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IMMUNOLOGICAL TESTS IN DIAGNOSTICS AND DETERMINATION OF TUBERCULOSIS INFECTION ACTIVITY

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Annotation. The article presents data on the use of immunological tests for the diagnosis of tuberculosis infection (test with tuberculous recombinant allergen containing ESAT6-CFP10 protein (ATR) and interferon-gamma release assay (IGRA)). Currently, studies are underway to create new immunological tests for the differentiation of latent tuberculosis infection and active tuberculosis..
Key words: immunodiagnosis, tuberculosis, latent tuberculosis infection, methods, detection, tests.

Tuberculosis (TB) is one of the important public health problems worldwide. Particular attention is paid to preventive measures to reduce the infection of the population. One of the goals of the World Health Organization (WHO) strategy is to create new immunological tests with the ability to increase the detection of active TB among people with latent tuberculosis infection (LTI). An ideal test should help distinguish LTI from initial TB as a long asymptomatic phase until the period of clinical symptoms of active TB [1, p. 5].

The IGRA test contains antigens of M. tuberculosis (MBT), ESAT6 and CFP10, which are not present in M. bovis. The specificity of this test makes it possible to differentiate LTI and the condition after BCG vaccination. Two test cases are used to diagnose LTI: (IGRA - Interferon Gamma Release Assays) and QuantiFERON

(QFT). The latter is produced in two versions - T-SPOT.TB (Oxford, Immunotec, United Kingdom) and QuantiFERON-TB Gold In-Tube (QFT-GIT, Celestis, Victoria, Australia). Tests are based on the synthesis of interferon-gamma (INF-μ) T cells in response to specific MBT antigens.

ESAT-6 and CFP10 begin expression during the multiplication of MBT, and the immune response to these antigens has a direct correlation with the activation and progression of LTI. IGRA tests are characterized by high prognostic significance in assessing the likelihood of developing a disease. Positive test results make it possible to identify individuals who are shown preventive chemotherapy [2, p. 49]. Screening strategy for selecting patients for preventive therapy increases the overall cost-effectiveness of treating TB.

A skin test using ATR is convenient to use in children, since IGRA tests involve intravenous manipulations. In developed countries, it is used to detect LTI at risk. One option for ATR is the intradermal Diaskintest. This test is highly specific, negative results in children after BCG vaccination are 100% [2, p. 54]. In people cured of extrapulmonary forms of TB, negative results also make up 100%. The dynamics of the results of ATR makes it possible to assess the development of tuberculosis infection.

In children and adolescents with a primary negative Diaskintest, after separation with MBT exciters, seroconversion (bend) occurs. Negative test results were observed in almost 50% of adult patients with TB after a 3-month course of chemotherapy. The WHO strategy provides for the creation of tests for the diagnosis of TB in children, systematic screening for the active detection of LTI cases, followed by a reduction in the size of this group.

ATR tests are convenient for use in primary care as screening instead of a Mantoux test. In the absence of clinical manifestations of TB and isolation of MBT, the dynamics of the results makes it possible to control the development of tuberculosis infection. Persons with positive test results have a high risk of developing it. Prescribing preventive therapy to these patients reduces the incidence of TB in both children and adults [3, p. 59].

Negative test results have negative prognostic value; these individuals do not get TB in the absence of chemotherapy. In the future, tests should be developed to assess the possibility of developing TB in the coming months (the availability of developing TB). It is important to assess not only the likelihood of a possible activation of the infection with positive test results, but also to determine the factors that provoke the activation of MBT: alcoholism, smoking, taking tumor necrosis factor alpha (TNF-α) inhibitors, HIV infection, diabetes, malnutrition, young age.

The phase of an early or incipient TB precedes the clinical symptoms of the active course of the disease [4, p. 705]. MBT can be detected in sputum approximately 1 year before the clinical manifestations of TB. The WHO program suggests the need for tests of two groups with different goals: 1) tests for persistent infection; 2) tests for incipient TB [1, p.5].

The tests of the first group are supposed to be used as control in people with a high probability of developing severe TB (for example, in people with HIV infection or in those starting treatment with TNF-α blockers). IGRA tests are very well suited for evaluating persistent tuberculosis infection. Improved tests of the second group should not give positive results after successful chemotherapy.

Tests for incipient TB are most appropriate for recent infections if they come in contact with sick TB. To increase the sensitivity of these tests, it is necessary to repeat them in dynamics. Therefore, they should be inexpensive, easy to use, semi-quantitative with the determination of the bacterial load. Assessing the dynamics of these tests makes it possible to make informed decisions about preventive or complete chemotherapy courses.

Tests for nascent TB are promising for public health, their rational implementation increases the potential of the strategy to track patients' contacts with TB. The ability to conduct these tests in dynamics allows not only to identify individuals with a high probability of transmission of infection, but also to prescribe preventive treatment. The result is a significant reduction in the incidence of TB in the population.

In recent years, attempts have been made to create tests to differentiate between LTI and active TB. According to the authors, ELISPOT tests can help solve this problem

[5, p. 280]. If T-SPOT.TB is based on INF-μ products, then ELISPOT is based on IL-2 synthesis.

Research is ongoing on the production of other cytokines in LTI and active TB. Activation of innate and adaptive immunity in LTI is supported by the inflammatory process at the sites of MVT localization [6, p. 101].

Recent studies have confirmed a more pronounced immune response with active TB than with LTI [7, p. 505]. However, many researchers believe that the production of IL-2, IL-13, INF-μ is higher with LTI than with active TB. INF-μ production in IGRA tests makes it possible to distinguish LTI and active TB from healthy control, however, it does not make it possible to differentiate LTI from active TB as a disease. At present, the benefits of determining any cytokines as compared with INF-μ as the basis of the tests have not been convincingly proven. Determination of INF-μ in IGRA tests is most appropriate in real conditions with a small amount of laboratory resources [8, p. 77].

ATR tests provide an opportunity to identify individuals with LTI with a high risk of developing active TB. The presence of positive ATR results in children at risk confirms the presence of LTI, more often it involves a course of chemotherapy. As a result, both the incidence of TB in risk groups and in the population as a whole decreases.

The use of ATR tests helps to detect timely activation of tuberculosis infection in patients with HIV and in the group receiving TNF-α blockers. Children with positive ATR results are highly likely to develop TB, especially for children from family contacts with sick TB bacteria.

The ATR test is highly sensitive, highly specific, inexpensive, and does not require highly qualified personnel. The test remains negative until the development of tuberculosis infection with replication of MBT. A positive test result can confirm the need for a preventive course of chemotherapy. The use of ATR tests may be contraindicated in patients with severe immunodeficiency, for example, in the late stages of HIV infection. In these cases, it will be rational to use IGRA tests [9, p. 6].

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