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LATENT TUBERCULOSIS INFECTION IN CHILDREN AND ADOLESCENTS: PREVENTIVE TREATMENT ISSUES

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Abstract. Preventive chemotherapy (PCT) for latent tuberculosis infection (LTBI) is considered one of the ways to reduce the incidence of tuberculosis (TB) in the world. A number of issues of PCT in children have not yet been fully resolved, including the effectiveness of preventing the active form of tuberculosis, taking into account possible side effects. The purpose of the study was to evaluate the effectiveness of a course of PCT in children with latent tuberculosis infection based on the generally accepted main criterion (absence of disease for 2 years) and additional ones (dynamics of a test with the recombinant tuberculosis allergen (ATR), treatment tolerance and course completion). On the basis of the Anti-tuberculosis dispensary No. 3 in St. Petersburg, a cohort of children aged 0–17 years was analyzed — 150 people, taken for dispensary observation in group VI A (altered sensitivity to tuberculosis allergens according to the ATR or Mantoux test). All children underwent phthisiatric examination; 134 children were subject to preventive chemotherapy (positive ATR test), which the parents of 34 children refused. The children were divided into three groups: I group (55 people) children who do not have family contact with a TB patient; II group (45 people) — children in contact with a TB patient (children of the first and second groups received PCT) and children of the third group — 34 children did not receive PCT (refusal). As a result of comparison of the three groups, reliable data were obtained on the effectiveness of PCT according to the criteria of preventing the disease and reducing the results of the ATR test. In no case did any adverse events requiring drug discontinuation occur, which made it possible to achieve high rates of completion of preventive chemotherapy courses. The conclusion is made about the need for preventive work with refusing parents to form their adherence to preventive treatment.

Keywords: *latent tuberculosis infection; children; teenagers; preventive treatment*

ЛАТЕНТНАЯ ТУБЕРКУЛЕЗНАЯ ИНФЕКЦИЯ У ДЕТЕЙ И ПОДРОСТКОВ: ВОПРОСЫ ПРЕВЕНТИВНОГО ЛЕЧЕНИЯ

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Резюме. Одним из путей снижения заболеваемости туберкулезом (ТБ) в мире считается превентивная химиотерапия (ПХТ) латентной туберкулезной инфекции (ЛТИ). Ряд вопросов ПХТ у детей до сих до конца не решен, в том числе об эффективности предупреждения активной формы туберкулеза с учетом возможных побочных эффектов. Целью исследования было оценить эффективность курса ПХТ у детей с латентной туберкулезной инфекции на основе общепринятого основного критерия (отсутствие заболевания в течение двух лет) и дополнительных (динамика пробы с аллергеном туберкулезным рекомбинантным (АТР), переносимость лечения и завершенность курса). На базе Противотуберкулезного диспансера № 3 г. Санкт-Петербурга проанализирована когорта детей в возрасте от 0 до 17 лет: 150 человек, взятых на диспансерное наблюдение по VI А группе (измененная чувствительность к туберкулезным аллергенам по пробе с АТР или Манту). Всем детям было проведено фтизиатрическое обследование. 134 ребенка подлежали превентивной химиотерапии (положительная проба с АТР), от которой родители 34 детей отказались. Дети были разделены на три группы: I группа (55 человек): дети, не имеющие семейного контакта с больным ТБ; II группа (45 человек): дети из контакта с больным ТБ (дети I и II групп получили ПХТ) и III группа: 34 ребенка не получили ПХТ (отказ). В результате сопоставления трех групп получены достоверные данные об эффективности ПХТ по критериям предотвращения заболевания и снижения результатов пробы с АТР. Ни в одном случае не возникло нежелательных явлений, требовавших отмены препаратов, что позволило достигнуть высоких показателей завершенности курсов превентивной химиотерапии. Сделан вывод о необходимости профилактической работы с отказывающимися родителями для формирования их приверженности к профилактическому лечению.

