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INTEGRATED APPROACH TO THE STUDY OF LONG-TERM DYNAMICS OF HIV INFECTION, TUBERCULOSIS AND THEIR COMBINED FORMS MORBIDITY OF THE RS (Y) POPULATION

Abstract In the paper the authors show the dynamics of the incidence of tuberculosis, HIV infection and their mixed forms in the Republic Sakha (Yakutia) on the base of the integration method. Differences in the TB incidence of native and non-native population are revealed. The authors present the possible mechanisms of interaction between M. tuberculosis and HIV, and their reflection in the epidemic process basing on an analysis of the literature review. The important role of tuberculosis mixed - forms and HIV infection in its development is shown.

Keywords: epidemiology, HIV infection, tuberculosis, mixed-forms, integration method.

Introduction.

Traditionally, epidemiology considers the epidemic process of certain infections separately. However, the phylogenesis of all causative agents of infectious diseases was happening under close and selective interaction of certain forms with development of various biocoenoses in the host's organism and the environment. The relations established between the biocoenosis co-members may be both integrated and competing, which, undoubtedly, has an impact on manifestations of the epidemiological process (EP) of certain infections. We have elaborated the concept of integrated-competing development of EP [12] stating that the self-regulation may take place not only in individual parasitogenic systems [2], but also between individual kinds of microorganisms in the formed biocoenoses, as a result of the integrated-competing relations. This leads to certain problems of revealing the interspecific interaction of individual groups of causative agents. The integrated technique helps to reveal such interactions and their manifestations on the population level of the epidemiological process [8].

Tuberculosis and HIV infection, being socially significant infections, represent a global problem causing tension in the national preventive care systems [7]. From the end of the 20th century, the WHO has faced the global challenge of the simultaneous increase in the tuberculosis and HIV incidence, with a definite relation established between these two nosological entities. Most authors relate the deteriorated tuberculosis epidemiological situation with the rapid increase in the HIV pandemic [7, 11, 14]. According to O.P. Frolova et al. [10], tuberculosis causes 66.5% of deaths in HIV patients, and it has become its opportunistic infection, since microbacteria are considered more virulent than other pathogens [15]. HIV infection is a significant factor of developing tuberculosis as a result of the activated latent process or an indirect impact on the mechanism of microbacteria tuberculosis (MBT). Tuberculosis and HIV infection causative agents in co-infected patients acquire new properties when exposed to anti-bacterial preparations and intensive antiretroviral therapy. As a result of the drug resistance and mutations formed, their main biological properties are modified, which leads to increased influence of one infection on the other [7]. The objective assessment of different authors forecast the increase in tuberculosis incidence among HIV-infected people in Russia, thus, it is critical to take urgent preventive measures [4, 11].

The analysis of professional publications shows that most authors study the potential influence of HIV infection on the spread of tuberculosis. At the same time, some researchers also notice that nowadays, in certain regions, HIV infection EP is starting to hamper tuberculosis EP [4]. This allows us to assume that the epidemiology of tuberculosis and HIV infection has an interdependent nature. There has been no such research in the republic so far.

Aim of the Research.

To study the several-years' trend of HIV infection and tuberculosis incidence in the Sakha Republic (Yakutia) and their mixed forms, and to assess the epidemiological situation with the use of the integrated approach.

Research Materials and Methods.

The main research technique - epidemiological - was applied by several methods under the

traditional algorithm [3]. The material for the coupled epidemiological analysis was the data from the federal statistics for the Sakha Republic (Yakutia) - "Information on infectious and parasitic diseases" (Form 2), "Information on tuberculosis patients" (Form 3), "Information on active tuberculosis incidence" (Form 8), the records of infection nidus epidemiological examination (Form 357/y), "Personified registry of tuberculosis patients with HIV infection" (Form 263/y-TB), record books of infectious diseases (Form 60) for the period 1992-2012. The statistical processing of the material was done by the standard epidemiological techniques [9].

Results and Discussion.

The retrospective analysis of the several-years' tuberculosis incidence trend in the republic in 1992-2012 showed two periods in EP development: the first - 1992-1998, when the mean annual incidence rates varied within 56.96‰ (Rinc=1.2%); and the second - 1999 to 2012, with some increase - 78.49‰ (Rinc=1%). Before 2005, the tuberculosis incidence rates in the republic were a little lower than in the RF or comparable, and since 2007 there appeared so-called scissors; the first remained the same with the rest of Russia demonstrating the disease reduction trend (Fig. 1).

Fig. 1. Active tuberculosis incidence trend in the Sakha Republic (Yakutia) and the Russian Federation in 1992-2012 (per 100 thousand people).

