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Latent Tuberculous Infection: Influence on Patient's Quality of Life

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Abstract

Latent tuberculosis infection is an asymptomatic condition in which patients carry the bacteria, but do not show any sign of illness, however they are at risk of disease activation at any time in the future. Understanding of influence of latent tuberculosis infection on the physical and mental well-being of these patients is important as successful strategies to reduce the tuberculosis burden globally. Our purpose is to explore patients during diagnosis and treatment of latent tuberculosis infection, measure their quality of life. Materials and methods: during 2017–2019 was examined 100 children 4–7 years age. Children were divided in 3 groups. First group (n = 40) - a children with LTI. Group of the comparison (n = 40) has comprised preschool age children with tuberculosis. Group of the checking (n = 20) have constituted the preschool age healthy children. Estimation of children health was conducted by analysis health factors: social, genetic, biological. In addition were studied criteria of health. It was used study anamnestic data, questioning, estimation quality of life, anthropometry, data of objective examination, laboratory data and parameters of functioning, electrocardiography, vegetative nervous system spectrography (VNS-spectrography), manual ergometry. Physical development valued with the help of specialized tables. Leukocyte intoxication index is calculated on formula Shemitova V.F. Variety heart rhythm (VHR) was studied by method VNS-spectrography on vegetotester “VNS-Micro” with computer program “Polispectr” of company “Neyrosoft”. Interpretation source vegetative tone and vegetative reactivity was realized according to recommendation N.A. Belokon. Vegetative provision of activity was valued on tolerance to steady-state load by method manual ergometry (MEM) in help of manual dynamometer. Quality of life was defined with the help of questionnaire PedsQL version 4.0 (the Russian version). Results and their discussion: in children with active tuberculosis, specific process has a most negative influence upon quality of life, comparatively temporary negative influence has LTI. Revealed changes in general have brought to reduction of QL indicators both in first and second group. With provision of latency currents of infecting with mycobacteria of tuberculosis, indicators of quality of life should be considered as one of defining, reflecting psychological component adaptation of child, and can be recommended to enter in program of examination and dispensary observation of children with LTI. Conclusions: our study has shown that preschool age children with LTI have rather significant deflections of health condition, revealing by symptoms of intoxication, expressed breaches adaptation and regulation mechanisms. Results of study have logistical confirmed need of improvement of the preventive maintenance and dispensary observation at children with LTI and active

participation in its base of the interdepartmental approach. All of this allows newly taking a look at problem of the latent tuberculous infection at preschool age children and role general practitioner in preventive maintenance of the development such dangerous diseases as tuberculosis.

Keywords: quality of life, latent tuberculosis infection, treatment, children and adolescents, well-being

1. Introduction

Tuberculosis is a main infectious reason of deaths in the world and one of 10 leading reasons of deaths in the world. From tuberculosis in 2020 have all over the world died 1,85 million people (including four hundred thousand people with HIV), but had suffered 10,4 million people. In 2020 1,3 million children had ill of tuberculosis, and 250 000 children have died from it (including children with HIV-associated by tuberculosis). Tuberculosis is one of the main reasons to deaths of the people with HIV. Serious problem became the tuberculosis with multi drug resistance. However, in global scale number of patients with tuberculosis falls approximately on 2% per annum [1]. Latent tuberculosis infection (LTI) is a state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens without evidence of clinically manifested active TB. A direct measurement tool for M. tuberculosis infection in humans is currently unavailable. One-third of the world's population is estimated to have LTI: they do not have active TB disease but may develop it in the near or remote future, a process called "TB reactivation". The lifetime risk of reactivation for a person with documented LTI is estimated to be 5–10%, with the majority developing TB disease within the first five years after initial infection. However, the risk is considerably higher in the presence of predisposing factors.

At present statistics data persuasively show that in some country of the world number of children, for the first time infected with tuberculosis mycobacterium, continues to grow. For instance, in some region to Russia amount such children forms more than 2% whole baby population of the country. Most often primary infecting children of the preschool age, diseases range in this age group on 52% exceeds the general range of diseases amongst baby population [2, 3].