Ключевые слова: *латентная туберкулезная инфекция, дети, подростки, превентивное лечение*

INTRODUCTION

According to the World Health Organization (WHO), in modern conditions the priority direction for reducing tuberculosis (TB) is the prevention and treatment of latent tuberculosis infection (LTBI) [1]. WHO experts believe that without addressing the challenge of LTBI diagnostics and treatment, the task of reducing tuberculosis incidence in all countries will not be solved [2, 3].

Latent tuberculosis infection is a condition in which mycobacterium tuberculosis (MBT) is present in the human body, causing positive reactions to immunological tests, including to TB allergens in the absence of clinical and radiological signs of tuberculosis [4]. Over the past decade, an intradermal test with a recombinant tuberculosis allergen (ATR or Diaskintest) containing MBT antigens: ESAT-6 and CFP-10 has been used in the Russian Federation to diagnose LTBI and TB, as well as to determine indications for preventive treatment of children. The ATR test (compared to the Mantoux test) allows for more effective identification of patients at high risk for developing tuberculosis [5–8]. Thus, according to E.M. Bogorodskaya et al., among children aged 8–17 years who fell ill in Moscow in 2021, 33 out of 43 (76,7%) were detected using screening with immunological tests before the onset of clinical manifestations of the disease (according to the results of an intradermal test with ATR) [9].

Due to their anatomical and physiological characteristics, children are most sensitive to TB infection and have a high risk of developing the disease, especially in the presence of comorbid pathology [10–12].

According to clinical guidelines existing in the Russian Federation, children with LTBI are recommended the reventive treatment with anti-tuberculosis drugs (ATDs): preventive chemotherapy (PCT) [4]. Traditionally, the effectiveness of preventive therapy is assessed by the main criterion — the absence of tuberculosis within two years after its implementation [4]. However, even in the absence of preventive treatment, 5–10% of infected persons are at risk of developing the disease, according to WHO data. This is why there are conflicting views on the issues of organizing preventive therapy, mandatory nature of its implementation, and search for effective and safe chemotherapy regimens using anti-tuberculosis drugs with high bactericidal activity continues [13–15].

In this regard, when choosing the tactics for managing children with LTBI, it is necessary to take into account the other possible criteria for the effectiveness and safety of chemotherapy: completion of PCT courses, tolerability of treatment in children, and dynamics of immunodiagnostic samples.

AIM

The aim of the study is to evaluate the effectiveness of preventive treatment courses in chil-

dren with LTBI, taking into account the main and additional criteria.

MATERIALS AND METHODS

A cohort of children (0–17 years old, n=150) observed in the dispensary department No. 1 of the Interdistrict Petrograd-Primorsky Anti-tuberculosis dispensary No. 3 in St. Petersburg in connection with MBT infection in the period from 2018 to 2021 was analyzed. The ratio of boys and girls was 56 and 44%, respectively (Table 1).

Inclusion criteria for the study: all children infected with MBT and registered in group VI A of medical follow-up. Exclusion criteria: presence of active tuberculosis. Of the 150 children, 134 had a TB positive ATR test result, the remaining 16 had a TB negative ATR test result and were referred with altered tuberculin sensitivity according to the Mantoux test with 2 tuberculin units (TU) (16 children aged 0 to 7 years). These 16 children were not indicated for preventive treatment, only observation. The remaining 134 children with indications for a course of chemotherapy (TB positive ATR test) were divided into three groups: group I — without established contact with a tuberculosis patient (n=55); group II included household contacts with a patient with active TB (n=45) and group III included children whose parents refused preventive treatment despite indications (n=34), including 14 from the foci of tuberculosis infection. Among tuberculosis contacts (children of group II), family contacts predominated 34 (75,6%): including 24 (53,3%) with a person with bacterial excretion. Among the 14 children in group III (who refused chemotherapy) and those with contact, 9 (64,3%) had family contacts, including 5 (35,7%) with a person with bacterial excretion. The remaining 5 (35,7%) children had no established tuberculosis contact.

