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DEPARTMENT OF PHTISIOPULMONOLOGY

“Clinical case of a combination of tuberculosis and new coronavirus infection covid-19”

METHODOLOGICAL GUIDE

FOR EXTRACLUDOR INDEPENDENT WORK IN THE DISCIPLINE “PHTHISIATRICS”

For 6th year students of the medical-pediatric and medical-preventive faculties, 4th year students of the dental faculty.

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1. Introduction. Basic requirements for anti-tuberculosis drugs activities during the COVID -19 pandemic

The global development of the new coronavirus infection COVID -19 (hereinafter referred to as COVID -19) pandemic has become a serious challenge for national healthcare systems. The main approaches to preventing the spread of COVID -19 are self-isolation and social distancing .

The spread of COVID -19 in the Russian Federation has made it necessary to maximize the mobilization of the available resources of medical organizations of all profiles to combat this disease. It is logical that timely diagnosis and treatment of patients with COVID -19 and prevention of the spread of the disease for any medical worker during a pandemic is an absolute priority.

At the same time, even in the context of large-scale anti-epidemic measures during a pandemic, it is necessary to understand that tuberculosis is a socially significant infectious disease and the suspension of anti-tuberculosis measures cannot be justified by any “special” circumstances.

It should be remembered that untimely detection of tuberculosis and interruptions in treatment lead to the spread of the disease, the development of drug resistance of the pathogen and, as a consequence, to the unfavorable development of the tuberculosis situation in a particular region and in the country as a whole.

It is important to note that there is growing evidence indicating that in the majority of patients with tuberculosis, COVID -19 occurs in a severe form with the development of viral pneumonia, leading to acute respiratory distress syndrome and respiratory failure.

In this regard, along with measures to respond to the COVID -19 epidemic , every possible effort must be made to maintain the system of providing the necessary types of medical care to patients with tuberculosis.

COVID -19 pandemic, the anti-tuberculosis service of the Russian Federation, along with the tasks of diagnosing, treating and preventing the spread of tuberculosis, has new important tasks, including preventing the spread of COVID -19 among contingents and employees of anti-tuberculosis organizations.

The restrictions imposed by quarantine measures and the self-isolation regime require a revision of traditional approaches to providing anti-tuberculosis care to the population, changing the functional structure of anti-tuberculosis organizations and routing tuberculosis patients for the period of anti-epidemic measures.

The main approaches to organizing anti-tuberculosis care in the context of the COVID -19 epidemic are:

- organization of medical care for tuberculosis patients

mainly at the patient's home;

- ensuring timely detection of tuberculosis cases with

bacterial isolation and isolation of these patients, mainly at the patient's home;

- strict restrictions on the conduct of diagnostic and treatment measures

on an outpatient basis in anti-tuberculosis dispensaries and hospitalization in anti-tuberculosis hospitals;

- strict adherence to all principles of infection control in

anti-tuberculosis organizations, which should be extended to all patients and medical workers, regardless of the patient's bacterial excretion factor and include: strict restrictions on the movement of patients within medical organizations; isolation in separate rooms and observation for 14 days of all patients admitted to the hospital, strict adherence to the "mask" regime by patients and the use of personal respiratory protection equipment by medical personnel;

- daily monitoring of possible manifestations of COVID -19 as in patients

tuberculosis, and among medical workers of anti-tuberculosis organizations;

- development and approval in the executive authorities of the subject

Federations in the healthcare sector have a procedure for routing persons with active tuberculosis and COVID -19 in isolated cases of infection and in the event of a mass outbreak of COVID -19 among tuberculosis patients;

- practicing procedures for personnel of anti-tuberculosis organizations

when identifying COVID -19 patients and preparing the anti-tuberculosis organization to work in conditions of a nosocomial outbreak of COVID -19.

The implementation of these principles will allow anti-tuberculosis organizations to continue providing effective anti-tuberculosis care and will make a tangible contribution to the overall efforts of the medical services of the constituent entities of the Russian Federation in the fight against the COVID -19 epidemic.

2. Organization of detection and diagnosis of tuberculosis in the context of the COVID -19 pandemic

In the context of the COVID -19 pandemic , timely diagnosis of tuberculosis is of particular importance.

2.1 Diagnosis of tuberculosis when patients visit primary health care organizations and medical organizations providing specialized, including high-tech medical care (with the exception of organizations specializing in phthisiology)

All persons who seek medical help with complaints of cough for 3 weeks or more are subject to examination for tuberculosis. In the context of the new coronavirus infection COVID -19 pandemic , it is necessary to screen such patients not only for tuberculosis, but also for COVID -19. When diagnosing tuberculosis, a microbiological (by AFB microscopy) or molecular genetic (PCR) examination of sputum is performed, as well as a radiation examination of the chest organs (X-ray or CT- study).

Sputum for analysis is collected by the patient independently at home after instructions from medical personnel.

Sputum collection for testing for AFB and MBT DNA is carried out over 2 consecutive days, with a minimum interval between collections of 2-3 hours. Sputum examination using AFB microscopy, as well as MBT DNA PCR, should be carried out three times.

To exclude the disease of the new coronavirus infection COVID -19 in patients with cough, the material obtained by taking a smear from the nasopharynx and/or oropharynx is examined by PCR for SARS - CoV -2 RNA.

Sputum (if available) can be used as additional material for research. At the same time , at the beginning of the disease, the most informative material is obtained by taking a smear from the nose, at a later date - sputum.

If a patient has a cough and a temperature of more than 37.5 $^{\circ}$ C, the case of illness is suspected of COVID -19. In this case, as soon as possible - within 24 hours, the material obtained by taking a smear from the nasopharynx and/or oropharynx is examined using PCR for SARS - CoV -2 RNA and computed tomography . At the first negative result of a smear test from the nasopharynx and/or oropharynx using PCR for SARS - CoV -2 RNA , a repeat test is carried out within 48 hours, then on the 11th day of observation. Examination and management of such patients is carried out in accordance with temporary guidelines

Ministry of Health “Prevention, diagnosis and treatment of the new coronavirus infection COVID -19” with strict adherence to sanitary and epidemiological standards in an outpatient (at home) or inpatient setting (infectious diseases hospital), depending on the severity of the condition.

Instructions for collecting and transporting sputum for the purpose of diagnosing tuberculosis and COVID -19 in a patient at home are given in Appendix 1.

Health care workers who collect, package and transport clinical samples and conduct laboratory tests must be trained in biosafety requirements and rules when collecting and handling material suspected of being contaminated with microorganisms II pathogenicity groups, strictly observe infection safety measures and use personal protective equipment.

It should be noted that changes in the lungs detected during a computed tomography scan may be caused by COVID -19, while the result of PCR diagnostics for SARS - CoV -2 may be negative. According to studies, when diagnosed by PCR in the first seven days from the onset of the disease, the SARS - CoV -2 virus is detected in almost 70% of patients, then the rate begins to decrease from the 15th day from the onset of the disease and amounts to no more than 45.5%. If there are changes characteristic of coronavirus infection (see Appendix 2), a repeat PCR test for SARS - CoV - 2 RNA and consultation with an infectious disease specialist are necessary .

If COVID -19 is ruled out , a TB doctor will consult with a TB doctor and conduct an additional examination for tuberculosis. A consultation with a phthisiatrician can be carried out in the form of a telemedicine consultation, at home while the patient is self-isolating, or in another medical institution if the patient is currently hospitalized there.

If a diagnosis of tuberculosis is made with a negative COVID -19 status , a TB doctor, when visiting a patient at home, assesses the severity of his condition. In case of mild or moderate severity, while ensuring infection safety measures, tuberculosis treatment and observation at home are organized in conditions of self-isolation of the patient. A patient with tuberculosis is prescribed one of the chemotherapy regimens depending on drug resistance data (ID : KR16/1 “Tuberculosis in adults”). It is mandatory to ensure control over the intake of anti-tuberculosis drugs, incl . using information and communication technologies. If it is necessary to carry out therapeutic and diagnostic measures in

In an outpatient setting , it is necessary to provide the patient with medical transport to transport the patient to the anti-tuberculosis medical organization and back.

