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The potential of the IGRA (Interferon Gamma Release Assay) test for the diagnosis of ocular tuberculosis. Review and comparative analysis with the tuberculosis skin test

Potencial do teste IGRA (Interferon Gama Release Assay) para o diagnóstico de tuberculose ocular. Revisão e análise comparativa com o teste tuberculínico cutâneo (PPD)

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Abstract

Precise detection of latent tuberculosis infection is becoming increasingly important due to increased use of immunosuppressive drugs and the human immunodeficiency virus epidemic , which increased the risk of reactivation to active tuberculosis (TB).The QuantiFERON® TB Gold IGRA Test has advantages over the skin test for TB, otherwise known as a Mantoux tuberculin test, for example, requires only a blood sample collection; there is no need for the patient to return to the laboratory for reading and interpretation of the results; The results are objective, do not require interpretation of the reader or interference of subjective criteria; it is an in vitro test, so there is no "booster effect" (potentiation of the tuberculin reaction); the test is not affected by prior BCG vaccination or infection with other species of mycobacteria. Limitations are described, although rare, as cross-reactions of this method with infections by some species of non-tuberculosis mycobacteria (including Mycobacterium kansasii, Mycobacterium szulgai and Mycobacterium marinum). There is still little data on the IGRA test in certain populations, such as in children, immunocompromised patients and pregnant women. In these groups, the interpretation of the test can be difficult and more studies are needed.

Keywords: *IGRA; Quantiferon; PPD; Mantoux; Intradermal test; Tuberculosis; Uveitis*

Resumo

A detecção precisa da infecção latente por tuberculose está se tornando cada vez mais importante devido ao aumento do uso de medicamentos imunossupressores e da epidemia do vírus da imunodeficiência humana, o que aumentou o risco de reativação à tuberculose ativa (TB). O Teste IGRA QuantiFERON® TB Gold apresenta vantagens frente ao teste de PPD como por exemplo, requer somente uma coleta de amostra sanguínea ; não há necessidade que o paciente retorne ao laboratório para leitura e interpretação dos resultados; Os resultados são objetivos, não requerem interpretação do leitor ou interferência de critérios subjetivos; trata-se de um teste in vitro, portanto não há "efeito booster" (potenciação da reação tuberculínica); o teste não é afetado por vacinação prévia por BCG ou infecção por outras espécies de micobactérias. Limitações são descritas, apesar de raras, como reações cruzadas deste método com infecções por algumas espécies de micobactérias não-tuberculosis (incluindo Mycobacterium kansasii, Mycobacterium szulgai e Mycobacterium marinum). Ainda há poucos dados sobre o teste IGRA em certas populações, como por exemplo, em crianças, pacientes imunocomprometidos e mulheres grávidas. Nestes grupos, a interpretação do teste pode ser difícil e mais estudos se fazem necessários.

Descritores: IGRA, Quantiferon; PPD; Mantoux; Teste intradérmico; Tuberculose; Uveites.

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Introduction

According to World Health Organization estimates, one-third of the world's population is currently infected with microorganisms of the Mycobacterium tuberculosis complex, while most infections remain latent in the immune system of their hosts and may progress to the active form and contagious disease. The identification of individuals with latent tuberculosis is mandatory in strategies to eliminate tuberculosis, since the development of the disease can be prevented by preventing its transmission.[1,2]

In addition, the use of TNFα inhibitors in the treatment of chronic inflammatory diseases such as rheumatoid arthritis, ankylosing spondylitis or Crohn's disease has increased in the last decades. Patients using anti-TNFα antibodies are at increased risk of developing infections, particularly the spread of extrapulmonary tuberculosis caused by the reactivation of latent Mycobacterium tuberculosis infection. For this reason, screening for latent tuberculosis prior to the initiation of TNFα inhibitor becomes essential, although it is known to be problematic, especially in the presence of immunosuppressive therapy, since neither the imaging techniques nor the cutaneous tuberculin tests demonstrate sufficient accuracy.

Latent tuberculosis was traditionally diagnosed in a conventional way, by the tuberculin skin test - also known as "PPD" or "Mantoux". The PPD test is based on cellular intradermal immune response to the cellular antigens of mycobacteria, making it non-specific for pathogenic microorganisms of the M. tuberculosis complex and leading to false positive results in cases of exposure to environmental mycobacteria and vaccination by Bacillus Calmette-Guérin (BCG).[1-3]

The intradermal test is one of the oldest diagnostic methods in use to date, and has been introduced routinely since 1910. Although it has been used routinely for over a century, there are some important limitations associated with this method, such as the need for personnel trained to administer it, subjectivity of interpretation and reading of results, and the booster effect when initial administration of PPD may promote subsequent reactions to the test. One of the major limitations of the tuberculin test is the low specificity, especially in individuals vaccinated by BCG, or in those infected with certain species of non-tuberculosis mycobacteria. The test may also show low sensitivity, especially in immunocompromised individuals. Another important limitation to be mentioned is the patient's need to return to the laboratory 48 to 72 hours after the application to read the results, which is not always achieved and increases the risk of patients with latent tuberculosis of not being identified in the population.[1-4]

