearance;
- To define the criterions of TB patient recovery;
- To study epidemiological, clinical, radiological and other criterions evident for regression and recovery of TB;
- To have a clear understanding about residual changes which are almost always accompany the recovery of tuberculosis and their significance for possible reactivation (exacerbation or relapse of TB in the future).

4. Basic knowledge and skills are necessary for topic studying (interdisciplinary integration)

1.Pharmacology department To classify anti-TB drugs, doses, ways and multiplicity of the anti-TB drugs intaking. To be able to prescribe a recipe of anti-TB drugs. To know physical and chemical properties of anti-TB drugs, pharmacology dynamic, doses and ways of the drugs intaking. To know possible side effects of drugs and the methods of their deletion.

2. The department of introduction of internal diseases. To apply the methods of physical examination of TB patient, laboratory and functional investigations and to define the volume of TB patient examination in the presence of side effects of

the drugs. To be able to distinguish pathological changes from normal results of the investigations.

5. The tasks for student's independent work during the preparation for the class.

5.1. The list of the main terms, parameters and characteristics which a student has to master during the preparation for the class.

DOTS – strategy (directly observed treatment short-course) The program of TB patient treatment carrying out under the direct control after the standardized chemotherapy regimens depending on treatment and dispensary follow up category.

DOTS + program This is standardized 5-components chemotherapy regimen for patients suffering from multi-drug-resistant tuberculosis (MDR) (TB with multiple drug resistance towards two drugs of the first line: isoniazid and rifampicin): 2 drugs of first line – Ethambutol + Pyrazinamide and 3 drugs of second line – fluoroquinolons + Ethionamide + Kanamycin must be administrated before the obtaining of the results of drug sensitivity with using of individual scheme of treatment subsequently.

Complex treatment This is combination of specific (etiologic) and non-specific treatment and also using of surgical methods of treatment.

Combinative treatment This is an administration of no less than 4 anti-TB drugs in the initial phase for every patient.

Control of treatment This is a taking of drug at a presence of medical workers, close relatives or ьvoluntaries with a purpose to supply taking drugs regularly.

Two phases of treatment First intensive phase is directed to inhibit the multiplication of Mycobacterium tuberculosis, its significant reducing and part sterilization of a zone of specific inflammation. In second, continuative phase daily or intermittent chemotherapy is provided for clinical recovery of patient (persistent stopping of bacilli excretion, resolving of infiltrates and healing of caverns) or for treatment before surgical intervention.

Anti-TB drugs Antituberculosis drugs Treatment category This is a group of patients defined on 4 determinants: type of TB (defined on the ground of the disease history), site of TB, severity of the disease and presence of TB bacilli in examined material (sputum).

New case of tuberculosis (NCTB) A patient with newly diagnosed tuberculosis, who never was treated with anti-TB drugs or was treated less than 1 month.

Relapse of TB (RTB) A case of repeated diagnosis of active tuberculosis in patient who in the past successfully completed a full course of chemotherapy and was considered as made a full recovery.

Chronic TB (CTB) A patient with positive result of microscopic or cultural examination of the sputum after the course of supervised treatment approximately after 2 years of unsuccessful treatment.

The drugs of first line (essential drugs) The drugs (isoniazid, rifampicin, pyrazinamide, streptomycin, ethambutol, thioacetazone) which are administered to NCTB or RTB who excretes drug bacilli (patient of 1- 3 categories).

The drugs of second line (reserved drugs) The drugs (kanamycin, amicacin, capreomycin, ofloxacin/ciprofloxacin, ethionamide/prothionamide, PAS, cycloserin) which are used in individual schemes of chemotherapy in patients of category 4 with the resistance towards the drugs of first line and also in patients of other categories with the resistance of MBT towards the drugs of first line or with adverse reactions induced by drugs.

Intermittent regimen The taking of daily dose of anti-TB drugs 2-3 times a week. Extensive forms of TB Tuberculosis involved two and more segments of lungs or 2 and more organs.

Intensive phase The stage of TB patient treatment directed on the inhibition of MBT multiplication, removing acute manifestation of the disease and part sterilization of specific inflammation zone.

Continuation phase The stage of TB patient (daily or intermittent chemotherapy) carrying out to reach clinical recovery of the patient (persistent stopping of bacilli excretion, resolving infiltrates and healing of cavern) or to prepare the patient for surgical intervention).