Based on the results of the examination, it is possible to identify a combination of two infections - tuberculosis and COVID -19. In this case, the patient must be isolated and sent by ambulance to an infectious diseases hospital or specialized medical organizations repurposed for the treatment of COVID -19 and tuberculosis.

2.2 In regional (territorial, district, republican) medical organizations of the constituent entity of the Russian Federation, providing specialized medical care in the field of phthisiology.

Mandatory diagnostic studies when making a diagnosis of tuberculosis are: microbiological studies, including the study of two samples of diagnostic material using fluorescent microscopy, a cultural method (on liquid and solid media), molecular genetic testing for the presence of DNA markers of Mycobacterium tuberculosis and mutations of resistance to anti-tuberculosis drugs, at least to rifampicin . When detecting resistance to rifampicin, it is necessary to study mutations associated with resistance to reserve drugs, at least to fluoroquinolones . When obtaining MBT growth, carrying out species identification of the isolated cultures and determining the sensitivity of MBT to anti-tuberculosis drugs by the cultural method. In the absence of resistance to rifampicin using the molecular method, the phenotypic sensitivity of MBT is determined by the method of absolute concentrations to streptomycin, isoniazid , rifampicin , ethambutol or by the method of proportions to streptomycin, isoniazid , rifampicin , ethambutol , pyrazinamide . When detecting resistance to rifampicin by the molecular method, the phenotypic sensitivity of MBT is determined by the method of proportions, at least to levofloxacin , moxifloxacin , ethionamide / prothionamide , capreomycin , kanamycin , amikacin .

In patients hospitalized for treatment of tuberculosis, if additional symptoms of intoxication and/or respiratory disorders or new changes during control computed tomography appear, it is necessary to perform a sputum or other material examination using PCR for SARS - CoV -2 RNA . If a positive result is obtained, the patient must be isolated and sent by ambulance to an infectious diseases hospital, specialized medical organizations repurposed for the treatment of COVID -19 and tuberculosis.

The structural unit of a medical organization for the treatment of COVID -19 and tuberculosis is located in a separate building or a complex of medical buildings

organizations. Placing a structural unit of a medical organization for the treatment of COVID -19 in the same building with other structural units of an anti-tuberculosis medical organization is possible if there is an isolated supply and exhaust ventilation system of the dedicated structural unit that maintains negative pressure in areas of high risk of the spread of tuberculosis and coronavirus infections, and the presence of two separate from other entrance areas (for staff and patients).

In the premises of structural units of a medical organization for the treatment of COVID -19 , the use of air recirculation both in mechanical ventilation systems and through autonomous air purifiers and air conditioners (split systems) is not allowed.

If it is impossible to comply with these conditions, placing a structural unit of a medical organization for the treatment of COVID -19 in the same building with other structural units of an anti-tuberculosis medical organization is not allowed. The provision of assistance must be carried out under conditions of strict adherence to the anti-epidemic regime, which ensures protection against cases of nosocomial infection with COVID -19 and preventing the spread of infection beyond the boundaries of the structural unit of the medical organization for the treatment of COVID -19. The introduction of COVID -19 into a tuberculosis hospital is most dangerous due to the combination of two infectious diseases with damage to the bronchopulmonary system and the risk of a complicated course of both COVID -19 and tuberculosis.

COVID -19 must be developed and approved .

Transportation of the patient is carried out in compliance with all infection safety measures and the availability of personal protective equipment for medical personnel. After hospitalization of the patient, final disinfection of all premises is carried out after his stay.

Further examination and treatment of tuberculosis patients with COVID -19 is carried out under the simultaneous supervision of a phthisiatrician and an infectious disease specialist. When contacting a patient, it is mandatory for medical personnel to use personal protective equipment.

3. Differential diagnosis of pneumonia, including those caused by the new coronavirus infection COVID -19, and respiratory tuberculosis

For an accurate and timely diagnosis, a differential diagnosis of respiratory tuberculosis with community-acquired pneumonia, viral pneumonia caused by COVID -19 and Pneumocystis pneumonia in patients with HIV infection is required. Differential diagnosis should be carried out taking into account the most characteristic clinical, laboratory and radiological manifestations. The characteristic signs of these diseases are outlined in Appendix 2.

4. Treatment of patients with tuberculosis and COVID -19

Treatment of COVID -19 in patients with tuberculosis is similar to treatment in the general population. However, when treating co-infection of COVID -19 and tuberculosis, it should be taken into account that tuberculosis therapy, regardless of the location of the infectious process, is long-term and consists of using a combination of drugs that suppress the proliferation of MBT (bacteriostatic effect) or destroy them in the patient's body (bactericidal effect). In the treatment of tuberculosis, various chemotherapy regimens are used, including from four to seven drugs in the intensive phase of treatment, from two to five in the continuation phase.

When co-infecting tuberculosis and COVID -19 , one of the main difficulties is the possible drug interaction of drugs for the treatment of tuberculosis with drugs recommended for the treatment of COVID -19. In this regard, it is necessary to adjust anti-tuberculosis therapy and carefully monitor the side effects of drug therapy that may develop during the treatment of patients in this category.

Detailed information on the treatment of tuberculosis is given in the clinical recommendations "Tuberculosis in adults", on the treatment of coronavirus infection in the methodological recommendations of the Russian Ministry of Health "Prevention, diagnosis and treatment of a new coronavirus infection (COVID -19)".

According to the Temporary Methodological Recommendations for drugs, recommended for etiotropic treatment of this infection in adults are chloroquine , hydroxychloroquine , mefloquine .

Chloroquine , hydroxychloroquine , mefloquine are antimalarial drugs that are supposed to prevent the virus from entering the cell. In exceptional

In cases where there are contraindications to the use of antimalarial drugs, lopinavir / ritonavir (an antiretroviral drug for the treatment of HIV infection) is used to treat COVID -19 . However , clinical studies have not proven the effectiveness of this drug against COVID -19 and many countries have abandoned its use.

At the same time, in patients with combined tuberculosis-HIV and COVID -19 infection who have been taking lopinavir / ritonavir for a long time , it is recommended to continue taking this drug, and if necessary, by decision of the medical commission, in combination with hydroxychloroquine .

Considering the lack of objective evidence of the effectiveness of the use of the above drugs for COVID -19, the lack of corresponding indications in the instructions for the drugs, the prescription of treatment must necessarily be accompanied by obtaining the voluntary informed consent of the patient (or his legal representative).

A number of drugs for the treatment of COVID -19 have a similar mechanism of action to anti-tuberculosis drugs, and their drug interactions may complicate the implementation of joint therapy. However , full treatment of coronavirus infection is a priority, and etiotropic therapy for tuberculosis should be adjusted by a medical commission taking into account drug interactions and the patient's individual tolerance to drugs. It should be noted that interactions between drugs must be considered taking into account the relatively short duration of etiological treatment of COVID -19 (maximum 14 days).

In addition, it must be remembered that correction of tuberculosis therapy should not violate the basic principles of tuberculosis therapy (a combination of drugs with bactericidal and bacteriostatic action against Mycobacterium tuberculosis, corresponding to the resistance of the isolated pathogen), and if it is impossible to prescribe full-fledged regimens to the patient, the commission should consider the possibility of complete short-term withdrawal anti-tuberculosis therapy for the period of treatment of COVID -19. Inadequate therapy for tuberculosis, even for 2 weeks, can contribute to the formation of drug-resistant strains of Mycobacterium tuberculosis.

Possible drug interactions for the treatment of co-infection with COVID -19 and tuberculosis are presented in Appendix 3.

One of the main drugs for the treatment of drug-sensitive tuberculosis is rifampicin (in special cases it can be replaced with other drugs of the group: rifabutin , for example, in patients with HIV infection when using an antiretroviral therapy regimen incompatible with rifampicin , or rifapentine in the continuation phase of treatment) . All drugs from the rifampicin group activate the cytochrome P450 system and can reduce the concentration of antimalarial drugs, negatively affecting their therapeutic effect.