TST (Tuberculin Skin Test) and IGRAs (Interferon-Gamma Release Assays) are the main tests currently available for the diagnosis of LTI. Persons with LTI have negative bacteriological tests: the diagnosis is based on a positive result of either a TST or IGRA test indicating an immune response to Persons with LTI have negative bacteriological tests: the diagnosis is based on a positive result of either a skin (tuberculin skin test, TST) or blood (Interferon-gamma release assay, IGRA) test indicating an immune response to M. tuberculosis. However these tests have limitations as they cannot distinguish between latent infection with viable microorganisms and healed/treated infections; they also poorly predict who will progress to active TB.

Either TST or IGRAs can be used to identify candidates to LTI treatment in high and upper-middle-income countries with estimated TB incidence less than 100 per 100,000. IGRAs should not replace TST in low and other middle-income countries.

Who should be tested and treated for LTI? The risk of progression to active disease is considerably higher in infected individuals who belong to specific high risk populations. Major risk factors for TB activation include: HIV infection, recent contact with an infectious patient, initiation of an anti-tumor necrosis factor (TNF)

treatment, receiving dialysis, receiving an organ or hematologic transplantation, silicosis, being in prison, being an immigrant from high TB burden countries, being a homeless person, being an illicit drug user.

Today latent tuberculous infection (LTI) often turn researchers attention as condition, characterized by presence positive tuberculin skin reaction in the background of absence of clinical and roentgenological sign of local (active) tuberculous process. Importance of the problem LTI is in growing of children with such condition. As well as high range of diseases amongst children from this groups speaks that preventive work with infecting by tuberculous mycobacteria children is conducted in insufficient volume [4, 5].

In spite of value of the problem, the role general practitioner in system primary public health care of children with LTI is passive, consists only in discovery of this group children by method tuberculin skin test and issue to phthisiatrician. That has served the cause to persisting study.

2. Purpose of the study

Study health condition of children preschool age with latent tuberculous infection for development of organizing measures on improvement of the preventive maintenance of the tuberculosis and dispensary observation in primary public health care.

3. Problems of the study

1. Study of realized organizing measures on preventive maintenance of tuberculosis and dispensary observation in Uzbekistan and other countries by literature data.
2. Value epidemiological, social and biological risk factors of development infecting by tuberculous mycobacteria of preschool age children with latent tuberculous infection.
3. Reveal the deflections of health and quality of life at children of preschool age with latent tuberculous infection.
4. Develop the organizing measures of preventive maintenance of tuberculosis and dispensary observation of children, infected by tuberculous mycobacteria, in primary public health care.

4. Scientific novelty

For the first time children of preschool age with latent tuberculous infection will be elaborated physician-biological and social factors, which can be reasons low resistivity and infecting with mycobacteria of tuberculosis.

Deflections of health preschool age children will revealed on base clinic-functional complex study with latent tuberculous infection. Will revealed and portioned on groups anamnestic, clinical and laboratory markers of latent tuberculous infection beside of preschool age children.

Will installed influence of latent tuberculous infection on parameters preschool age children's quality of life.

Will scientifically motivated measures of the preventive maintenance of the tuberculosis and dispensary observation for infected children in primary public health care.

5. Materials and methods of study

During 2017–2019 was examined 100 children 4–7 years age on the base of Samarkand state antituberculous sanatorium, kindergarten № 84 of Samarkand.

For including children in conducted study obligatory condition was presence BCG vaccination at birth, attendance by children educational institution.

In study were excluded children, which parents were not agree to participate in study, children with delay psychomotor developments, having chronic diseases with symptoms of intoxication, children, have had sharp disease before 1 month back.

Children were divided in 3 groups. First group ($n = 40$) - a children with LTI, which were engulfed by dispensary observation and got the chemoprophylaxis in sanatorium. “Sharp turn” of tuberculin skin tests was noted at 3 (7,5%) children, increase of test result on 6 mm and more for one year - at 19 (47,5%), hyperergic result of test - at 12 (30%); annual increase test results with papule size on 12 mm and more - at 3 (7,5%), unchangeable sizes of the test in more than 3 years - at 3 (7,5%) children. Group of the comparison ($n = 40$) has comprised preschool age children, treated in Samarkand state tuberculosis hospital. Group of the checking ($n = 20$) have constituted the preschool age children from 1 groups of health with presence correct scar of BCG vaccination. In all group distribution children on sex and age had not a reliable difference.

