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Tuberculosis in children in the Russian Federation at the present stage

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The literature review presents data on peculiarities of tuberculosis epidemiology, incidence rate and clinical pattern in children in the Russian Federation. Over the last 5 years, the age structure of the children developing tuberculosis has significantly changed: the share of children of small and preschool age increased, whereas the share of 7-14-year-old children decreased. Tuberculosis of thoracic lymph nodes predominates in the structure of clinical forms of tuberculosis of respiratory organs in children; small forms predominate, which indicates improvement of diagnostic capabilities. However, a rather large number of children with calcination stage of the tubercular process is observed. Further improvement of early detection of a tubercular infection is a powerful tool of preventing complicated and progressive forms of tuberculosis in children.

Keywords: tuberculosis, children, tuberculosis of thoracic lymph nodes, epidemiology, diagnosis, vaccinal prevention.

Tuberculosis incidence rate in children is a “barometer” of epidemical situation on tuberculosis [1]; it is considered an important prognostic parameter reflecting shifts in the epidemical situation [2]. Some researchers mention such a peculiarity of the current epidemiological situation on pediatric tuberculosis as the incidence rate increase, especially among preschool- and primary school-aged children [3].

Age structure of the children, who had developed tuberculosis, changed significantly in the past 5 years: there was an increase in the share of children of 0-2 and 3-6 years of age and decrease in the share of 7-14-year-old children [4, 5]. In her publications, L.A. Baryshnikova indicates that dynamics of the age structure of children from 1991-1993 to 2006-2008 was characterized by decrease in the share of school-aged children (7-14 years) from 31.4 to 18.6% in the setting of a tendency to increase in the share of younger children (0-2 years of age) from 13.3 to 15.9% [6, 7].

Overall, the tuberculosis incidence rate among 0-14-year-old children in the Russian Federation doubled (from 9.4 to 19.1 per 100,000 children) in the period from 1992 to 2001. The incidence rate underwent only insignificant changes in the subsequent 5 years; it plummeted down to 15.3 per 100,000 persons in 2008 and to 14.7 in 2009 [8].

Mortality from tuberculosis of the child population reduces to few cases owing to the existing techniques to protect children from the disease. But unfavorable age group (in terms of mortality from tuberculosis) consists of children aged from 0 to 2 years (0.4 per 100 thousands eligible children) [8, 9]. This fact demonstrates the importance of vaccine prevention of tuberculosis in young children and an X-ray examination of the newborn environment [8].

Tuberculosis diagnosis is the method of early detection of the primary infection and development of tuberculosis in children employed in Russia [10, 11]. However, it is widely debated whether such diagnosis is rational for cohort examination of children [12]. Tuberculin tests in the setting of cohort BCG vaccination are not capable of reliably determining the level of children's infection with mycobacteria tuberculosis (MBT) and distinguish between postvaccinal and infectious allergies [10-12]. Several factors distort tuberculin sensitivity. The reaction result is affected by allergic diseases, recent infections, age, vaccines and individual skin sensitivity parameters; all these aspects complicate interpretation of the results [11-13].

Skin test using Diaskintest (DST) – recombinant protein CFP10-ESAT6 – has served to resolve the problem [12]. According to several authors, DST test may be used as an effective screening method of examining children in order to identify persons with various manifestations of tuberculous infection [14, 15].

The rate of negative DST results in healthy MBT-infected patients was 56.6%, the rate of positive test results in patients with tuberculosis – 87.9%. The obtained results prove that DST may be used in combination with other methods for tuberculosis diagnosis in children [16]. DST may be used in the process of complex examination of children at specialized establishments for differential diagnosis of infectious and postvaccinal allergies; it also improves effectiveness of diagnosing complicated BCG vaccination in infants [17]. Use of DST tests together with computed tomography of chest improves effectiveness of tuberculosis diagnosis in children [15, 18, 19].

The incidence rate observed in high tuberculosis risk group children despite phthisic supervision stirs special alarm [8, 20]. The incidence rate among the children contacting with bacteria-discharging persons in 2009 exceeded the incidence rate observed in the corresponding age groups in Russia altogether 30 times [8]. Other authors observed a 50-60-fold higher incidence rate among the children residing in tuberculous infection centers (and a tendency to annual growth) than in the population in general [21]. High incidence rate among the children residing in tuberculous infection centers is caused by poor housing conditions, bacillary patients, asocial behavior and noncompliance with sanitary standards; undernourishment of children due to low quality of life of the family, not always feasible isolation of children from patients with tuberculosis, untimely and incomplete chemoprophylaxis and low quality of vaccinal prevention of tuberculosis [21-23].

Specific biomedical tuberculosis risk factors consist in absence of ineffectiveness of BCG vaccination [9, 10]. According to multiple published data, BCG vaccination is an important preventive anti-tuberculous measure; it decreases children's tuberculosis-associated morbidity and mortality and prevents development of acute progressive forms of the specific process (miliary tuberculosis, meningitis, caseous pneumonia) [24, 25]. It has been proven that BCG vaccination shifts "fetal" Th2-polarized immune response to various antigens in infants towards a more effective "adult" Th1 response characterized by production of $\text{INF } \gamma$ and IL 2 – activators of effector lymphocytes and macrophages [26].

The question of immunization significance remains controversial. Some scientists consider impact of vaccinal prevention on epidemic process parameters insignificant and conclude that there are no reasons for cohort application thereof [27]. However, most authors uphold the need in maintaining traditional approaches towards organization and realization of specific prevention of tuberculosis [21, 23, 25].