All children underwent a full examination, which contains taking the anamnesis, including an epidemiological anamnesis, results of immunodiagnostics (Mantoux tests with 2 TU, ATR tests according to the indications of in vitro tests: QuantiFERON® or TB-FERON), radiological imaging, as well as laboratory tests.

To prevent the transition of LTBI to the active form of tuberculosis, children of groups I and II were prescribed PCT in accordance with the Federal Clinical Guidelines (FCG), a regimen of two anti-tuberculosis drugs: isoniazid (H) + pyrazinamide (Z) for 3–6 months in the absence of data on drug resistance (DR) at the source of infection. Children from contacts with DR to H (n=5) were administered rifampicin (R) for 4 months; in case of multiple drug resistance (MDR) (n=4), no treatment was carried out, only monitoring in accordance with the FCG [4].

The effectiveness of the PCT courses was assessed based on four criteria: absence of the disease for two years after the courses of PCT, completeness of the courses, tolerance to anti-tuberculosis drugs and dynamics of immunodiagnostic samples.

All parents gave voluntary informed consent for the study.

Statistical analysis was performed using MS Excel 2010 and the SPSS 17.0 software package. To determine the reliability of differences, Student's t-test for absolute values and Pearson's χ^2 test for relative variables were used. Statistical significance was considered at a level of $p < 0,05$.

RESULTS AND DISCUSSIONS

In 16 children (aged 0 to 7 years) who were referred to the anti-tuberculosis dispensary due to a change in tuberculin sensitivity according to the Mantoux test with 2 TU, ATR remained TB negative during dynamic monitoring without the prescription of PCT after 6–12 months. The results of the clinical and radiological examination did not reveal any pathology. Based on this, the children were removed from medical check-up and excluded from our further study.

Table 1. Age and sex composition of children infected with mycobacterium tuberculosi included in the study

Таблица 1. Возрастно-половой состав детей, инфицированных микобактериями туберкулеза, включенных в исследование

Разделение по половой принадлежности / Gender division	Возраст / Age			
	0–3 года / 0–3 years (n=12)	4–7 лет / 4–7 years (n=38)	8–14 лет / 8–14 years (n=59)	15–17 лет / 15–17 years (n=41)
Дети (муж.) / Children (men)	7 (58,3%)	20 (52,6%)	42 (71,2%)	15 (36,6%)
Дети (жен.) / Children (women)	5 41,7%)	18 (47,4%)	17 (28,8%)	26 (63,4%)

Table 2. Comprehensive assessment of the effectiveness and safety of preventive chemotherapy for latent tuberculosis infection in children

Таблица 2. Комплексная оценка эффективности и безопасности превентивной химиотерапии при латентной туберкулезной инфекции у детей

Критерии оценки эффективности / Performance evaluation criteria	Проведение ПХТ / Carrying out PCT		III группа (отказ от ПХТ) / III group (refusal from PCT) (n=34)
	I группа (без контакта с МБТ) / I group (without contact with MBT) (n=55)	II группа (с контактом с МБТ) / II group (with contact with MBT) (n=45)	
Заболевание в течение 2 лет / Illness for 2 years	1 (1,8%) P_{I-II}= 0,32401; *χ^2= 1,515	3 (6,7%) *P_{II-III}= 0,00932; *χ^2= 3,395	7 (20,6%) *P_{I-III}= 0,00445; *χ^2= 9,049
Нежелательные явления, связанные с приемом ПТП / Adverse events associated with taking PTPs	10 (18,2%) P_{I-II}= 0,10539; *χ^2= 3,030	15 (33,3%)	–
Гиперферментемия / Hyperenzymemia	6 (10,9%) P_{I-II}=1,00000; χ^2=0,001	5 (11,1%)	
Клинические симптомы со стороны ЦНС / Clinical symptoms from the central nervous system	4 (7,3%) *P_{I-II}=0,04312; *χ^2=4,594	10 (22,2%)	
Завершенность / Completeness	50 (90,9%) P_{I-II}=0,74143; χ^2=0,230	40 (88,9%)	
Завершенность с перерывами / Completeness with breaks	5 (9,1%) *P_{I-II}=0,02819; *χ^2=5,802	12 (26,7%)	
Уменьшение чувствительности к АТР / Decreased sensitivity to ATR	38 (69,1%) P_{I-II}=0,52782; χ^2=0,520	28 (62,2%) *P_{II-III}=0,00283; *χ^2=9,942	9 (26,5%) *P_{I-III}=0,00016; *χ^2=15,315