Estimation of children health was conducted by analysis health factors: social, genetic, biological. In addition were studied criteria of health: physical development, functional condition, level to resistivity, psychomotor development, sharp and chronic diseases in anamnesis, presence of congenital development defects.

It was used study anamnestic data, questioning, estimation quality of life, anthropometry, data of objective examination, laboratory data and parameters of functioning, electrocardiography, vegetative nervous system spectrography (VNS-spectrography), manual ergometry. Information about each child is received information from history of disease and history of child development. Was conducted analysis factor risk of contamination with mycobacteria tuberculosis: physician-biological, social, genetic. Efficiency of vaccination BCG valued on presence scar, size less 4 mm was indicate as faulty vaccination. Physical development valued with the help of specialized tables. Leukocyte intoxication index is calculated on formula Shemitova V.F. Children observed by other specialists.

In help of cluster method all data were generalized. Variety heart rhythm (VHR) was studied by method VNS-spectrography on vegetotester “VNS-Micro” with computer program “Polispectr” of company “Neyrosoft”. Registered more than 500 cardiac cycles. Interpretation source vegetative tone and vegetative reactivity was realized according to recommendation N.A. Belokon. Vegetative provision of activity was valued on tolerance to steady-state load by method manual ergometry (MEM) in help of manual dynamometer.

Quality of life was defined with the help of questionnaire PedsQL version 4.0 (the Russian version), for 5–7 age children. Statistical processing was organized on PC Pentium 4. Made descriptive sample method, method one-factorial analysis of variance, Chi-square, U-criterion of Mann-Uitni, factor of Spearmen correlation, criterion of Fisher, reliable were considered differences $p < 0,001$.

6. Results and their discussion

Our study is indicating that at preschool age children with LTI there are deflections of health condition and quality of life. Premorbid background complicated by risk factors of developing tuberculous infection. Amongst specific risk factor, in the main group priority value has a contact with the source of infection (45,0%), presence of the disease at close relatives (42,5%), faulty vaccination BCG - 1-4 mm, absence of the incidence with chemoprophylaxis children with "sharp turn" of tuberculin skin test (17,5%). Reliable difference at frequency specific factor risk with group children, who had treatment in Samarkand state antituberculous sanatorium, was not revealed. Factors, having importance, as at children with LTI, so at children with evident form of the disease, were contact with tuberculous patients and faulty vaccination of BCG.

Important social risk factors at children with LTI were: not working parents (82,5%), asocial lifestyle of family (50,0%), unsatisfactory home conditions (77,5%), alcoholism of parents (72,5%), large families (55,0%). Nearly similar factors detected at children with evident form of tuberculosis. Biomedical risk factors at children with LTI in the first group were polydeficient anemia (35,0%), chronic nonspecific lungs disease (27,5%), preeclampsia and eclampsia during pregnancy in mother's anamnesis (45,0%) - realistically often, than at children with evident tuberculosis. During of cluster analysis are determined as significant factors - early begin artificial feeding (65,0% - on 55,0% often, than in checking group, $p < 0,01$), extensive tooth decay (32,5%, $p < 0,001$), presence to anemia light degree (27,5%, $p < 0,01$) - as at children with LTI, so and at children with evident forms of the tuberculosis. These risk factors promoted lowered resistivity of the children organism, and according to opinion O.B. Nechaeva, could become the reason infecting children with mycobacteria tuberculosis and it persisting in child organism, and speak about insufficiency of mechanism immunological protection. Low resistivity of organism was one of the important sign at group of children with LTI.