The problem facing scientists all over the world is creation of new vaccines on the basis of genetic engineering [28]. Still, BCG vaccine remains one of the primary vaccines in all countries; according to many authors, extensive use of this vaccine is especially important nowadays, as the epidemical situation on tuberculosis remains stringent [21, 25].

Tuberculosis of intrathoracic lymph nodes (TITLN) prevails in the structure of clinical forms of respiratory tuberculosis; according to different authors, it is diagnosed in 68.0-84.7% of the cases [4, 5, 9, 29, 30]. High percentage of minor forms of tuberculosis among patients with TITLN

(50-67%) is associated with improved diagnostic capabilities and frequent use of multispiral computed tomography for examining children [2, 23, 24, 31].

The primary characteristic features of minor TITLN include moderate clinical symptoms, no convincing diagnostic criteria revealed by means of regular radiographic and laboratory diagnosis; this makes it rather difficult to interpret the child's condition [3, 29], especially if Diaskintest and multispiral computed tomography have not and/or could not have been performed.

According to other published sources, decrease in the effectiveness of tuberculosis diagnosis in children at early stages of infection development is becoming more distinct; the process is often identified at the stage of involution or involutional changes [3, 32]. In 2005-2010, Professor Yu.E. Ovchinnikova examined 3-14-year-old children with TITLN and determined that the process was revealed at the infiltration stage only in half of the patients; in the other half, the process was identified at the stage of calcination and densification. Chronic course of the disease with concurrent infiltrative changes in certain groups of intrathoracic lymph nodes and calcification in other groups thereof was identified in 1 out of every 4 children. In most children, the pathology of intrathoracic lymph nodes was disseminated and bilateral; 1/3 of the patients developed complications [30]. Other authors also highlight the fact that TITLN often acquires chronic course characterized by formation of large calcified foci [9]. TITLN complications are observed in 11.6-30% of the cases [4, 5, 20, 29].

Increase in the rate of secondary forms of tuberculosis in children has been observed in recent years [20, 30, 31], especially of infiltrative pulmonary tuberculosis (11-13%) [1]. One of the characteristic features of the current situation is the significant increase in the amount of bacteria-discharging children among the tuberculous patients [33]. According to other sources, processes characterized by bacterial discharge and pulmonary tissue destruction in children are only rarely observed [20]. G.A. Gufranova et al. observed that the amount of bacteria-discharging children decreased significantly in the past 3 years; however, bacterial discharge is registered among children (including children with drug resistance [DR]) every year [4].

Increase in the rate of diagnosing acutely progressing forms of tuberculosis (miliary tuberculosis, meningitis, caseous pneumonia) and in the specific weight of the MBT-discharging DR patients has been observed recently [4, 30]. MBT DR-induced tuberculous process is characterized by severity of the patients' overall condition and functional disorders; it is hard to treat; it leads to the development of chronic forms of the disease [7, 23, 32].

Extrapulmonary forms of tuberculosis are observed only in 16.3% of the cases in children. In infants, osteoarticular tuberculosis is observed more often than any other forms of extrapulmonary tuberculosis (65.9%). Meningeal and central nervous system tuberculosis is observed in 12.1% of the infants. The rate of these forms of extrapulmonary tuberculosis diminishes with age, whereas the rate of peripheral lymphatic and urogenital tuberculosis increases: it reaches its maximum in children of 7-14 (34.6%) and 5-6 (37.8%) years of age [5, 32].

One of the adverse factors affecting spread of tuberculosis in the world in whole and in Russia in particular is the increase in the amount of HIV patients, including HIV-infected children [34]. Increase in tuberculosis rate among HIV patients is a serious problem for Russia: 101 children with these concurrent pathologies – HIV and tuberculosis – were revealed in 2009 [9].

By December 31, 2009, 4,048 under-14 children with HIV infection were registered in the Russian Federation, 85% of whom were under-7 children. The amount of children with tuberculosis concurrent with HIV increased 1.5 times from 2007 to 2010; the overwhelming majority of these children was comprised of under-7 children: 83.6% in 2007, 91.0% in 2008 and 78.0% in 2009 [34]. HIV-infected children are more susceptible to tuberculosis [35].

The HIV infection incidence rate in the Siberian Federal District (SFD) in 2010 was 1.9 times higher than in Russia altogether (78.1 per 100,000 persons). At the same time, an increase in primary incidence and prevalence of HIV infection among under-14 children was observed; most

of these children were infected with HIV in the perinatal period (77%). The incidence rate of HIV infection among under-14 children in 2010 was 6.1 per 100,000; the prevalence rate thereof amounted to 39.2 per 100,000. Every second child with HIV infection in the District featured HIV-associated diseases, among which tuberculosis was the fourth most widespread after bacterial infections, viral infections and fungal diseases. Since 2009, the following causes of death of children with HIV infection have been registered in the SFD: cytomegalovirus infection, pneumocystic pneumonia, fungal diseases and tuberculosis [36].

Thus, risk of tuberculosis development, form, severity and outcome of the specific process in childhood depend on a complex set of exogenous and endogenous factors, such as BCG vaccination effectiveness and duration of the contact with a tuberculous patient. Currently, despite a generally adverse epidemiological situation, the structure of clinical forms of tuberculosis and rates of complicated diseases and bacterial discharge in children vary. Tuberculosis diagnosis requires using DST and consolidating data on the use thereof. Detection of an active process at early stages of tuberculous infection development is a powerful means of preventing complicated and progressive forms. Analysis of tuberculous pathomorphological peculiarities in children in order to improve timely diagnosis of the disease is a relevant issue in the current context.

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