When using treatment regimens for COVID -19, including hydroxychloroquine , chloroquine , mefloquine , it is necessary in patients with drug-sensitive tuberculosis receiving I and III chemotherapy regimens, replace rifampicin with rifabutin , rifapentine (in the continuation phase) with rifabutin . The replacement with rifabutin is due to the fact that, as shown by pharmacokinetic studies in vivo , the inducing properties of rifabutin in relation to the cytochrome 450 system are significantly less pronounced than those of other drugs from this group (rifampicin and rifapentine). In this regard, it is assumed that there will be no decrease in the concentration of drugs for the treatment of COVID -19 below therapeutic levels. It is recommended to use rifabutin at a dose of 150 mg * 1 time / day daily. 2-3 weeks after
After treatment for COVID -19 with antimalarial drugs ends, taking into account the long half-life and accumulation of drugs in organs and tissues, rifabutin can be discontinued and rifampicin can be resumed .

cardiotoxicity and prolong the QT interval are used to treat multidrug-resistant tuberculosis on the ECG. These include fluoroquinolones III - IV generation (levofloxacin , sparfloxacin , moxifloxacin) and a representative of the diarylquinoline class - bedaquiline . Hydroxychloroquine , chloroquine , mefloquine , and azithromycin can have a similar effect .

When treating patients on IV chemotherapy regimen, it is recommended to switch patients to a less cardiotoxic fluoroquinolone - levofloxacin . When treating patients according to V chemotherapy regimen, it is possible to temporarily discontinue fluoroquinolones for the period of treatment of COVID -19.

Monitoring for cardiotoxicity requires instrumental and clinical monitoring, including the QT interval . An ECG is prescribed before the start of treatment, monitoring is carried out once every 5 days. QT interval duration corrected is estimated using the Bazett formula , it should not exceed 480 ms . Upon reaching the threshold value, on the recommendation of a cardiologist individually

beta-blockers are prescribed (bisoprolol , carvedilol , nebivolol , metoprolol). If there are complaints of arrhythmia, palpitations, pain and discomfort in the heart area, episodes of weakness and dizziness, or syncope , an emergency ECG is prescribed.

Combined therapy with the oxazolidinone class antibiotic linezolid and antimalarial drugs may increase the neurotoxicity of the drugs and increase the risk of developing optic neuritis. Clinical monitoring is required. If characteristic complaints of decreased visual acuity, changes in color vision , pain in the eye, or headache appear, consult an ophthalmologist or neurologist.

To correct an excessive immune response in the treatment of COVID -19 , the interleukin-6 inhibitor tocilizumab is used . Considering that tocilizumab contraindicated in active tuberculosis, the drug can be prescribed only by decision of a medical commission, provided that the benefit to the patient outweighs the possible risks. The commission must include a TB doctor and a resuscitator . When tocilizumab is co-administered with linezolid , a significant decrease in platelet levels is possible. It is necessary to monitor a complete blood count before starting the combined use of drugs and then once every 3-4 days during the entire period of treatment for COVID -19.

The development of thrombocytopenia may also occur when linezolid is combined with interferon-beta . The principles for monitoring thrombocytopenia are similar.

Pathogenetic therapy for tuberculosis during treatment of COVID -19 is not recommended.

5. Organization of home treatment and dispensary observation of tuberculosis patients during the coronavirus pandemic

In the context of the new coronavirus infection pandemic and self-isolation, treatment and dispensary observation of tuberculosis patients is carried out mainly at home, with the mandatory provision of infection control measures and infection safety of persons living with the patient.

Day hospitals in anti-tuberculosis organizations, which provide daily visits to patients, are subject to closure during the pandemic.

A patient with tuberculosis is prescribed one of the chemotherapy regimens depending on drug resistance data in accordance with the requirements of the clinical guidelines “Tuberculosis in adults”, ID : KR16/1.

It is important to organize control by medical personnel over the administration of each dose of anti-tuberculosis drugs during the main course of chemotherapy.

In organizing supervised treatment, priority is the use of information and communication technologies such as Skype , WhatsApp etc., with the help of which medical workers monitor patients' intake of TB drugs.

For this purpose, a remote control room is organized in the anti-tuberculosis organization, and a responsible employee is determined.

The medical record of treatment of a patient with tuberculosis (form 01-TB/u) is maintained in accordance with the requirements.

All patients registered or registered with anti-tuberculosis medical organizations during the coronavirus pandemic must be in self-isolation at all times. It is important to prevent patients from being in the corridors, offices, and halls of the medical institution.

Organization of work in foci of tuberculosis infection, carrying out final and ongoing disinfection, identification and examination of contact persons is carried out taking into account the epidemiological significance of the identified foci.

Strengthening all infection and epidemic control measures is mandatory.

Basic principles of organizing medical care for tuberculosis patients:

1. Conducting telemedicine consultations (or consultations using other information and communication technologies) specialists anti-tuberculosis medical organization in case of suspected tuberculosis in a patient for primary health care specialists.

2. Completing the clinical minimum of tuberculosis screening for everyone persons who have been coughing for more than 3 weeks (Order of the Ministry of Health of the Russian Federation dated December 29, 2014 No. 951 "On approval of methodological recommendations for improving the diagnosis and treatment of respiratory tuberculosis") by primary health care institutions with sputum collection for AFB at home.

3. Organization of controlled treatment of tuberculosis patients on an outpatient basis at home, subject to the patient's self-isolation regime.

4. Registration of written informed consent of the patient for provision of medical care on an outpatient basis (at home) in compliance with the isolation regime for the treatment of tuberculosis.

5. Determining the need for hospitalization of patients in anti-tuberculosis hospital or changes in the organizational form of treatment of the patient by the medical commission of the anti-tuberculosis organization.

6. Informing patients about the symptoms of a new coronavirus infection COVID -19 and the algorithm of actions if suspicious symptoms occur (call your local physician, inform your local phthisiatrician).

7. Compliance with infection control measures by healthcare workers, providing care to patients with tuberculosis at home (use of personal protective equipment: disposable gown, respirator, gloves; treating hands with a disinfectant solution; disposal of personal protective equipment as class B waste).

8. Conducting consultations with a phthisiatrician for patients receiving treatment once every 10-14 days by visiting your home or remotely at home using telecommunication technologies.

9. Conducting consultations with narrow specialists according to indications via on-site visits at home or remotely at home using telecommunications technologies.

10. Organization of consultations with a psychologist, narcologist, social worker using telecommunication technologies for patients who allow interruptions in treatment.

11. Conducting laboratory and instrumental monitoring of adverse reactions of anti-tuberculosis drugs according to indications.

12. Conducting laboratory monitoring of the effectiveness of the ongoing course of chemotherapy with collection of diagnostic material at home at least once a month in the intensive phase of treatment and once every two months in the continuation phase.

13. Carrying out an X-ray examination at the beginning of treatment, during the transition to the continuation phase and at the end of treatment, as well as when bacterial excretion resumes or other signs of disease progression (interim planned x-ray examinations temporarily are suspended).

14. Delivery of a patient for an x-ray examination by a medical professional transport of the anti-tuberculosis organization.

15. Consulting district TB specialists on examination issues patients, correction of treatment, summing up the results of courses of therapy using information and communication technologies (telemedicine consultations) or through correspondence consultations.

16. Establishing a diagnosis of tuberculosis and placing the patient under the supervision of an anti-tuberculosis institution, as well as summing up the results of the patient's main course of treatment based on the results of the examination in absentia with written notification to the patient.

17. Examination of patients according to II , III , IV dispensary observation groups according to indications.

18. Changing the work of dispensary outpatient departments of anti-tuberculosis institutions and redistributing personnel to provide video-controlled treatment of tuberculosis patients, as well as treatment and examination of patients at home to the required extent.

Organization of outpatient treatment of tuberculosis patients in self-isolation can be carried out in the following organizational forms: video-controlled treatment at home, hospital at home; mobile nursing teams.

When determining the organizational form of treatment for patients with tuberculosis who are already receiving the main course of treatment on an outpatient basis, or who are being discharged from the hospital of an anti-tuberculosis institution, as well as in patients with newly diagnosed tuberculosis or a relapse of the disease requiring a course of therapy, it is necessary to give preference to video-controlled treatment under the following conditions :

- technical support for daily treatment monitoring using information and communication technologies;
- mode of self-isolation of the patient;
- missed doses of no more than 15% of doses prescribed by the treatment regimen;
- absence of children and pregnant women in the patient's place of residence;
- the presence of a separate room in the place of residence of a patient with bacterial excretion .
- the patient does not have concomitant diseases that complicate the course of tuberculosis.