At preschool age children with LTI exist the subclinical signs of infecting MBT, basically manifestations of intoxication. Deflections in physical development (PhD) are discovered at 62,5% ($p < 0,001$) of the first group, at each third child from this groups it was connected with low mass of the body (30,0%, $p < 0,01$). Deficit of body mass is probably connected with reinforcement of the processes catabolism, which is called to provide the compensation and adaptation during chronic stressful situation. Intoxication phenomena in the first group children were also expressed as pale skin cover (47,5%, $p < 0,001$), anemia light degree (27,5%), fast heart rhythm (25,0%). These signs were importance as well as in group of the comparison. Intoxication was confirmed by leukocyte intoxication index by V.F. Shemitova. In the main group children this index was positive more than at half of examined person (75,0%).

Condition of peripheral lymph elements in the first group and group of the comparison in principal did not differ, that is indicate of generalities in reactions lymphatic system of children in response to persistence MBT in child organism. However, by comparing these factors in the first group and group of healthy children, noted brightly expressed differences: lymphatic elements dense and elastic consistencies (77,5%), plural (85,0%), size more than 5 mms (85,0%), with perifocal inflammation phenomena (22,5%, $p < 0,01$), unrepresentative localization lymphadenopathy - an cubital (20,0%), parotid (42,5%), occipital (35,0%) in first group was realistically often than in checking group ($p < 0,01$).

Functional systolic noise of heart existed at absolute majority examined children of first (90,0%) and the second group (87,5%). This on 52,5% and 47,5% accordingly often, than at children of checking group (42,5%, $p < 0,001$).

In the first group children with LTI were noted such signs as headaches (27,5%, $p < 0,01$), intolerance of transport (27,5%, $p < 0,01$), pains in chest (17,5%, $p < 0,05$), reduction to concentrations and attention (82,5%, $p < 0,05$), hyperactivity (50,0%, $p < 0,05$), emotional lability (67,5%, $p < 0,05$), petulance (67,5%, $p < 0,05$). During checkup of children with LTI is realistically often discovered marbling of skin cover (100%) and hyperhidrosis of distal extremities (62,5%), than in group healthy children ($p < 0,01$). These signs were significant at group children with LTI, as reasons of the functional breaches to specific organic pathology. Supposedly, these signs can be indicative of sanitary action quality, which conducted in primary section of health care.

Vegetative status at 45,0% children with LTI during cardiography is characterized sympathicotonia (in 20,0% often, than at healthy children, $p < 0,05$), at each fourth child of the main group was noted hypersympathicotonia (25,0%, $p < 0,01$). Considering fact of the final determination of vagus regulation of heart at 5–6 years old and domination of parasympathicotonia at children this age group, sympatic directivity of vegetative regulation, including hypersympathicotonia at children with LTI, follows to consider as overstrain adaptive regulation mechanism on background of chronic stress. It is important to emphasize that sympathicotonia at children of the main group had a relative character and was realized by reason of reduction compensatory of vagal influence that is one of the mechanism of the overstrain adaptational regulation, leaving for frames compensatory and adaptive reactions [5]. Accordingly, neither reliable increase of tension index (TI) (71,0 2,64 u.u.), nor index of Amo at children with LTI (25,6 1,04%), in contrast with checking group (64,5 2,6 u.u. and 30,1 1,2% accordingly), was not received. In this time, was reduced contribution parasympathitonic influences on initial vegetative status, it was indicated by reliable increasing at children with LTI initial vegetative tonus (IVT) and index of vegetative rhythm (IVR) factors in 12,5% and 15,0% accordingly, in contrast with data of checking group ($p < 0,05$). Such point of view was confirmed identity of mechanism adaptation and regulation of protection at children with chronic infectious disease – tuberculosis. Clinooorthostatic tests has allowed to install that surplus reaction on orthostasis was noted at each fourth child with LTI (25,0%) and at each fifth child with active tuberculosis (20,0%); the normal reaction existed at each fourth child of the main group (25,0%) and only at 5,0% ($p < 0,05$) children of the comparison group. Asympathicotonia of vegetative regulation (AST VR) registered at 50,0% children with LTI - in 1,9 times often, than in checking group ($p < 0,05$). It indicate of essential reduction compensator-adaptive reactivity of vegetative answer at preschool age children of main group, as well as at children with tuberculosis, which AST VR was noted in 2,5 times often (69,2%, $p < 0,05$), than at children of the checking group. Organized cluster analysis has confirmed objectivity and importance of determination VR because revealed AST VR is significant manifestation as at children with LTI, so and at children with active tuberculosis.