The discovery of the mycobacterial proteins ESAT-6, CFP-10 and TB 7.7 - all expressed specifically by pathogenic strains of the M. tuberculosis complex - leveraged the development of more specific diagnostic tests for latent tuberculosis (TBL), that is, people with tuberculosis positive test (more commonly with positive tuberculin test) but no evidence of active infection. IGRA (Interferon Gamma Release Assay) tests - interferon gamma detection assays in blood samples - have been developed, and have proven to be excellent tools for the aid of latent tuberculosis. The test principle is the measurement of the in vitro levels of interferon gamma produced by T cells that have been stimulated by purified or synthesized TB antigens.[3,4]

In the United States, there are the Centers for Disease Control and Prevention (CDC), and they publish updated guidelines for the use of gamma interferon release assays to detect Mycobacterium tuberculosis infection. In these guidelines they caution that although sensitivity and specificity are inherent characteristics of the tests with no "gold standard", estimates of test performance may occur as a result of the differences in study population and error classification rate of diagnosis (for example, as a result of differences in the prevalence of M. tuberculosis and infection by non-tuberculous mycobacteria, malnutrition and immunosuppression). In addition, since PPD and IGRA are indirect tests measuring the immune responses and not direct tests to detect the causative organism or components of the organism, sensitivity assessments among people with active tuberculosis with culture may not provide reliable estimates of sensitivity to the latent stage. Immunological differences that allow the progression of the infection to the disease may affect the results of the immunological test (Table 1). In addition, treatment may alter the immune responses and may alter test results. Estimates of specificity among low-risk populations may underestimate specificity because some people may have infection resulting from unrecognized exposure.[1-7]

Technique used for the IGRA test

The Interferon Gamma Release Assay (IGRA) has two internationally traded techniques: QuantiFERON-TB Gold In-Tube (QTF) and T-SPOT. Both are approved by the FDA (US Food and Drug Administration), Health Canada and EC (European Committee), but only QTF is registered in Brazil.

Blood is collected directly into three separate tubes: the negative control tube containing only heparin, the positive control tube containing phytohemagglutinin as mitogen, and a third tube containing specific peptides for M. tuberculosis ESAT-6, CFP-10 and TB7.7. The tubes are incubated at 37°C for 18 hours and centrifuged to obtain plasma samples which are stored at -20°C until ELISA is performed.

Therefore, QFT is a test of cell-mediated immune responses (CMI) to antigenic peptides that mimic mycobacterial proteins. These proteins ESAT-6, CFP-10, and TB7.7 are absent in all BCG strains and in most non-tuberculous mycobacteria, with the exception of M. kansasii, M. szulgai, and M. marinum. Typically, individuals infected with organisms of the M. tuberculosis complex have lymphocytes in the blood to recognize these and other mycobacterial antigens. This recognition process involves the production and secretion of cytosine IFN-γ. Detection by immunoenzymatic assay (ELISA) of IFN- is used to identify in vitro cellular immune responses associated with M. tuberculosis infection.

An individual is considered to be infected with M. tuberculosis when the concentration of IFN- measured in IU/mL is higher than the cutoff of the test.[7]

IGRA and BCG Vaccination

As the QTF-G response is based on the release of IFN-č by T lymphocytes previously sensitized with M. tuberculosis after exposure to two proteins present on the bacterial cell wall: ESAT-6 and CFP-10, since these antigens are absent in the BCG and most of the mycobacteria present in the environment, prior exposure to these bacteria and BCG immunization do not induce a positive test result.[8,9]

Table 1
Benefits of IGRA compared to PPD

	IGRA	IGRA	PPD	PPD
Only day for the exam?	Yes	Patient needs to attend only once for the exam (It is not necessary for the patient to return to the laboratory for reading and interpretation of the result)	No	Patient needs to attend twice for the exam (the patient must return to the laboratory fo reading and interpretation to the result)
High sensitivity?	Yes	95% sensitivity - accurately identifies patients infected with TB	No	70% sensitivity – more unidentified diagnoses
High specificity?	Yes	98% specificity - less unnecessary follow-up and treatment	No	Variable; 59% in populations vaccinated with BCG - false positives result in unnecessary and costly follow-up
Objective results?	Yes	Objective and controlled laboratory test (they do not require interpretation of the reader nor interference of subjective criteria)	No	Subjective measurement of skin induration (require interpretation from the reader or may be subject to subjective criteria)
Effective in patients vaccinated with BCG?	Yes	Not affected by BCG vaccination	No	Results affected by BCG vaccination
Risk of Booster Effect?	No	There is no risk in the methodology	Yes	Booster Effect:When many years have passed since a person has been infected with tuberculosis,, heir initial skin test may be negative due to decreased immunity. Subsequent tests may be positive, however, the initial placement of tuberculin stimulates the immune response to the test. This phenomenon is referred to as the "booster effect" or reinforcement. The Booster effect may be misinterpreted as a new skin test conversion (i.e., a recent TB infection).