For patients for whom it is impossible to organize video-controlled treatment, or for whom dose omissions exceed 15-20%, organize outpatient treatment in a hospital setting at home under the following conditions:

- self-isolation regime of the patient;
- absence of children and pregnant women in the patient's place of residence;
- the presence of a separate room in the place of residence of a patient with bacterial excretion .

If it is impossible to organize the above forms of treatment in regional anti-tuberculosis dispensaries or tuberculosis rooms, ensure the issuance of anti-tuberculosis drugs for 7-14 days. In this case, the dispensary/office nurse is required to conduct a daily telephone survey about the patient's medication intake and condition.

Indications for hospitalization of a patient with tuberculosis in a 24-hour hospital:

- progressive pulmonary heart failure, hemoptysis, pulmonary hemorrhage, spontaneous pneumothorax);
- common forms of tuberculosis with symptoms of intoxication;
- tuberculous meningoencephalitis ;
- tuberculous pleurisy with persisting exudate and/or signs of respiratory failure;
- the presence of bacterial excretion when the patient lives together with people at risk for tuberculosis, children 0-17 years old, or the patient lives in a communal apartment or dormitory;
- the patient has concomitant diseases that complicate the course of tuberculosis and pose a threat to the development of adverse reactions;
- the patient has a history of severe allergic reactions;
- the occurrence of adverse reactions to anti-tuberculosis drugs that are not amenable to drug correction and/or life-threatening .

Table 1

Organization of treatment of tuberculosis patients during the COVID -19 pandemic

Organizational form of treatment	Number of times a nurse visits a patient	Frequency of doctor visits	Frequency of patient examination
Hospital at home	Daily	1 time every 10 days	CBC, OAM, sputum examination for MBT, biochemical blood test 1 r. per month - intensive phase of treatment, 1 r. at 2 months - continuation phase. X-ray examination:
Travel nursing teams	Daily	1 time every 10 days	
Video monitoring my treatment	Daily communication using information and communication technologies	Once a month, communication using information and - communication technologies at least once a week, increase frequency if necessary	

		monitoring the patient's condition	- before starting treatment; - when transferring to the continuation phase of treatment; - at the end of treatment.
Tuberculosis room	Daily, if not possible - telephone survey	1 time every 10 days	

6. Organization of preventive treatment of tuberculosis persons in contact with patients who release bacteria

Organization of treatment of patients with tuberculosis with bacterial excretion at home requires simultaneous provision of preventive treatment to persons in close contact living in the same apartment.

As a rule, at the time of identification of a patient with tuberculosis with the release of Mycobacterium tuberculosis, persons living in close contact are infected with mycobacteria and require preventive treatment.

Basic principles of organizing medical care for persons in contact with patients with bacterial tuberculosis :

1. Examination of contacts to exclude clinical symptoms tuberculosis (cough, fever, weight loss and night sweats) and determining the skin reaction to ATP administration.
2. Evaluation of a skin test with recombinant tuberculosis allergen through 72 hours remotely using information and communication technologies, or during a visit from a medical worker at a tuberculosis office at home.
3. Carrying out an X-ray examination or computer tomography for contacts with a positive or questionable result of the ATP test.
4. Systematic observation of contact persons by a TB doctor through information and communication technologies such as Skype , Viber , WhatsApp and etc.
5. Prescribing preventive treatment for tuberculosis to persons in contact with patients with bacterial excretion with a questionable or positive result of a skin test with ATP in the absence of clinical symptoms of tuberculosis and pathological changes in the lungs and intrathoracic lymph nodes.

6. Prescribing preventive treatment for tuberculosis to persons in contact with patients in whom bacterial excretion is determined by sputum smear microscopy, regardless of the result of the ATP test in the absence of clinical and radiological signs of active tuberculosis in the contact person.

7. Carrying out preventive treatment to contact persons under direct supervision of medical personnel through information and communication technologies, or during direct home visits.

8. Determining a preventative treatment plan for a contact person based on the result of determining the patient's drug sensitivity

9. Psychological and social support for contact persons receiving preventive treatment of tuberculosis.

Tuberculosis preventive treatment regimens

1. Contact persons with a patient with Mycobacterium tuberculosis sensitive to first-line drugs, may receive one of the following preventive treatment regimens:

а) isoniazid and rifampicin daily for 3 months;

б) isoniazid and rifapentine once a week for 3 months (12 doses);

в) isoniazid and rifapentine daily for one month;

г) isoniazid and rifabutin daily for one month (when prescribing COVID -19 prevention regimens with hydroxychloroquine , chloroquine , mefloquine for the period of their use);

д) isoniazid daily for 6-9 months (if the above regimens are contraindicated).

HIV-positive contacts of a bacillary patient with a pathogen sensitive to first-line anti-tuberculosis drugs should receive preventive treatment with isoniazid for 6-9 months.

2. Contact persons with a patient who has been diagnosed with bacterial excretion and Mycobacterium tuberculosis is resistant to isoniazid , but sensitive to rifampicin should receive rifampicin in combination with one of the drugs (ethambutol , pyrazinamide , levofloxacin), depending on the drug sensitivity data of the pathogen of the patient- bacterial isolate , daily for 4 months.

3. Contact persons with a bacterial-distributing patient with multiple Drug-resistant pathogens can receive preventive treatment with a combination of 3 drugs. In this case, preventive treatment is prescribed

patients at risk of developing tuberculosis by decision of the medical commission, taking into account the data on the drug resistance of the pathogen in the patient who excreted the bacteria . Inclusion of first-line anti-tuberculosis drugs into the preventive treatment regimen is possible only if the sensitivity of the pathogen is confirmed in a patient who is a bacteria-excreting patient .

7. Features of infection control in a tuberculosis hospital

Infection control measures during the period of epidemic rise in the incidence of COVID - 19 should be aimed at preventing the nosocomial spread of both tuberculosis infection and infection caused by the SARS - CoV -2 virus among patients, staff and visitors of TB medical organizations. The set of preventive measures is based on the specific features of the mechanisms of spread of the corresponding infections. It must be taken into account that both tuberculosis infection and SARS - CoV -2 infection are spread by air (via bioaerosols), and for SARS - CoV - 2 infection, in addition, contact and airborne droplets are also epidemically significant routes of spread .

To reduce the risk of unreasonable introduction of SARS - CoV -2 infection into TB hospitals, the following restrictive quarantine measures are recommended:

- Hospitalization of patients with tuberculosis must be justified

limited:

- Only patients with a previously microbiologically confirmed diagnosis of tuberculosis (smear microscopy for AFB, rapid molecular genetic methods), which represent an increased

epidemiological risk (with a positive AFB smear) , as well as for other indications defined in paragraph 6 of these recommendations. All tuberculosis patients admitted to the TB hospital must be isolated for 14 days from other patients until they receive two negative test results for COVID - 19, c subsequent transfer to a specialized department.

- In case of emergency hospitalization of patients with signs of acute respiratory viral infection or

elevated temperature that cannot be explained by the underlying disease (active tuberculosis), they must be quarantined (box or separate

room with a bathroom in a dedicated isolated quarantine block) for a period of at least 14 days with testing for COVID -19 on the 1st, 2nd, 10th day.

- If hospitalization is not urgent, for persons with

signs of acute respiratory viral infection or elevated temperature, which cannot be explained by the underlying disease (active tuberculosis), the date of hospitalization is postponed to a later date (at least 21 days), and if chemotherapy is necessary, it should be organized on an outpatient basis.

- Exclusion of leaves of hospitalized patients for any reason

reasons.

- Eliminating the possibility for hospitalized patients to leave

territory of a phthisiological medical organization.

- Prohibition of all visits to patients by outside visitors.
- Excluding visits from hospitalized patients

other departments of the hospital, except with the permission of a doctor for treatment and - diagnostic purposes.

- Ensuring remote notification of relatives about the condition

patients in compliance with the requirements for the protection of personal information.

- Carrying out thermometry of all employees of the medical organization before

the beginning of the working day with the immediate removal from work of all persons with elevated temperature.

- Conducting continuous monitoring of the condition of hospitalized patients

patients for the appearance of acute respiratory symptoms, fever unmotivated by the underlying disease, the development of pneumonia, the onset or progression of respiratory failure.