Distinctive feature of LTI was safety of normal structure of the wave variability of cardiac rhythm VCR that demonstrated harmony of vegetative provision. Wave characteristic of vegetative spectrum at children of the main group reliable difference, in contrast with data of healthy children, not identified. At children, suffered with tuberculosis, frequency of spectrum VCR was characterized by essential reduction of general power spectrum and all its components due to low compensator parasympathetic influences in structure vegetative balance that was indicative of reduction variability heart rhythm and reserve of powers adaptational mechanism at children with chronic tuberculous infection. Further study has shown that group LTI on spectral feature is not uniform. So at 36,8% children of main group to factors

of the spectral features were a similar of healthy children ($M_{\text{healthy}} \pm \delta$) - a group "A", but at 63,2% children with LTI wave features of spectrum approached to similar factor of the group children with tuberculosis ($M_{\text{suffered}} \pm \delta$) - a subgroup "B". All factors of VNS-spectrum between subgroup "A" and "B" children with LTI were received reliable differences: in subgroup "B" importance of factors total power of the spectrum (TP), waves very low frequency (VLF), low frequency (LF), high frequency (HF), were realistically below on 64,6%, 57,0% and 71,8% accordingly, than at children of subgroup "A". Also, data of children in subgroup "B" were realistically lower, than at children of the checking group VLF on 57,8%, LF - on 58,4%, HF - on 65,6%. Follows to note that factor TP in subgroup "B" was even realistically below (on 19,2%), than at children with active forms of the tuberculosis. At the same time, VNS-spectrum factors between subgroup data "A" and group of healthy children reliable difference was not received. Considering fact, that tuberculosis is an upshot of the early period of primary tuberculous infection, it should be assumed quite justified to performing VNS-spectrography at children with LTI, and if there disorders of spectral wave structure, estimate this as disadvantage trend to disease of tuberculosis and need of taking urgent preventive measures against LTI. Results of spectrogram in examined children shown in **Table 1**.

During of study vegetative provision to activity on data of MEM, determined that tolerance to steady-state load at children with LTI decreased: importance of endurance indicator was 11,6 0,44 (sec), factor of functioning in isometric mode - 143,85,64 (u.u.) - that were on 36,9% and 48,6% less, than at children of checking group. In the main group 44,7% children (on 35,3% more, than at checking group, $r < 0,001$) have not were able completely restore of hemodynamic indicators for 3 minutes after performing the test.

Factors of VNS-spectrum	Children group:				p
	Healthy children (n = 20)	LTI (n = 40)		Children with active tuberculosis (n = 40)	
		Having importance $M_{\text{healthy}} \pm \delta$ (n = 12)	Not having importance $M_{\text{suffered}} \pm \delta$ (n = 28)		
		3	A		
TP, ms ²	8076,0 ± 347,27	7834,0 ± 681,56	2776,0 ± 149,90	3437,0 ± 175,29	P _{A-B} < 0,05 P _{A-2} < 0,05 P _{B-2} < 0,05 P _{B-3} < 0,05 P ₂₋₃ < 0,05
VLF, ms ²	1608,5 ± 69,16	1580,9 ± 129,63	679,0 ± 56,71	533,5 ± 27,21	P _{A-B} < 0,05 P _{A-2} < 0,05 P _{B-3} < 0,05 P ₂₋₃ < 0,05
LF, ms ²	2304 ± 99,10	2221,1 ± 264,32	959,6 ± 82,10	1003,0 ± 51,15	P _{A-B} < 0,05 P _{A-2} < 0,05 P _{B-3} < 0,05 P ₂₋₃ < 0,05
HF, ms ²	4124,1 ± 177,33	4032,0 ± 479,81	1137,2 ± 184,8	1900,2 ± 96,90	P _{A-B} < 0,05 P _{A-2} < 0,05 P _{B-3} < 0,05 P ₂₋₃ < 0,05

Table 1.
Spectrogram data of examined children ($M \pm m$).