* Различия достоверны. / Differences are significant.

Thus, further analysis included 134 children with a TB positive ATR test when taken for medical follow-up.

The analysis of cases of the disease within two years after the course of PCT and other performance evaluation criteria are given in Table 2.

Within two years after the course of preventive chemotherapy, the disease was detected in 1 (1,8%) person in group I, 3 (6,7%) children in group II, and significantly more frequently in 7 (20,6%) children in group III. Based on the results of phthisiological diagnostics, the following forms of tuberculosis of the respiratory organs were established: tuberculosis of the intrathoracic lymph nodes (TITLN), primary tuberculosis complex (PTC), and focal pulmonary tuberculosis. Thus, in group I, TITLN was diagnosed in 1 child, in group II — TITN in 1 child and PTC in 2 children. In children of group III (who refused chemotherapy), TITLN was diagnosed in 6 children and focal tuberculosis was diagnosed in 1 child.

Analysis of the completion of the PCT courses showed that almost all children in groups I and II finished it entirely: 90,9 and 88,9%, respectively. The differences between groups are statistically insignificant (p >0,05).

The tolerability of PCT was significantly worse in children with tuberculosis contacts, including 3 patients who received an individual regimen: DR to H — R intake for 4 months. The frequency of adverse events (AE) during taking ATDs is presented in Table 2. At the follow-up examination during the intake of ATDs in children of group I, asymptomatic hyperenzymemia (increased levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST)) was observed in 10,9% of cases, and clinical symptoms from the central nervous system (CNS) were observed in 7,3%. In children of group II, hyperenzymemia was ob-

Table 3. Dynamics of immunodiagnostic samples of patients

Таблица 3. Динамика иммунодиагностических проб пациентов

Показатель / Index	I группа / Group I (n=55)	II группа / Group II (n=45)	III группа / Group III (n=34)
Увеличение папулы / Enlarged papule	10 (18,2%) P_{I-II}=1,00000; χ^2=0,053	9 (20%) *P_{II-III}=0,00001; *χ^2=20,377	24 (70,6%) *P_{I-III}=0,00001; *χ^2=24,443
Уменьшение папулы / Papule reduction	38 (69,1%) P_{I-II}=0,52782; χ^2=0,520	28 (62,2%) *P_{II-III}=0,00283; *χ^2=9,942	9 (26,5%) *P_{I-III}=0,00016; *χ^2=15,315
Без динамики / No dynamics	7 (12,7%) P_{I-II}=0,57747; χ^2=0,495	8 (17,8%) *P_{II-III}=0,00283; *χ^2=9,942	1 (2,9%) *P_{I-III}=0,07002; *χ^2=4,223
Частота гиперергических реакций до лечения / на момент взятия на учет (III группа) / Frequency of hyperergic reactions before treatment / at the time of registration (III group)	25 (45,4%) P_{I-II}= 0,68558; χ^2= 0,300	18 (40,0%) *P_{II-III}= 0,04108; *χ^2= 4,729	22 (64,7%) *P_{I-III}= 0,08578; *χ^2= 3,125
Частота гиперергических реакций после лечения / при контрольном обследовании (III группа) / Frequency of hyperergic reactions after treatment / during control examination (III group)	10 (5,4%) P_{I-II}=0.40481; χ^2=0,970	5 (11,1%) *P_{II-III}= 0,00026; *χ^2=14,577	17 (50,0%) *P_{I-III}=0,00211; *χ^2=10,065
Конверсия в отрицательный результат / Conversion to negative result	10 (18,2%) P_{I-II}=0,40481; χ^2=0,970	5 (11,1%) *P_{II-III}=0,00001; *χ^2=70,536	0 (0%) *P_{I-III}=0,00001; *χ^2=56,269