- Ensuring immediate isolation of patients with suspected ARVI,

pneumonia or COVID -19 in a box or a separate room with a bathroom in a dedicated isolated quarantine block.

To reduce the risk of nosocomial spread of both tuberculosis and infection caused by SARS - CoV -2, when symptoms suspicious for COVID -19 are detected in hospitalized patients or the diagnosis of coronavirus infection is confirmed, the following measures are recommended:

- Immediate isolation of the patient in an infectious disease ward or separate

a ward with a bathroom in a dedicated isolated infectious disease unit for the isolation and treatment of patients with mixed tuberculosis/ SARS - CoV -2 infection.

- Before entering a block, box or allocated ward there must be

a vestibule has been organized for changing clothes and disinfecting hands, objects and protective clothing.

- Units (boxes, wards, blocks) where such patients are kept

must be marked indicating the high risk of infection, prohibiting entry for unauthorized persons, and the need for proper use of PPE .

- Access to such units should be strictly limited to only

employees directly involved in the provision of medical care.

- The room where such patients are placed should be

At least one of the following effective habitat control measures is provided around the clock :

- mechanical ventilation with the creation of negative pressure in the room with an air exchange rate of 6 - 12 per hour;
- maximum natural ventilation - constant intensive ventilation (open windows with closed entrance doors);
- ultraviolet bactericidal radiation in the upper part of the room using properly installed shielded irradiators;
- the use of open (unshielded) ultraviolet irradiators for 30 minutes every 6 hours is allowed only in the absence of people in the room and in combination with constant intensive natural ventilation (airing).

Please note that:

- the use of room air conditioners (split systems) in high

risk in the absence of other effective environmental control measures (ventilation, UVBI shielded) significantly increases the risk of the spread of infectious aerosols (tuberculosis, SARS - CoV -2, etc.);

- the use of air purifiers (air recirculators), including with

UVBI lamps do not provide a significant reduction in the risk of airborne infections (via bioaerosols) due to low specific efficiency, and therefore cannot be recommended for high-risk areas in the absence of other effective measures.

In areas of high risk of infection - premises where patients with mixed infection stay , it is mandatory to:

- carrying out regular effective disinfection of surfaces and

objects;

- proper hand washing or disinfection;
- compliance with personal hygiene requirements;

- ensure that everyone present in the room performs

cough hygiene requirements;

- whenever possible, it is necessary to strive to comply with safe

distances - at least 1.5 - 2 m from a potential source of infection;

- use of personal protective equipment (PPE):

• to prevent the spread of SARS - CoV -2 infection by contact, the following PPE registered by Roszdravnadzor for medical use is used: protective suits, gowns, aprons, caps, non-sterile gloves, shoe covers, etc.;

• to prevent the spread of tuberculosis and SARS - CoV -2 by air (via bioaerosols) - the use of certified respirators of a protection class of at least FFP 2, when carrying out aerosol-generating procedures (tracheal intubation, provocation and collection of sputum, toilet of the upper respiratory tract, collection of biological material for research etc.) - protective shields or glasses;

• 24-hour controlled use of medical (surgical) masks is mandatory for all hospitalized patients in the anti-tuberculosis hospital.

During this period, personnel should be provided with the use of medical masks throughout the working day in areas of low and medium risk of infection, and in areas of high risk of infection for tuberculosis and SARS - CoV -2 - the correct use of respirators.

To ensure maximum protection of personnel from the spread of infection through bioaerosols , personnel must be trained in the correct use of respirators and provided with the ones that comply with GOST 12.4.294-2015, TR CU 019/2011 “On the safety of personal protective equipment” or the European standard EN 149:2001+A1:2009 respirators of protection class FFP 2 or FFP 3.

During the COVID -19 pandemic , it is recommended to refrain from using respirators with an exhalation valve, as they do not prevent the spread of infection from the individual using it. For individual selection of models and sizes of respirators appropriate for each member of staff, it is necessary to conduct a fit test of respirators, the methodology of which is available at the link: https :// youtu . be /8 kPqLp 85 d 9 w .

Information on carrying out disinfection measures in high-risk areas, on the rational, long-term and reuse of PPE is contained in section 7. “Prevention of coronavirus infection” of the temporary guidelines

Ministry of Health of the Russian Federation “Prevention, diagnosis and treatment of new coronavirus infection (COVID -19).”

The handling and disposal of all waste from units for the treatment of patients with mixed infection tuberculosis/SARS-CoV-2, as well as other waste from a medical anti-tuberculosis organization, must be carried out in accordance with the requirements of SanPiN 2.1.7.2790-10 "Sanitary and epidemiological requirements for the handling of medical waste", which is classified as extremely epidemiologically hazardous waste of Class B.

8. Drug prevention of coronavirus infection

As a drug for chemoprophylaxis For COVID -19 , hydroxychloroquine is being considered ; if it is not available , mefloquine may be used .

In a number of countries, in a tense epidemic situation, drug prophylaxis is carried out with chloroquine , hydroxychloroquine and mefloquine . Considering the increase in morbidity and the high risks of spreading infection in our country, it is advisable to prescribe drug prophylaxis to certain groups of the population, including people with tuberculosis or people with LTBI. The principles for prescribing drug prophylaxis are similar to those in the general population.

table 2

Drug prevention of coronavirus infection

Group	Recommended scheme
Post-exposure prophylaxis for persons with tuberculosis or persons with latent tuberculosis infection (LTBI) after a single contact with a confirmed case of COVID -19	1. Hydroxychloroquine Day 1: 400 mg 2 times (morning, evening), then 400 mg once a week for 3 weeks; 2. Mefloquine Days 1 and 2: 250 mg 2 times (morning, evening), day 3: 250 mg per day, then 250 mg once a week for 3 weeks.
Prevention of COVID -19 in persons with tuberculosis or persons with LTBI who are in the focus of infection	1. Hydroxychloroquine Day 1: 400 mg 2 times with an interval of 12 hours, then 400 mg once a week for 8 weeks; 2. Hydroxychloroquine 400 mg daily for 7 days; 3. Mefloquine Days 1 and 2: 250 mg 2 times with an interval of 12 hours,

	Day 3: 250 mg per day, then 250 mg once a week for 8 weeks.

When using COVID -19 prevention regimens, including hydroxychloroquine , chloroquine , mefloquine , it is necessary in patients with tuberculosis receiving I and III chemotherapy regimens, replace rifampicin or rifapentine with rifabutin .

9. Features of providing medical care to children with tuberculosis in the context of the COVID -19 pandemic

9.1 Features of tuberculosis in children depending on age

9.1.1. Young children.

Due to the anatomical and physiological characteristics of the body of a young child, tuberculosis is characterized by more pronounced clinical manifestations, the development of a complicated course and a tendency to generalization. In a child under 12 months of age, detection of the disease is possible when seeking medical help or during an examination based on established contact with an adult with tuberculosis. It is in young children that the risk of developing miliary tuberculosis and tuberculous meningitis with a fatal outcome is high.

9.1.2. Teenagers.

The anatomical and physiological characteristics of adolescence lead to the rapid progression of tuberculosis, the severity of alterative-necrotic inflammation in the lung tissue, and the development of a complicated course with bacterial excretion . In adolescence, secondary forms of tuberculosis, characteristic of adults, develop, while maintaining the features of the primary period (high sensitization). Late detection and diagnosis, inadequate treatment measures contribute to the development of relapse of tuberculosis in young people and chronicity of the process.

9.2 Features of tuberculosis in children depending on the presence of vaccination against tuberculosis

Vaccination against tuberculosis (BCG, BCG-M) is the main method of preventing severe, rapidly progressing forms of the disease in young children. Among children not vaccinated against tuberculosis, complicated forms of TVGLU (61.7%), generalized tuberculosis (6.5%), bacterial excretion are recorded (11.7%), including massive (3.9%), and death is observed. (9.1%).

9.3 Features of COVID-19 in children

Children are susceptible to COVID -19 just like adults. Given the high proportion of asymptomatic and mild forms, children are currently considered as potential sources of infection. The main infection of children occurs in family centers or medical institutions (maternity hospitals).