Aspects of QL	LTI n = 40 (M ± σ)	Suffered with TB n = 40 (M ± σ)	Healthy n = 20 (M ± σ)
Physical functioning	44,5 ± 2,5	40,2 ± 2,1	88,1 ± 3,4
Emotional functioning	52,1 ± 3,3	53,2 ± 2,4	83,8 ± 3,9
Social functioning	57,2 ± 2,1	42,7 ± 2,1	89,5 ± 2,2
preschool functioning	65,4 ± 2,0	48,0 ± 5,1	77,9 ± 1,3
psychosocial functioning	52,3 ± 2,4	47,9 ± 3,4	83,3 ± 2,8
Total scales	54,8 ± 2,6	46,1 ± 2,4	84,9 ± 2,5

Table 2.
Quality of life indicators in examined groups (in points).

Assessment of life's quality have revealed that at children with LTI quality of life realistically has a low indicators, than at children from checking group, as in opinion of children, as in opinion of tutors.

Indicators of life's quality (QL) in examined groups are presented in **Table 2**.

Indicators of the physical functioning at healthy children were double above than at children with LTI and active tuberculosis - 88,1 ± 3,4 (against 44,5 ± 2,5 and 40,2 ± 2,1 points). Presence of the clinical manifestation of disease is greatly reflected on children's ability to coping with obstacle, run, participation in athletic games. At children with LTI indicators of their physical functioning also were low - 44,5 ± 2,5 that directs that LTI has an influence upon the general condition of organism, that reveals in general weakly expressed malaises at this groups children. This brings them to independent restriction of the daily physical load. At children with active tuberculosis, physical functioning indicators were low. These patients were revealed at peak period of disease that brings sharply expressed change of general condition patients and expressed in practically full refusal of physical loads, daily duties, in accordance with physical activity.

Lowest indicators of emotional functioning noted at children with LTI and active tuberculosis - 52,1 ± 3,3 and 53,2 ± 2,4 points, that indicated of negative influence of tuberculosis to nervous system. Children from this groups more annoyed, moody, whining, feel discomfort from clinical symptoms of disease, at them is often noted presence of alert on cause of contact with persons of opposite sex. Amongst children with active tuberculosis, we have revealed changes in emotional status that is connected with understanding of incurability of diseases, despondency from joining of tuberculosis. High indicators of emotional functioning are registered at healthy children - 83,8 ± 3,9. However, at part of these children is noted presence discomfort from need to visit kindergarten.

During analysis of social functioning highest indicators noted at groups of healthy children – 89,5 ± 2,2 points, and this is indicative of adaptation of children, both to condition of kindergarten, and to acquisition of new friend relationships with other children. In group children with LTI indicators of social functioning were 57,2 ± 2,1 points. This reflects presence of such problems as compelled temporary cessation of the social relations in group in by reason of receiving of preventive treatment in tuberculous sanatorium. Amongst children with active tuberculosis fixed the lowest indicators of social functioning - 42,7 ± 2,1 points. As judged by answer respondent of these groups, awe for its future is from realizations contagiousness of diseases, as well as incurability of it.

Preschool functioning practically does not suffer at healthy children - 77,9 ± 1,3 points, only at a part children is revealed by restlessness, absence of attention, as well as inattentive attitude to performing of tasks. At children with active

tuberculosis this scale of functioning has a low indicators - $48,0 \pm 5,1$ points. These patients often skip the occupations in case of its condition, impossibility concentration during occupation. At children with LTI life in school is evaluated of $65,4 \pm 2,0$ points, the main problems of this group carried temporality - a restriction of visit the kindergarten at period of stay in sanatorium.

Scale of psychosocial functioning is a total scale emotional and social functioning. According results of this scale higher indicators were noted in group of healthy children - $83,3 \pm 2,8$ points, comparatively low in group children with LTI - $52,3 \pm 2,4$ points, and realistically low in group of patient with active tuberculosis - $47,9 \pm 3,4$ points.

