MOLECULAR GENETIC STUDIES MAKE IT POSSIBLE TO IDENTIFY DRUG RESISTANCE AND ADJUST THE TREATMENT OF A PATIENT WITH TUBERCULOSIS

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Annotation: This article molecular genetic studies make it possible to identify drug resistance and adjust the treatment of a patient with tuberculosis

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Tuberculosis is one of the acute medical and socio-economic problems both in Russia and around the world. A particularly unfavorable trend in the epidemiology of TB in recent years is the increase in patients shedding Mycobacterium Tuberculosis (TB) with Multidrug Resistance and Extensive Drug Resistance. These forms of tuberculosis are characterized by severe course, low efficiency of therapy and high mortality. With an incorrect combination of anti-tuberculosis chemotherapy drugs, the selection of antibiotic-resistant strains of mycobacteria occurs, which leads to the spread of drug-resistant tuberculosis.

The existing traditional methods for isolating MBT and determining drug resistance on dense nutrient media are characterized by insufficient sensitivity and long-term results (more than 2.5 months).

The use of the automated system VASTES MGIT 960 using liquid nutrient media made it possible to increase the detection of MBT by 30% and reduce the time for obtaining the results of the patient's examination to 14-17 days.

Faster isolation of the causative agent of tuberculosis and determination of MBT drug resistance (3-4 days) became possible after the development of high-

tech methods for determining gene mutations in Mycobacterium tuberculosis, in particular, by polymerase chain reaction (PCR).

PCR is the most sensitive method for diagnosing tuberculosis. With the help of PCR, it is possible to determine the type of pathogen with 100% certainty.

This is a rather complex examination based on the search for various fragments of Mycobacterium tuberculosis DNA in the material from the patient. The method allows you to detect even a small number of bacteria - 5-10 cells in the analysis.

All body secretions are subject to PCR research: sputum, urine, intra-articular fluid, cerebrospinal fluid, biopsy specimens and much more.

In BU "RPTD" two modifications of PCR are used:

- PCR in real time (PCR RT);

- genotyping technique based on DNA-STRIP technology (HAIN TEST).

The use of molecular genetic methods in the examination of a patient with tuberculosis makes it possible to confirm the diagnosis of tuberculosis in the early stages, to select adequate therapy for each patient, to avoid the development of drug-resistant tuberculosis, to achieve a shortening of the treatment time and complete recovery of the patient with tuberculosis.

The speed of obtaining the results of the study (3-4 days) and the high accuracy of the data obtained made it possible to recommend the inclusion of molecular genetic methods in the scheme for examining a patient with tuberculosis at all stages of his observation in an anti-tuberculosis dispensary - order of the Ministry of Health of the Russian Federation No. 109 dated March 21, 2003 events in the Russian Federation", Order of the Ministry of Health of the Russian Federation No. 932n dated November 15, 2012 "On Approval of the Procedure for Providing Medical Care to Patients with Tuberculosis".

In 2019, the Republican Tuberculosis Dispensary conducted 1920 molecular genetic studies to determine the type of pathogen, of which 30% were positive and 1119 drug sensitivity determinations of MBT to the main anti-tuberculosis drugs, which made it possible to identify drug resistance and adjust treatment in 44% of the examined TB patients.

In 2019, in the Republican TB Dispensary of the Ministry of Health of Chuvashia, in 75.0% of newly diagnosed TB patients, the use of high-tech methods for isolating the causative agent of tuberculosis and determining MBT drug resistance made it possible to confirm the diagnosis of tuberculosis.

Quality-assured bacteriological examination is an essential element for diagnosis and management of patients infected with susceptible or resistant TB bacteria. Phenotypic DST remains the mainstay for the detection of drug resistance in *M. tuberculosis* and is based on detection of bacterial growth in the presence of antibiotics. Traditional solid-media culture techniques are reliable and cheap but

slow, with an overall turnaround time of 6–12 weeks when a patient specimen is taken. Automated liquid-media systems are faster (average turnaround time of 14–21 days), and are recommended for use even in low- and middle-income countries. Whatever the test used, results from the Supranational Reference Laboratory Network have clearly shown that, while DST for rifampicin, isoniazid, fluoroquinolones and second-line injectables is reliable in solid- and liquid-media systems, there is more controversy around the standardisation of DST for other drugs (ethambutol, pyrazinamide and other SLDs). The WHO policy of testing for SLD susceptibilities suggests testing MDR-TB isolates for sensitivity to amikacin, kanamycin, capreomycin and newer fluoroquinolones (moxifloxacin at two concentrations or ofloxacin/levofloxacin plus high concentration of moxifloxacin). For fluoroquinolones, testing of the drug in use in the country is recommended.

Recently, with the insights from mycobacterial genomics, molecular techniques to detect antibiotic resistance have been established. They offer advantages like turnaround times of hours and the possibility of omitting microbiological culture. A prerequisite is the knowledge of specific genetic mutations that are undoubtedly associated with resistance.

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