In general, COVID -19 is milder in children than in adults. An analysis of cases of COVID -19 infection in children in different countries since the beginning of the pandemic shows that in 90% of cases, children have asymptomatic, mild or moderate cases of the disease. The frequency of severe and extremely severe cases of the disease does not exceed one percent. It is known that the risk of severe disease in the population is higher in people with chronic diseases of the cardiovascular system, respiratory system, diabetes mellitus, and malignant neoplasms. A higher risk of severe forms of infection caused by SARS - CoV -2, as well as other coronavirus infections, is observed in young children, children with concomitant pathologies, especially congenital malformations, as well as with HIV/tuberculosis co-infection.

Clinical symptoms in children correspond to the clinical picture of an acute respiratory viral infection caused by other viruses: fever, cough, sore throat, sneezing, weakness, myalgia. The severity of the febrile reaction can be different: fever up to 38 °C is observed in half of sick children, in a third of children an increase in body temperature is recorded from 38.1 to 39.0 °C. Other symptoms, relatively rare symptoms, with a frequency of no more than 10%, in children hospitalized in the PRC were diarrhea, weakness, rhinorrhea , and vomiting. Tachycardia is observed in half of hospitalized children, tachypnea in a third. Children rarely experience a decrease in saturation of less than 92%.

Risk groups for poor prognosis of severe co-infection (tuberculosis + COVID -19) in children:

- newborns and young children;
- children not vaccinated with BCG (BCG-M);
- unfavorable premorbid background, especially congenital defects

development, diseases of the cardiovascular system, respiratory organs, diabetes mellitus, malignant neoplasms, Kawasaki disease;

- immunodeficiency states of various origins;
- co-infection with other infectious diseases, especially

respiratory syncytial virus infection in young children.

9.4 Features of the prevention and detection of tuberculosis in children and adolescents during the COVID -19 pandemic

9.4.1. Routine vaccination of children against tuberculosis during a pandemic.

When deciding on a temporary restriction on routine preventive vaccinations against tuberculosis, one should be guided by the current, including temporary, regulatory documents of Rospotrebnador and the Russian Ministry of Health. The Regional Office for Europe of the World Health Organization (WHO/Europe) recommends based on the epidemiological situation as a whole, minimizing the possibility of exposure to COVID -9 by reorganizing vaccination work. Priority should be given to vaccination of newborns with BCG (BCG-M), as well as primary vaccine complexes, especially when it comes to vaccines containing measles, rubella or polio components, and other combination vaccines.

9.4.2. . Routine examination of children and adolescents for tuberculosis during the epidemic.

In a pandemic, there are limited opportunities for conducting preventive medical examinations [orders of the Ministry of Health of the Russian Federation dated March 16, 2020 No. 171 “On the temporary procedure for organizing the work of medical organizations in order to implement measures to prevent and reduce the risks of the spread of the new coronavirus infection (COVID - 19) ” ; dated March 19, 2020 No. 198n “On the temporary procedure for organizing the work of medical organizations in order to implement measures to prevent and reduce the risks of the spread of the new coronavirus infection (COVID -19)”; letter of the Ministry of Health of Russia dated March 19, 2020 No. 15-2/705-07]. Routine examination of children and adolescents using immunodiagnostics is not carried out. Accordingly, detection of the disease is possible mainly from among those who have applied for medical help with complaints, or from those who are registered with a TB doctor in risk groups for tuberculosis (contact with tuberculosis patients, altered sensitivity to tuberculosis allergens).

Recommended:

- all children who seek medical help with complaints

respiratory in nature (cough, shortness of breath, chest pain), increased body temperature for more than 7 days, purulent-inflammatory processes in various organs and tissues for more than 14 days (lymphadenitis, osteitis, etc.) immunodiagnosis of tuberculosis infection - skin samples with s ATP;

- children who sought medical help with respiratory complaints

nature (cough, shortness of breath, chest pain) conducting a plain chest x-ray;

- anti-tuberculosis institutions providing anti-tuberculosis

helping children and adolescents switch to the use of remote technologies - correspondence consultations with patients based on the results of studies;

- children in contact with tuberculosis patients should undergo immunodiagnostics

strictly by appointment, if possible - at home. The issuance of medical reports and recommendations is carried out using remote technology in compliance with the requirements for working with personal data. Provide medical care at home. If it is necessary to conduct an in-person examination, the aphthisiatrician in a medical organization must comply with the time for pre-registration of the patient for an appointment with separation of patients;

- delivery of anti-tuberculosis drugs, if necessary,

carried out at home by employees of the local anti-tuberculosis service;

- conducting an examination: collecting urine, sputum, blood (in extreme cases)

necessary), otherwise - carried out at home.

- preventive treatment of latent tuberculosis infection in children

carry out at home.

9.5 Features of diagnosing tuberculosis in children and adolescents during the COVID -19 pandemic

1. Children with suspected/presence of pneumonia are recommended to undergo an ATP test. Children with positive and questionable reactions to the ATP test are recommended to consult a TB doctor.

2. Collecting an anamnesis from a child suspected of having tuberculosis during the COVID -19 pandemic should include collecting an extensive epidemiological history, including the following information:

- stay of adults from the child's environment in other countries and in other regions of the Russian Federation;
- date of return from another state/subject of the Russian Federation;
- having contact with persons infected with COVID -19;
- previous examinations of people from the child's environment for COVID -19 (if available);
- previous examinations of the child for COVID -19 (if available).

3. General blood and urine tests, biochemical blood test (total protein, fractions, glucose, ALT, AST, bilirubin, urea).

4. Examination of sputum (or upper respiratory tract washings) for AFB.
5. Blood tests for HIV, hepatitis, syphilis.
6. Computed tomography of the chest.
7. Conducting telemedicine consultations with medical specialists if indicated.

If it is impossible to exclude the tuberculosis etiology of the disease, it is recommended to transfer the child to a boxed department of an infectious diseases hospital, examination for COVID -19, joint management by an infectious disease specialist and a phthisiatrician until a final diagnosis is established. When confirming the diagnosis of tuberculosis, tactics are in accordance with paragraph 8.7.1.

9.6 Features of treatment of combined infection tuberculosis + COVID -19 in children and adolescents

Treatment measures for COVID -19 in children are carried out in accordance with temporary guidelines. Interferon-alpha preparations are recommended as antiviral therapy for children with COVID -19 in cases of moderate and mild illness ; in cases of severe severity, intravenous immunoglobulins are used. Interferon-alpha can reduce the viral load in the initial stages of the disease, relieve symptoms and reduce the duration of the disease. Umifenovir is used in patients with COVID -19, but there is no evidence of its effectiveness and safety. In children, the drug can be used over the age of 6 years. Oseltamivir and other anti-influenza drugs can only be used in patients infected with the influenza virus. Research is currently being conducted on the effectiveness of chloroquine phosphate and hydroxychloroquine sulfate, including in combination with azithromycin for coronavirus infection. According to research, the use of chloroquine phosphate and hydroxychloroquine sulfate is possible in patients whose body weight is more than 50 kg. If there are contraindications to the prescription of chloroquine and hydroxychloroquine, it is possible to prescribe protease inhibitors (lopinavir + ritonavir) by decision of the medical commission. Antibacterial therapy is indicated if there are signs of a bacterial infection joining the COVID -19 infection . Recovery in children mainly occurs within 1-2 weeks.

Treatment of children while taking anti-tuberculosis drugs should be accompanied by careful monitoring of adverse reactions.

9.7 Possibilities for preventing COVID -19 in children and adolescents with tuberculosis

9.7.1. Anti-epidemic measures.

Anti-epidemic measures to prevent COVID -19 are carried out in accordance with current sanitary legislation, taking into account the fact that young children and adolescents are at increased risk of developing severe forms of tuberculosis, and therefore more severe manifestations of COVID -19 disease.

The priority area is the provision of specialized medical care at home.