Total scale has revealed the regularity - at children with active tuberculosis specific process has a most negative influence upon quality of life, comparatively temporary negative influence has LTI.

Revealed changes in general have brought to reduction of QL indicators both in first and second group. With provision of latency currents of infecting with mycobacteria of tuberculosis, indicators of quality of life should be considered as one of defining, reflecting psychological component adaptation of child, and can be recommended to enter in program of examination and dispensary observation of children with LTI.

Base on the above data introduces following picture of developing deflections mechanism of health condition at children with LTI:

- complex disadvantage physician-social factor leads to chronic stressful situation,
- that provokes adaptive and regulator overstrain and
- leads to immunological insufficiency,
- which clinical revealing low resistivity,
- that in condition not efficient immunization BCG and contact with bacterial isolation,
- is realized as infecting child with tuberculosis mycobacteria, with development LTI,
- it supporting chronic stressful reaction with transition in vicious circle and
- prospect of the failure to adaptation with transition in tuberculosis.

Social disorder connected with breach of main biorhythm regularities of life, high psychoemotional exhaustion on home conflicts background; it brings to reduction of child health and disadaptation of system activity. Certainly, this is an obligate ambience for persisting any infections, in this instance persisting of MBT.

In base of fetter of development LTI at preschool age children, were designed approaches to improvement of preventive maintenance and dispensary observation at participation general practitioner, marked active position of general practitioner in saving of children health, infected with MBT. Also was determinate of favorable current LTI group - "observation" group, overstrains of adaptation - "attention" group and disadaptation - "risk" group; as well as were improved questions of receivership in rendering physician-social help such children between phthisiatrician and family (social institution) with participation primary health care organization. Groups of dispensary observation of children with LTI in polyclinics are presented in **Table 3**.

Functional data	“Observation” group (favorable adaptation)	“Attention” group (overstrain adaptation)	“Risk” group (disadaptation)
Hypersympathicotonia	Absent	Absence/presence	Presence
Spectral features (TP, VLF, LF, HF)	Normal	Reduction	Reduction
Vegetative reactivity	Normal/HST/AST	Normal	HST/AST
System activity	Normal/reduction	Normal/reduction	Normal/reduction/sharp reduction

Table 3.
Groups of dispensary observations at children with latent tuberculous infection in polyclinic.

Consequently, in structure of medical-social help to children with latent tuberculous infection is defined staging of observations. First stage of medical help to children with LTI must be dispensary-polclinic section (district pediatricians, physicians of the educational institutions, general practitioner), which timely revealed children, infected with MBT (by tuberculin skin tests data), and direct to phthisiatrician this children for specialized help. Second stage must be to define the branch a physician-social help, realizing nonspecific rehabilitation of children with LTI, directed on elimination risk factor and consequence chronic physician-social stress. We suppose the expedient observation by general practitioner to children with LTI not less than three years, because long processes of astenization, reduced adaptation require time to value efficiency specific chemoprophylaxis and nonspecific correction. In addition, children with LTI from “attention” and “risk” groups pass the rehabilitation (third stage) on base of general profile sanatorium (more than 1 month). In case of favorable current of adaptation, (“observations” group) rehabilitees can be realized on area, in families or in social institution.

Therefore, our study has shown that preschool age children with LTI have rather significant deflections of health condition, revealing by symptoms of intoxication, expressed breaches adaptation and regulation mechanisms. Results of study have logistical confirmed need of improvement of the preventive maintenance and dispensary observation at children with LTI and active participation in its base of the interdepartmental approach. All of this allows newly taking a look at problem of the latent tuberculous infection at preschool age children and role general practitioner in preventive maintenance of the development such dangerous diseases as tuberculosis.