* Различия достоверны. / Differences are significant.

served in 11,1% of cases, and symptoms from the CNS were observed in 22,2%. Symptoms from the CNS included complaints of headache, drowsiness, fatigue (these changes were mild and short-lived). Hyperenzymemia was transient (an increase in enzymes to a level 20–30% above normal), did not require complete discontinuation of PCT, and was cured by hepatoprotective therapy (Liv-52, Karsil).

When assessing the dynamics of immunodiagnostic samples in children who received PCT, a decrease in the test with ATR was significantly more often observed compared to children without PCT, regardless of the presence of tuberculosis contact (Table 3).

The frequency of hyperergic reactions before treatment was higher in children from group I. According to the results of the treatment, a decrease in the frequency of hyperergy in children without tuberculosis contact by 8,4 times and in children with tuberculosis contact by 3,6 times was achieved. It is also worth noting that the average size of a papule before treatment was higher in children of group I. Conversion of the ATR test result was observed more often in children of the group I.

Thus, as a result of the work, high efficiency of the preventive treatment was established. It consisted primarily in preventing cases of transition LTBI to clinically expressed forms of tuberculosis within the next two years after PCT, as evidenced by a reliably high percentage of sick children in group III (refusal of PCT). Satisfactory tolerability of PCT in children of groups I and II, regardless of the presence of tuberculosis contact, should be noted: in no case were there serious AE requiring the discontinuation of PCT, which made it possible to achieve high rates of completion of PCT courses. It should be noted that the dynamics of the test with ATR are an important criterion for the effectiveness of preventive treatment. A clear effect of therapy was shown both in reducing the absolute values of the ATR test and in decrease the proportion of hyperergic reactions. On the contrary, in children of group III (refusal of PCT), where the number of sick people was higher, a decline in sensitivity to the test with ATR was significantly less common. Unmotivated refusals of parents from preventive treatment indicate insufficient work to form adherence to tuberculosis prevention [16]. Decreased sensitivity to ATR reduces the risk of developing a local form of TB in the future

and indications for the number of repeated preventive chemotherapy and shortens the duration of medical check-up [17].

CONCLUSION

1. Preventive chemotherapy covered 100 children (74,6%) out of 134 with a TB positive test with ATR, which is insufficient. The main reason is parental refusal, which requires strengthening preventive work to improve adherence to treatment.

2. As a result of the PCT course, more than half of the children achieved a decrease in the ATR test. The incidence of TB was significantly lower than in children without PCT (group III: refusals). Tolerability of therapy is satisfactory.

3. It is necessary to evaluate the effectiveness of PCT courses using not only the main (absence of TB for two years), but also additional criteria (completeness of courses, tolerability of anti-tuberculosis drugs and dynamics of the sample with ATR).

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

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Consent for publication. Written consent was obtained from legal representatives of the patients for publication of relevant medical information within the manuscript.