Recommended:

- in the case of a diagnosis of active tuberculosis and the presence of life-threatening conditions (including complicated tuberculosis, common forms of the disease), hospitalize children in a specialized anti-tuberculosis institution in an isolated ward for 14 days and test them twice for SARS - COV -2 using the PCR method upon admission and after 24 hours after the first examination. If the results are negative and there are no signs on CT that are characteristic of new coronavirus pneumonia, transfer the patient to the general ward;

- when a diagnosis of active tuberculosis is established and there are no life-threatening conditions, the patient is given a conclusion with a recommendation for treatment at home under the supervision of a local TB doctor and a nurse with the organization of home delivery of anti-tuberculosis drugs;

- if a patient with tuberculosis is suspected or diagnosed COVID -19, treatment is carried out in the infectious diseases department of hospitals, for patients with confirmed COVID -19 up to 2-fold negative nasal /oropharyngeal swabs for SARS - COV -2, for patients with suspected COVID -19 until the diagnosis is clarified. If the diagnosis of COVID -19 is excluded , the patient with tuberculosis, if indicated, is transferred to a dispensary and quarantined for 14 days, or discharged for outpatient treatment at home.

9.7.2. Drug prevention.

recombinant interferon 2 b can be used as a drug prevention of COVID -19 .

9.7.3. Prevention of infection through breastfeeding

In February 2020, Chinese experts in their consensus did not recommend continuing breastfeeding for mothers with “suspected” and “confirmed” cases of COVID -19. However, it is believed that spread from person to person occurs mainly through airborne droplets. Since COVID -19 is currently

While much is unknown, the appropriateness of initiating and continuing breastfeeding must be determined by the mother in coordination with her family and health care providers. Breast milk is the best source of nutrition for most babies.

A mother with confirmed or suspected COVID -19 infection should follow standard transmission precautions to avoid spreading the virus to her baby, including washing and sanitizing her hands before handling her baby and wearing a face mask while breastfeeding. When expressing breast milk with a manual or electric breast pump, the mother should wash her hands before touching any pump or part of the bottle. To feed expressed milk, it is necessary to identify a healthy family member.

Organization of treatment of children in children's anti-tuberculosis hospitals and sanatoriums:

In children's anti-tuberculosis hospitals and sanatoriums, transfer children to outpatient treatment, subject to the possibility of organizing treatment at home, in order to reduce the number of children in closed institutions.

In children's anti-tuberculosis hospitals and sanatoriums, carry out anti-epidemic measures specified in these recommendations for hospitals with tuberculosis patients.

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Instructions for the responsible medical worker for collecting at home and transporting sputum to the laboratory for the purpose of diagnosing tuberculosis and COVID -19

1. Taking diagnostic material, its packaging, labeling and transportation is carried out in accordance with SP 1.3.3118-13 “Safety of working with microorganisms I - II pathogenicity (danger) groups.”

2. Health care workers who collect sputum or other biomaterial must be trained in the requirements and rules of biological safety when collecting and working with material suspected of being contaminated with microorganisms II pathogenicity groups, strictly observe precautions and use personal protective equipment: respirators type FFP 2 or equivalent; eye protection glasses or face shield; anti-plague or laminated surgical gown or overalls, cap, rubber/latex gloves.

3. Persons responsible for collecting sputum should first (possibly by telephone) explain to the patient the reasons for the study and the need to cough up not saliva or nasopharyngeal mucus, but the contents of the deep parts of the respiratory tract, which is achieved as a result of a productive cough that occurs after several deep breaths.

4. It must be explained that the isolation of mycobacteria and other microorganisms, incl . SARS - CoV -2 is not constant and for a complete microbiological examination it is necessary to collect sputum 3 times and transfer it to a medical worker for delivery to the laboratory during 2 of his visits within 2 consecutive days.

5. Please note that storing sputum at room temperature no more than 2 hours are allowed.

6. The first sputum sample should be collected by the patient during the first visit of a medical worker, the second sample no more than two hours before the scheduled time of the second visit of the medical worker, the third sample - during the second visit of the medical worker.

7. During the visit, the medical professional must be in laminated surgical gown or overalls, cap, respirator class not lower than FFP 2, goggles, rubber or latex gloves. Not to be at a distance

less than 1.5-2 meters, choosing his position so that the direction of air movement is from him to the patient. The healthcare worker should provide the patient with containers for collecting sputum.

8. Recommend that the patient hold the bottle as close to his lips as possible and immediately

or spit sputum into it as it is coughed up. Sputum production increases after one or more deep breaths. Upon completion of sputum collection, the patient should close the bottle with a cap.

9. The health care professional should assess the quantity and quality of the collected material, enter this data in the direction.

10. To identify samples, containers are marked at the point of collection using self-adhesive labels/permanent marker with information to ensure unambiguous identification of the sample and its destination.

11. The label of the containers with the material indicates: the serial number of the sample corresponding to the number in the accompanying sheet, the surname and initials of the patient.

12. Containers with samples from each patient are placed in an individual sealed bag with absorbent material and additionally packaged in a common sealed bag.

13. The package is placed in a foam thermal container with cooling thermoelements.

14. The transport container is sealed and labeled. It is advisable to place a disposable indicator in the container that monitors the temperature from 2 to 8 °C.

15. Accompanying documents are placed in individual packaging separately from the biological material and firmly attached to the outside of the container.

16. It is allowed to transport sputum to the laboratory for no more than 48 hours at a temperature of 2 to 8 °C.

Differential diagnosis of respiratory tuberculosis and pneumonia caused by various etiological factors

Comparison criteria	Community-acquired pneumonia	Infiltrative tuberculosis	Pneumonia caused by Covid-19	Pneumocystis pneumonia
Complaints	An increase in temperature to febrile levels, weakness, cough with a small amount of sputum, sometimes chest pain	Weakness, sweating, low-grade fever, weight loss, cough with a moderate amount of mucopurulent sputum.	Increase in temperature to 38.5, sore throat, dry cough, shortness of breath, weakness, headache, decreased sense of smell and taste, signs of conjunctivitis, feeling of congestion in the chest, myalgia. It can occur without pronounced symptoms of intoxication, with minor manifestations of respiratory distress.	Weakness, shortness of breath during exercise, dry whooping cough, sometimes fever up to febrile levels. More often, symptoms of respiratory failure prevail over symptoms of intoxication.
Anamnesis	The disease begins acutely, patients usually tell the day and hour of illness, there is a history of hypothermia	More often, subacute development of symptoms, a history of contact with tuberculosis patients	There is not always a connection with catarrhal phenomena. Fever is usually noted from the first days of the disease. Shortness of breath increases in dynamics by 6-8 days from the onset of the disease. There may be indications of arrival from a COVID -19 epidemic focus or contact with a COVID -19 patient within the last 14 days	There is no direct connection with the presence of catarrhal phenomena during the last 5-7 days. Development with a gradual increase in symptoms over 2-4 weeks in patients with immunodeficiency conditions (HIV infection with severe immunodeficiency (the number of CD 4 T-lymphocytes less than 200 in 1 μl), organ transplantation, long-term therapy with GCS). Positive dynamics during biseptol therapy.
Objective status	Paleness of the skin. Classic objective	Decreased nutrition, “red cheeks”,	Normal nutrition, cyanosis, shortness of breath during exercise	Decreased nutrition, cyanosis of the nasolabial triangle,

	signs are lag of the affected side of the chest when breathing, increased vocal tremor, shortening (dulling) of percussion sound over the affected area of the lung, the appearance of bronchial breathing, the presence of a focus of fine bubbling rales or crepitus, increased bronchophony	inconsistency auscultatory picture of the volume of lesions in the lungs (“a lot is visible and little is heard”)	load, in severe cases at rest, tachycardia. Above the lungs, breathing is harsh or weakened vesicular up to the “dumb lung”	acrocyanosis . In the lungs , weakened vesicular breathing , fine bubble moist rales, crepitus
Pulse oximetry	Usually within normal limits, a slight decrease with a large volume of damage. Pulse oximetry is used to detect DN and assess the severity of hypoxemia;	In most cases within normal limits	Characteristic decrease in saturation	Characteristic decrease in saturation
X-ray	The main radiological sign is a local decrease in the airiness of the lung tissue (infiltration) due to the accumulation of inflammatory exudate in the respiratory sections. The changes are often unilateral and extend to one or two bronchopulmonary segments.	Localization of the process in segments 1, 2, 6 of the lung, characterized by the presence of areas of infiltration of a heterogeneous structure, with the formation of “dry decay cavities”, the presence of screening foci in the underlying sections and other lung	In mild cases, a normal radiograph; in severe cases, radiological signs of acute distress syndrome: large confluent infiltrates in the peripheral and lower parts of the lungs, air bronchography phenomena. CT scan is required to identify characteristic changes	X-rays at the early stages are not very informative . There may be a decrease in pneumatization in the area of the roots of the lungs, an increase in the interstitial pattern. As the severity of the condition increases, a cloud-like decrease in pneumatization like “butterfly wings” or “cotton lung”
MSCT signs	Combination of areas of consolidation of lung tissue with areas of “ dull”	Single or multiple solid nodules, isolated	Multiple areas of decreased pneumatization of lung tissue by type	Reduced pneumatization of the “frosted glass” type, gradually merging with each other, more often