7. Conclusions

1. Preschool age children with latent tuberculous infection have rather significant deflections in their health condition.
2. Anamnesis of children with latent tuberculous infection greatly burden with specific risk factor of infecting MBT. These are not enough effective BCG vaccination at 72,5% of examined person, tuberculosis at close relative (37,5%), as well as biomedical and social factors, provoking low level of resistance at 55,5% children of main group: early artificial feeding (65,5%), sharp diseases of respiratory tract (42,5%) and asocial family.
3. In spite of latent current of the primary tuberculous infection, at preschool age children there are realistically significant clinical signs: marbling of skin cover

(72,5%), sweating (80,0%), hyperhidrosis (52,5%), deflections of physical development (60,0%), lymphadenopathy (72,5%). At 47,5% children with latent tuberculous infection is defined toxicosis, by first degree of leukocyte intoxication index.

4. Initial vegetative tone at majority preschool age children with latent tuberculous infection identical of healthy children group indicators, with saving sympatic-parasympathetic activity; but at 21,1% children initial vegetative tone similar indicators of children with active tuberculosis and characterized hypersympathic directivity with reduction compensatory influences vagus nerve that reflects significant adaptational tension.
5. Spectral features variety of heart rhythm at 66,0% children with latent tuberculous infection similar data of children with active tuberculosis, which frequency spectrum is characterized by essential reduction to general power of the spectrum (TP) on 57,4% and all its component (LF on 56,5%, HF on 53,9% and VLF on 66,8%). It demonstrate significant overstrain adaptational mechanism of vegetative regulation functional systems of the organism child with latent tuberculous infection.
6. Latent tuberculous infection promotes reduction of adaptability processes of child organism, revealing in deficit of quality of life.
7. Well-timed taking by general practitioner on dispensary register children with latent tuberculous infection, differentiated approach depending on conditions mechanisms of adaptation and regulation, complex and interdepartmental medical examination are contribution to preventive maintenance of development tuberculosis at given contingent of children.

8. Practical recommendation

To pediatrician during estimation of health condition of children with latent tuberculous infection is recommended:

1. Use leukocyte intoxication index by V.F. Shemitova as subclinical markers of intoxication.
2. Use data of heart rhythm variety with determination of indicators: hypersympathicotonia in initial vegetative; the reduction of general power of spectrum and all its components; asympatic vegetative reactivity; reduction to system activity – tolerance to steady-state load and quality of life deficiency as markers of adaptation.
3. Define the groups of dispensary observations of children with latent tuberculous infection: “observations”, “attention” and “risk” considering data of adaptation and regulation mechanism: favorable adaptation; the overstrains of adaptation and disadaptation, which
4. Dispensary observation of children is with latent tuberculous infection must be realized in household polyclinic during 3 years in accordance with applicable scheme. Dispensary observation of children with LTI is presented in **Table 4**.

Action	Groups of dispensary observation		
	“Observations”	“Attention”	“Risk”
First year of observation			
Checkup by pediatrician	Once in half year	Once in quarter of year	
Volume of investigation	Assessment of risks, clinical examination, VNS-spectrography, cardiography, manual ergometry (MEM), study of quality of life (QL)		
Specialists checkups	Otophinalaryngology, stomatologist, on evidences - a neurologist, immunologist and others		
	Once in half year or on evidences		
Adaptation and regulation	Enriched feeding, dose physical loads, cleaning of chronic foci of infections		
	Sanitary actions	Energy-metabolic correction, optimizers CNS (by neurologist prescription), immunocorrection (by immunologist prescription)	
Estimation of efficiency	Absence clinic-laboratory and roentgenological manifestations of tuberculosis, positive dynamics of tuberculin skin tests, absence clinic-functional breaches of vegetative regulation and system activity (VNS-spectrography, cardiography, MEM, QL), normalization of physical development, increasing resistivity, improvement of current accompanying pathology		
2 and 3 years of observation			
Checkup by pediatrician	Once in half year		Once in quarter of year
Volume of investigation	Actions of first year observation		
Specialists checkups	Similar as actions of first year observation		
Adaptation and regulation	Similar as actions of first year observation + sanatorium treatment (at least 1 month)		
Estimation of efficiency	Similar as actions of first year observation		

Table 4.
Dispensary observation of children with latent tuberculous infection.

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