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Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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REFERENCES

1. Prakticheskiy spravochnik VOZ po tuberkulezu. Modul' 5. Vedeniye tuberkuleza u detey i podrostkov. [Management of tuberculosis in children and adolescents]. Vsemirnaya organizatsiya zdravookhraneniya. 2023. https://www.who.int/ru/publications/i/item/9789240046832. (in Russian).
2. WHO. Consensus meeting report: development of a Target Product Profile (TPP) and a framework for evaluation for a test for predicting progression from tuberculosis infection to active disease. World Health Organization. Geneva, 2017 (WHO/HTM/TB/2017.18). Licence: CC BY-NC-SA3.0 IGO. https://www.who.int/publications/i/item/WHO-HTM-TB-2017.18.
3. WHO, Latent tuberculosis infection: updated and consolidated guidelines for programmatic management. World Health Organization. Geneva. 2018. https://www.who.int/publications/i/item/9789241550239.
4. Klinicheskiye rekomendatsii. Latentnaya tuberkuleznaya infektsiya (LTI) u detey. [Latent tuberculosis infection (LTBI) in children]. Obshcherossiyskaya obshchestvennaya organizatsiya «Rossiyskoye obshchestvo ftiziatrov». 2016. http://roftb.ru/structure/. (in Russian).
5. Aksenova V.A., Baryshnikova L.A., Klevno N.I. i dr. Skrining detey i podrostkov na tuberkuleznuyu infektsiyu v Rossii — proshloye, nastoyashcheye, budushcheye. [Screening of children and adolescents for tuberculosis infection in Russia — past, present, future]. Tuberkulez i bolezni legkikh. 2019;97(9):59–66. (in Russian).
6. Lozovskaya M.E., Nikiforenko N.N., Klochkova L.V. i dr. Klinicheskiye i epidemiologicheskiye osobennosti tuberkuleza u detey rannego vozrasta v Sankt-Peterburge. [Clinical and epidemiological features of tuberculosis in young children in St. Petersburg]. Pediatr. 2018;5(9):5–12. (in Russian).
7. Slogotskaya L.V., Bogorodskaya Ye.M., Levi D.T. i dr. 10 let kozhnoy probe s allergenom tuberkuleznym rekombinantnym (Diaskintest®) i 110 let tuberkulinovoy probe Mantu — sravneniye effektivnosti. [10 years of skin test with recombinant tuberculosis allergen (Diaskintest®) and 110 years of Mantoux tuberculin test — comparison of effectiveness]. BIOpreparaty. Profilaktika, diagnostika, lecheniye. 2017;17(2):67–77. (in Russian).