	glass", the presence of bronchiolitis of the "tree in the buds" type, broncholobular foci of varying size and intensity	lobar or segmental consolidation without "frosted glass"; tree-bud-type nodules (bronchiolitis); pleural effusion; lymphadenopathy (including with calcification); location in C 1,2,6 lung segments	“frosted glass” round shape with or without consolidation, with or without thickening of septa (“cobblestones”); “reverse halo” or other signs of organizing pneumonia (in later phases of the disease); the location is predominantly peripheral, the nature of the lesion is bilateral . (in the basal sections)	from roots to periphery . subsequently , extensive diffuse areas of ground glass with areas of intact lung tissue, “geographic map” syndrome. The most common lesions are the middle and lower sections. Characterized by the absence of lesions in the subpleural cavities
General blood analysis	Leukocytosis >10-12 x 10^9/l with increased neutrophil levels and/or band shift >10%, accelerated ESR.	Moderate leukocytosis with a band shift (the presence of “young” forms and metamyelocytes in the blood is not typical), moderate lymphopenia and monocytosis , accelerated ESR.	Leukopenia, lymphopenia , elevated CRP levels, thrombocytopenia	Band shift of the leukocyte formula to the left without leukocytosis, moderate accelerated ESR
Test with ATP in standard dilution, IGRA -tests	usually negative	Positive, hyperergic	Hyperergic tests are not typical	Negative tests
Identification of the pathogen	Growth of the causative agent of pneumonia in sputum	Positive sputum results for AFB , MBT DNA PCR	SARS - CoV -2 RNA by PCR in a nasopharyngeal swab	Detection of Pneumocystis DNA by PCR in sputum and throat swabs

Interaction of TB drugs with drugs used to treat COVID -19

	Etiotropic therapy of COVID-19 1)				
PTT	Chloroquine	Hydroxychloroquine	Mefloquine	Tocilizumab *	INF beta
Isoniazid	Allowed	Allowed	Allowed	Allowed	Allowed
Rifampicin 2)	Forbidden	Forbidden	Forbidden	Allowed	Allowed
Rifabutin 2)	Carefully	Carefully	Carefully	Allowed	Allowed
Rifapentine 2)	Forbidden	Forbidden	Forbidden	Allowed	Allowed
Ethambutol	Allowed	Allowed	Allowed	Allowed	Allowed
Pyrazinamide	Allowed	Allowed	Allowed	Allowed	Allowed
Ethionamide	Allowed	Allowed	Allowed	Allowed	Allowed
Prothionamide	Allowed	Allowed	Allowed	Allowed	Allowed
Cycloserine	Allowed	Allowed	Allowed	Allowed	Allowed
Terizidone	Allowed	Allowed	Allowed	Allowed	Allowed
Streptomycin	Allowed	Allowed	Allowed	Allowed	Allowed
Aminosalicylic acid	Allowed	Allowed	Allowed	Allowed	Allowed
Capreomycin	Allowed	Allowed	Allowed	Allowed	Allowed
Kanamycin	Allowed	Allowed	Allowed	Allowed	Allowed
Amikacin	Allowed	Allowed	Allowed	Allowed	Allowed
Clavulanic acid	Allowed	Allowed	Allowed	Allowed	Allowed
Meropenem	Allowed	Allowed	Allowed	Allowed	Allowed
Levofloxacin 3)	Carefully	Carefully	Carefully	Allowed	Allowed

Moxifloxacin [3])	Carefully	Carefully	Carefully	Allowed	Allowed
Sparfloxacin [3])	Carefully	Carefully	Carefully	Allowed	Allowed
Linezolid [4])	Carefully	Carefully	Carefully	Carefully	Carefully
Bedaquiline [5])	Carefully	Carefully	Allowed	Allowed	Allowed
Imipenem + cilastatin	Allowed	Allowed	Allowed	Allowed	Allowed
Tioureidoimino methylpyridinium perchlorate	Allowed	Allowed	Allowed	Allowed	Allowed

Allowed - no drug interactions expected

Prohibited - serious drug interactions that preclude co-administration of drugs

Not advisable - potential drug interactions that require special (close) monitoring , changes in dosage or timing of medications

Possible drug interactions are presented taking into account the short duration of etiological treatment of COVID -19 (no more than 14 days)

1) The use of tocilizumab for active tuberculosis in accordance with the instructions is contraindicated; the drug may be prescribed by a medical commission, provided that the benefit of the prescription outweighs the risk of use. There are no contraindications to the use of chloroquine , hydroxychloroquine , interferon-beta for tuberculosis.

2) Rifampicin causes the induction of cytochrome P450 isoenzymes, accelerating the metabolism of drugs, and accordingly reduces the activity of antimalarial drugs (mefloquine , chloroquine , hydroxychloroquine), and therefore its administration together with antimalarial drugs is prohibited.

The use of rifapentine with chloroquine , hydroxychloroquine , mefloquine is prohibited, because may lead to a significant decrease in antimalarial drug concentrations.

In patients with tuberculosis receiving I and III Chemotherapy regimens need to be replaced by rifampicin with rifabutin , rifapentine (in the continuation phase) with rifabutin . Rifabutin is used according to the regimen of 150 mg * 1 time / day daily. 2-3 weeks after stopping treatment for COVID -19 , you can stop taking rifabutin and resume taking rifampicin .

3) No studies have been conducted on the combined use of drugs. Given the range of adverse reactions when prescribing fluoroquinolones with antimalarials, ECG monitoring should be performed for QT prolongation .

4) No studies have been conducted on the combined use of drugs. Considering the range of adverse reactions when prescribing antimalarials and linezolid , it is necessary to prescribe drugs under the supervision of a neurologist, ophthalmologist, taking into account a possible increase in the risk of developing optic neuritis, and when prescribing tocilizumab , interferon -beta with linezolid , it is necessary to monitor platelet levels, taking into account a possible increase in the risk of development thrombocytopenia.

5) studies have been conducted on the combined use of bedaquiline and antimalarial drugs. Given the range of adverse reactions when prescribing antimalarials and bedaquiline, ECG monitoring should be performed for prolongation of the QT interval .

LIST OF ABBREVIATIONS USED

ALT - alanine aminotransferase

AST - aspartate aminotransferase

ATP - recombinant tuberculosis allergen

HIV - human immunodeficiency virus

WHO - World Health Organization

DIC - disseminated intravascular coagulation

DNA - deoxyribonucleic acid

DN - respiratory failure

WHO/Europe - Regional Office for Europe of the World Health Organization

PRC - People's Republic of China

CT - computed tomography

AFB - acid-fast mycobacteria

LTBI - latent tuberculosis infection

MBT - Mycobacterium tuberculosis

IU - International Units of Measurement

INR - international normalized ratio

ARVI - acute respiratory viral infection

ICU - intensive care unit

PTP - anti-tuberculosis drug

PCR - polymerase chain reaction

RNA - ribonucleic acid

RSV - respiratory syncytial virus

PPE - personal protective equipment

SIC - sepsis-induced coagulopathy

ESR - erythrocyte sedimentation rate

CRP - C-reactive protein

TB - tuberculosis

SARS (SARS) - severe acute respiratory syndrome

UVBI - ultraviolet bactericidal radiation

ECG - electrocardiography

COVID -19 - infection caused by a new coronavirus SARS - CoV -2

MERS - Middle East respiratory syndrome

MERS - CoV - coronavirus that caused an outbreak of Middle East respiratory syndrome

MRSA - methicillin -resistant Staphylococcus aureus

SARS - CoV -2 is a new coronavirus that caused an outbreak of infection in 2019-2020.

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