Undeleted adverse reactions Adverse reactions which could not be to delete after reducing of the drug dosage and administration of adjacent therapy.

Deleted adverse reactions Adverse reactions which characterized by insignificant symptoms and organs function disturbances and could be deleted by reducing of the drug dosage and administration of adjacent therapy.

Criterions of TB patient recovery The batch of signs of good treatment response (completed and adequate main course of chemotherapy; persistent stopping of bacilli excretion, confirmed by microscopy and culture examination of the sputum; healing of caverns in lungs and resolving (or induration) of infiltration and lesions; deleting of clinical and laboratory signs of TB inflammation; restoration of functional abilities and capability of work).

The treatment is completed The patient with positive sputum smear at the start of treatment completed full course of treatment and no more than one negative result of sputum smear on 5^{th} month and later is recorded. The patient suffering from pulmonary or extrapulmonary tuberculosis with negative sputum smears after full course of the treatment.

Treatment failure New case of TB with smear sputum still positive during 5 months or more after starting chemotherapy or the patient interrupted the treatment from 2 up to 5 months after starting chemotherapy with positive sputum smear.

Interrupted treatment The patient interrupted the treatment for 2 or more months.

Recovery The patient completed full course of the treatment with recorded negative sputum smear in two or more sequent specimens after 5 months of the treatment and at the end of the treatment.

Theoretical questions for the class:

1. Enumerate the main principles of TB patient treatment.
2. Characterize the main methods of anti-TB drugs taking.
3. To indicate single and daily dosage of main anti- TB drugs.
4. What is the main method of TB patient treatment?
5. Why combinative anti-TB chemotherapy is used?
6. What does individual treatment mean?
7. What factors are conditioned the necessity of prolonged and non-interrupted anti- TB treatment?
8. What phases of TB patient treatment are defined? What are their aims?
9. What is the classification of anti-TB drugs?
10. Name the main clinical indications for using of combinative anti-TB drugs.
11. Enumerate the indications for administration of fluoroquinolons.
12. Name the criterions of TB patient recovery.
13. Enumerate the types of adverse reactions induced by the chemotherapy with anti-TB drugs.
14. Explain the difference between the adverse reaction and side effect of the drug.
15. Which adverse reactions are classified as serious ones?
16. What is the classification of side effects of drugs appearing as a result of prolonged anti-TB chemotherapy?
17. What is the mechanism of adverse reactions appearing?
18. Describe clinical signs of toxic reactions.
19. What is the management in case of allergic reactions?
20. What is the cause of disbacteriosis?
21. Clear the meaning of Yarish-Gerxgaimer reaction?
22. What are the kinds of drug-resistance of MBT?
23. What is the mechanism drug resistance?
24. What factors most frequently are the causes of drug resistance development?
25. Formulate a doctor's and patient's roles in the development of drug resistance?
26. What are the principles of modern anti-TB chemotherapy supplying the prevention of drug resistance?
27. Give the characteristic of bacilli excretion depending on the quantity of growing colonies of MBT during drug resistance test?
28. Why single used of daily dosage of anti-TB drugs is considered as the main one in Phthisiology?
29. What is the peculiarity of intermittent way of anti-TB drugs administration?
30. What ways of taking drugs are used in Phthisiology?
31. What is the advantage of intravenous method of taking anti-TB chemotherapy?
32. Which drugs are taken intravenously?
33. What are the indications for intravenous chemotherapy?

34. Enumerate the contraindications anti-TB chemotherapy?

35. What data is taken in account during the distribution of TB patients among treatment categories?

36. Which cases of TB are concerns to Category 1?

37. What tuberculosis disease is considered as extensive one?

38. Which cases of TB are concerns to Category 2?

39. Which cases of TB are concerns to Category 3?

40. Which cases of TB are concerns to Category 4?

41. What are standardized schemes of TB treatment in adults?

42. What is the peculiarity of TB patient treatment in Category 4?

43. Which standardized treatment regimen is used in multi-drugresistant (MDR) TB patients?

Practical work (tasks) which are doing within the class:

1. Which drug of mentioned below ones has anti-TB action?

A. Nitroxoline.

B. Ciprofloxacin.

C. Co-trimoxazole**.**

D. Amoxicillin.

E. Doxycyclin.

2. Which drug of mentioned below ones acts only on extracellular MBT?

A. Isoniazid.

B. Ethambutol.

C. Pyrazinamide.

D. Streptomycin.

E. Rifampicin.

3. **Which drug of mentioned below ones can induce a neuropathy?**

A. Isoniazid.

B. Ethambutol.

C. Pyrazinamide.

D. Streptomycin.

E. Rifampicin.

4. Which disease is a contraindication for isoniazid administration?

A. Chronic obstructive bronchitis.

B. Rheumatic fever.

C. Epilepsy.

D. Chronic pancreatitis.

E. Ulcer disease.

5. The patient P., 33 years old, is in the inpatient department of anti- TB dispensary. Diagnosis “Tuberculous meningitis” was confirmed by MBT found in cerebrospinal fluid. The administered treatment: isoniazid (intravenously) + PAS (intravenously) + rifampicin (per os) + streptomycin (intramuscular) + pyrazinamide (per os). **Which drug is of rational taking during lumbar puncture?**

A. Rifampicin.

B. PAS.

C. Streptomycin.

D. Amicacin.

E. Chlorine calcium complex of streptomycin.

6. The patient, 46 years old suffers from newly diagnosed fibrousecavernose tuberculosis. MBT resistant to isoniazid and kanamycin were found in the sputum.

What etiologic chemotherapy is necessary to administer in intensive phase of patient treatment?

7. The patient, 39 years old suffers from pulmonary fibrousecavernose tuberculosis during 6 years. Chemotherapy failed. Surgical methods of treatment are not indicated. The patient visited a doctor with the complaints on febrile fever, weakness, cough with sputum and haemoptysis. MBT resistant towards streptomycin were found in the sputum.

What treatment is necessary?

8. Primary tuberculous complex of moderate lobe of the right lung (phase of infiltration) was diagnosed in a child of 10 years old. MBT are not found.

What treatment is necessary for the patient in intensive phase?

9. Right sided caseous pneumonia was newly diagnosed in patient of 26 years old. MBT sensitive towards every of all anti-TB drugs are found in the sputum.

What treatment is necessary for the patient in chemotherapy intensive phase?

10. The diagnosis of right sided caseous pneumonia was made in a patient of 47 years old. The patient's state is severe. Fever is 39-40º C. Cough with the sputum, breathlessness in the rest are present. The patient is HIV-infected person. Dullness is heard over the right upper lobe of lungs during the percussion. The breathing is of bronchial one. Little number of moist rales of different calibers is aucultated. Blood test: leucocytes – 12,4x109/l, ESR – 38 mm/hour. X-ray picture: total shadowing of the right upper lobe with multiple parts of translucency. Nodular lesions of slight intensity with vague contours are in the lower lobes of both lungs. MBT are found in the sputum. **What kind of adjacent therapy is necessary to apply with anti-TB chemotherapy?**

The patterns of answers: 1.B. 2.D. 3. A. 4. C 5.E. 6. Isoniazid, rifampicin, ethambutol, pyrazinamide. 7. Isoniazid, rifampicin, ethambutol, pyrazinamide, ofloxacin 8. Isoniazid, rifampicin, pyrazinamide, vitamins of B group, hepatoprotectors 9. Isoniazid, rifampicin, pyrazinamide, streptomycin 10. Steroids, immune-correctors

Materials for the self-control:

A. The variants of independent student's task doing during the practical class:

1. To compose the table of the main principles of TB patient treatment using the references

2. To enumerate the main methods of TB patient treatment.

3. To compose the table of possible adverse reactions induced by essential anti-TB drugs using the references

4. To compose the table of the main anti-TB drugs and indicate their single and daily dose using the references

5. To compose the table of possible methods of taking anti-TB drugs.

6. To compose the table of the main criterions of TB clinical recovery and indicate the diagnostic methods used to prove the recovery.

B. The variants of situate task doing during the practical class:

1. To administer the chemotherapy regimen for new case of small form of TB.

2. To administer the chemotherapy regimen for new case of cavitary form of TB.

3. To administer the chemotherapy regimen for a patient suffering from cavitary form of TB with treatment failure at previous stage of chemotherapy.

4. To administer the chemotherapy regimen for a patient suffering from chronic cavitary form of TB.