8. Schwoebel V., Koura K.G., Adjobimey M. et al. Tuberculosis contact investigation and short-course preventive therapy among young children in Africa. Int J Tuberc Lung Dis. 2020;24(4):452–460. DOI: 10.5588/ijtld.19.0712.
9. Bogorodskaya Ye.M., Slogotskaya L.V., Shamuratova L.F. i dr. Skrining tuberkuleznoy infektsii u detey i podrostkov na osnove primeneniya dvukh vnutrikozhnykh testov: s tuberkulinom i allergenom tuberkuleznym rekombinantnym (ESAT-6/CFP-10) v Moskve v 2021 g. [Screening for tuberculosis infection in children and adolescents based on the use of two intradermal tests: with tuberculin and recombinant tuberculosis allergen (ESAT-6/CFP-10) in Moscow in 2021]. Tuberkuloz i bolezni logkikh. 2022;100(11):29–38. DOI: 10.21292/2075-1230-2022-100-11-29-38. (in Russian).
10. Glushakov I.A., Glushakova V.D. Faktory riska infitsirovaniya mikobakteriyami tuberkuleza detey i podrostkov s neyrosensornoy tugoukhost'yu. [Risk factors for infection with Mycobacterium tuberculosis in children and adolescents with sensorineural hearing loss]. Vestnik Tsentral'nogo nauchno-issledovatel'skogo instituta tuberkuleza. 2023;S1:228–229. (in Russian).
11. Boom W.H., Schaible U.E., Achkar J.M. The knowns and unknowns of latent Mycobacterium tuberculosis infection. J. Clin. Investig. 2021;131:e136222. DOI: 10.1172/JCI136222.
12. Dolla C.K., Padmapriyadarsini C., Thiruvengadam K. et al. Age-specific prevalence of TB infection among household contacts of pulmonary TB: Is it time for TB preventive therapy? Trans R Soc Trop Med Hyg. 2019;113(10):632–640. DOI: 10.1093/trstmh/trz049.
13. Baronova O.D., Aksenova V.A., Klevno N.I. i dr. Bezopasnost' i mediko-ekonomicheskaya effektivnost' preventivnogo lecheniya detey s latentnoy tuberkuleznoy infektsiyey. [Safety and medical and economic effectiveness of preventive treatment of children with latent tuberculosis infection]. Tuberkulez i bolezni legkikh. 2020;98(9):25–31. (in Russian).
14. Chin K.L., AnibarroL., SarmientoM.E. et al. Challenges and the Way forward in Diagnosis and Treatment of Tuberculosis Infection. Trop Med Infect Dis. 2023;8(2):89. DOI: 10.3390/tropicalmed8020089.
15. Cohen A., Mathiasen V.D., Schön T. et al. The global prevalence of latent tuberculosis: A systematic review and meta-analysis. Eur. Respir. J. 2019;54:1900655. DOI: 10.1183/13993003.00655-2019.
16. Khodorenko V.A., Yarovaya Yu.A., Lozovskaya M.E. i dr. Otsenka priverzhennosti roditeley k spetsificheskomu lecheniyu detey, bol'nykh tuberkulezom. [Assessment of parents' adherence to specific treatment of children with tuberculosis]. Children's medicine of the North-West. 2023;11(3):125–130. DOI: 10.56871/CmN-W.2023.11.42.010. (in Russian).
17. Prikaz Ministerstva zdravookhraneniya Rossiyskoy Federatsii ot 13.03.2019 № 127n. Ob utverzhdenii poryadka dispansernogo nablyudeniya za bol'nymi tuberkulezom, litsami, nakhodyashchimisya ili nakhodivshimisya v kontakte s istochnikom tuberkuleza, a takzhe litsami s podozreniyem na tuberkulez i izlechennymi ot tuberkuleza i priznanii utrativshimi silu punktov 16-17 Poryadka okazaniya meditsinskoy pomoshchi bol'nym tuberkulezom, utverzhdennogo prikazom Ministerstva zdravookhraneniya Rossiyskoy Federatsii ot 15 noyabrya 2012 g. № 932n. [On approval of the procedure for dispensary observation of patients with tuberculosis, persons who are or have been in contact with a source of tuberculosis, as well as persons suspected of tuberculosis and cured of tuberculosis and the recognition of paragraphs 16-17 of the Procedure for providing medical care to patients with tuberculosis, approved by order of the Ministry of Health, as invalid Russian Federation dated November 15, 2012 No. 932n]. (Zaregistrirovan 19.06.2019 № 54975). 2019: 24. https://ptd11.ru/files/act-127H-13-03-2019.pdf. (in Russian).

ЛИТЕРАТУРА

1. Практический справочник ВОЗ по туберкулезу. Модуль 5. Ведение туберкулеза у детей и подростков. Всемирная организация здравоохранения. 2023. https://www.who.int/ru/publications/i/item/9789240046832.
2. WHO. Consensus meeting report: development of a Target Product Profile (TPP) and a framework for evaluation for a test for predicting progression from tuberculosis infection to active disease. World Health Organization. Geneva, 2017 (WHO/HTM/TB/2017.18). Licence: CC BY-NC-SA3.0 IGO. https://www.who.int/publications/i/item/WHO-HTM-TB-2017.18.
3. WHO, Latent tuberculosis infection: updated and consolidated guidelines for programmatic management. World Health Organization. Geneva. 2018. https://www.who.int/publications/i/item/9789241550239.
4. Клинические рекомендации. Латентная туберкулезная инфекция (ЛТИ) у детей. Общероссийская общественная организация «Российское общество фтизиатров». 2016. http://roftb.ru/structure/.