The retrospective analysis of the several years' HIV infection incidence trend in the republic showed three periods (Fig. 2). The first - from 1996 to 1999 with its increase (Rinc=70%) and the peak in (13.1‰). The second period was marked by decrease in the incidence (Rdec= -21.8%). However, in (the third period) there appeared again the increase trend (Rinc=3.8%). The pattern of the curve reflecting the HIV infection incidence trend in the Sakha Republic (Yakutia) was in general similar to that of the RF but its peak fell on the year 2000, not 2001 as in the RF.

Fig.2. HIV infection incidence trend in the Sakha Republic (Yakutia) and the Russian Federation in 1992-2012 (per 100 thousand people)

At the same time, the incidence rates in the republic over the years analyzed were considerably lower than the Russia's average. Before 1996 Yakutia was considered an area free of HIV infection. In 1996-1998 the infection was detected mainly in arriving foreign citizens, with the intensive territorial infection of the population starting only in 2002. According to A.A. Kozhevnikov's survey [5], Yakutia is considered an area with low HIV infection which is explained by the fact that the local population restrains from drug abuse and random sex. It is known that starting from the mid-1990s, the three epidemics - drug abuse, HIV infection and tuberculosis - have been following each other [1]. The republic proves this trend and demonstrates the increased drug abuse affecting the spread of HIV infection [6].

The coupled analysis of the HIV infection and tuberculosis incidence in Yakutia showed that the increase in this nosological entity incidence coincides with the intensified HIV infection EP. In particular, the correlation analysis between tuberculosis and HIV infection incidence rates in 1999-2012 revealed the average bond strength line ($r=0.6$, $p<0.05$). Since the annual risk of tuberculosis activation in tuberculin-positive patients with HIV is very high and averages to 7.9% [13], we can assume that the epidemiological potential for developing tuberculosis in the population will increase progressively in accordance with the number of people infected by HIV.

At the same time, it should be noted that the interrelation between tuberculosis and HIV microbacteria is likely to occur in the human body, only, since the both infections are anthroponoses. HIV and MBT are two closely connected infectious agents, pathogenically, interacting with each other indirectly through many recipient's structures. HIV mainly targets at T-lymphocytes, therefore, in most cases, its first clinical manifestations appear as the lymphatic nodes reaction. At the same time we should state the fact of the incredible lymphotropy of MBT, especially at the initial infection of human beings with microbacterium tuberculosis. Therefore,

the lymphatic system organs represent the area of the most intensive interaction between the virus and microbacterium [7]. With the active tuberculosis process localizing in any organ, the specific inflammation development starts with the immune system's cell component disorder caused by both the toxic impact and other biological factors of the microbial effect. That is why the HIV and MBT interaction occurs indirectly, primarily through the immune system. HIV infection increases susceptibility to tuberculosis infection, resulting in the rapid development of the disease and thus affecting the disease spread indicators (incidence and prevalence). Here, cytokines play an important role, as they are able to activate or slowdown the virus replication in the human organism [4].

Therefore, all these facts prove the significant role of tuberculosis and HIV infection mixed forms in EP development. Our research has shown that HIV infection and tuberculosis mixed forms are registered in the republic since 1999 (Fig. 3).

Fig. 3. The incidence trend for HIV infection and tuberculosis mixed forms in the Sakha Republic (Yakutia) in 1999-2012 (per 100 thousand people)

At the same time, we witness a definite growing trend ($R_{inc}=8\%$). A similar trend is typical of the RF on whole [4, 7]. We have established that, with the mono HIV infection mortality in the republic over the past five years averages to 1.6% and of tuberculosis - 4.1%, their mixed forms lead to 11.9% mortality. Indeed, this combination is 'the devil's mixture' as foreign researchers call it [4]. We should emphasize that the mixed form patients are more dangerous as the infection source for contacting people than HIV-negative tuberculosis patients [16]. However, so far, we have not registered cases of mixed forms in the indigenous population of the republic, though they prove to be more susceptible to tuberculosis as a mono-infection. For example, against 49.0 per 100,000 persons in the non-aboriginal population, the Yakut people demonstrate 87.8 per 100,000 and the indigenous peoples of the North - up to 110.5. Unlike the newcomers and Yakuts with the dominating male patients ($71.3\pm 2.8\%$ и $58.8\pm 1.6\%$, respectively), the male-female break-down of tuberculosis patients in the indigenous people differed insignificantly (Fig. 4).

Fig. 4. Male-female break-down of active tuberculosis patients in the indigenous people of the North

Therefore, over analyzed period, the epidemiological processes for both tuberculosis and HIV infection in the republic were quite autonomous. However, HIV infection is starting to influence the tuberculosis EP activity, which is seen in the increase in the mixed forms and the average force line of the correlation bond between tuberculosis and HIV infection incidence figures. Due to higher epidemiological significance of the mixed forms, in comparison with the mono infections, the increase in their number aggravates the epidemiological situation with tuberculosis in the republic, already being alarming.

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