5. Аксенова В.А., Барышникова Л.А., Клевно Н.И. и др. Скрининг детей и подростков на туберкулезную инфекцию в России — прошлое, настоящее, будущее. Туберкулез и болезни легких. 2019;97(9):59–66.
6. Лозовская М.Э., Никифоренко Н.Н., Клочкова Л.В. и др. Клинические и эпидемиологические особенности туберкулеза у детей раннего возраста в Санкт-Петербурге. Педиатр. 2018;5(9):5–12.
7. Слогоцкая Л.В., Богородская Е.М., Леви Д.Т. и др. 10 лет кожной пробе с аллергеном туберкулезным рекомбинантным (Диаскинтест®) и 110 лет туберкулиновой пробе Манту — сравнение эффективности. БИОпрепараты. Профилактика, диагностика, лечение. 2017;17(2):67–77.
8. Schwoebel V., Koura K.G., Adjobimey M. et al. Tuberculosis contact investigation and short-course preventive therapy among young children in Africa. Int J Tuberc Lung Dis. 2020;24(4):452–460. DOI: 10.5588/ijtld.19.0712.
9. Богородская Е.М., Слогоцкая Л.В., Шамуратова Л.Ф. и др. Скрининг туберкулезной инфекции у детей и подростков на основе применения двух внутрикожных тестов: с туберкулином и аллергеном туберкулезным рекомбинантным (ESAT-6/CFP-10) в Москве в 2021 г. Туберкулез и болезни легких. 2022;100(11):29–38. DOI: 10.21292/2075-1230-2022-100-11-29-38.
10. Глушаков И.А., Глушакова В.Д. Факторы риска инфицирования микобактериями туберкулеза детей и подростков с нейросенсорной тугоухостью. Вестник Центрального научно-исследовательского института туберкулеза. 2023;S1:228–229.
11. Boom W.H., Schaible U.E., Achkar J.M. The knowns and unknowns of latent Mycobacterium tuberculosis infection. J. Clin. Investig. 2021;131:e136222. DOI: 10.1172/JCI136222.
12. Dolla C.K., Padmapriyadarsini C., Thiruvengadam K. et al. Age-specific prevalence of TB infection among household contacts of pulmonary TB: Is it time for TB preventive therapy? Trans R Soc Trop Med Hyg. 2019;113(10):632–640. DOI: 10.1093/trstmh/trz049.
13. Баронова О.Д., Аксенова В.А., Клевно Н.И. и др. Безопасность и медико-экономическая эффективность превентивного лечения детей с латентной туберкулезной инфекцией. Туберкулез и болезни легких. 2020;98(9):25–31.
14. Chin K.L., AnibarroL., SarmientoM.E. et al. Challenges and the Way forward in Diagnosis and Treatment of Tuberculosis Infection. Trop Med Infect Dis. 2023;8(2):89. DOI: 10.3390/tropicalmed8020089.
15. Cohen A., Mathiasen V.D., Schön T. et al. The global prevalence of latent tuberculosis: A systematic review and meta-analysis. Eur. Respir. J. 2019;54:1900655. DOI: 10.1183/13993003.00655-2019.
16. Ходоренко В.А., Яровая Ю.А., Лозовская М.Э. и др. Оценка приверженности родителей к специфическому лечению детей, больных туберкулезом. Children's medicine of the North-West. 2023;11(3):125–130. DOI: 10.56871/CmN-W.2023.11.42.010.
17. Приказ Министерства здравоохранения Российской Федерации от 13.03.2019 № 127н. Об утверждении порядка диспансерного наблюдения за больными туберкулезом, лицами, находящимися или находившимися в контакте с источником туберкулеза, а также лицами с подозрением на туберкулез и излеченными от туберкулеза и признании утратившими силу пунктов 16-17 Порядка оказания медицинской помощи больным туберкулезом, утвержденного приказом Министерства здравоохранения Российской Федерации от 15 ноября 2012 г. № 932н. (Зарегистрирован 19.06.2019 № 54975). 2019: 24. https://ptd11.ru/files/act-127H-13-03-2019.pdf.