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Meta-analysis studies have concluded that the diagnostic specificity of IGRAs for TBL is greater than 95%, whereas specificity is not affected by BCG vaccination. The PPD has a specificity of 97% in populations not vaccinated by BCG, whereas in populations where BCG is administered the specificity is much lower (around 60%) and variable, depending on the age group vaccinated and the number of doses administered of BCG, and the sensitivity of IGRA is reduced in individuals with HIV infection and children.

Because QFT is not affected by BCG, it is an extremely useful test for the evaluation of TBL in BCG-vaccinated individuals, particularly in countries where BCG is given during chidhood or multiple times.[8,9]

Factors influencing the IGRA result

Although IGRA seems not to be affected by most non-tuberculous mycobacterial (NTM) infections that may cause mycobacteria to be false positive, M. marinum or M. kansasii express ESAT-6 or CFP-10 and can therefore produce cross reaction.[10]

Like any other diagnostic tests, IGRA is susceptible to variability by numerous factors at multiple levels, including assay manufacture, preanalytical processing, analytical factors, and immunomodulation.

On the other hand, several risk factors were associated with negative results of IGRA, including immunodeficiency, young or advanced age, tuberculin test negative (TST), extrapulmonary tuberculosis, disseminated tuberculosis, concomitant tuberculosis and smoking. However, these studies were limited by an observational design implemented in single centers, and most of them did not include a large number of patients with culture-confirmed tuberculosis.[10-11]

An international, multicenter, retrospective and cross-sectional study was carried out by the European Tuberculosis Network Testing Group (TBNET - www.tb-net.org) to identify risk factors associated with IGRA false-negative results in patients with active tuberculosis.

Clinical data and laboratory results of patients enrolled at 25 participating centers with a confirmed diagnosis of active tuberculosis (i.e., positive culture of M. tuberculosis and/or positive M. tuberculosis specific nucleic acid amplification assay) and who had a routine IGRA investigation by the T-Test SPOT. TB or the QFT-GIT were analyzed. Data was collected from 771 patients (221 patients with tuberculosis had negative IGRA).

There is evidence that IGRA false-negative results can be observed more frequently in young children. However, since there were no children <5 years old enrolled in the present study, they could not address this possible relationship.

In contrast to previous investigations, immunodeficiency, concomitant treatment of tuberculosis, disseminated tuberculosis, extrapulmonary tuberculosis, and smoking could not be identified as risk factors for false negative results from the IGRA test.

In addition to the association with old age, it is still not clear why some individuals with active tuberculosis have specific adaptive immune responses non-specific to M. tuberculosis at the time of tuberculosis diagnosis. Results from previous studies have suggested different etiologies for false-negative IGRA test results that were not evaluated in this study.[10-11]

Moreno et al. analyzed 520 patients with this goal. The factors associated with the indeterminate results of Quantiferon Gold-Test in-Tube (QFT-G-IT) in a univariate analysis were inflammatory bowel disease, disease activity, lymphopenia, and medium to high doses of corticosteroids. In a subsequent multivariate analysis, only lymphopenia (defined as <1500 cells) was associated with indeterminate QFT-G-IT results. Lymphocyte count was the only factor independently associated with an increase in the number of indeterminate QFT-G-IT results in patients with different autoimmune diseases. They also concluded that the use of medium and high doses of corticosteroids should be considered before the QFT-G-IT test.[12]

Latorre et al. evaluated the impact of immunosuppressants and immune-mediated inflammatory diseases (IMID) on Gold In-Tube QuantiFERON-TB (QFN-G-IT) and T-SPOT.

In the present study, patients with IDIM who required screening for latent tuberculosis infection (TBL) were included and classified in: (i) 50 patients with inflammatory rheumatic diseases, (ii) 50 patients with psoriasis, and (iii) 30 patients with Crohn's disease. A total of 44 healthy individuals without immunosuppression were also included as controls. Tuberculin skin tests (PPD), T-SPOT.TB and QFN-G-IT were carried out.

The authors observed that immunosuppressants intale was more frequent in patients with Crohn's disease and psoriasis.

Positive results of IGRAs and PPDs were reduced in patients with Crohn's disease, while the rate of undetermined T-SPOT.TB results was increased in this group compared to the other IMIDs analyzed and controls. When the response to IFN-č was studied, cytosine levels after mitogenic stimulation were significantly lower in Crohn's and inflammatory rheumatic diseases than in psoriasis. Interestingly, patients with psoriasis were the only ones who did not receive corticosteroids. In addition, a negative correlation was observed between the secreted IFN-č after mitogenic stimulation and corticosteroid dose.

The authors concluded that the clinical accuracy of IGRA for the diagnosis of TBL seems to be differentially affected by the IMID type. In particular, Crohn's disease and/or its concomitant immunosuppressive profile may negatively affect the accuracy of T SPOT.TB and QFN-G-IT when compared to psoriasis or inflammatory rheumatic diseases. Therefore, it is important to be prudent in diagnosing TBL in this type of patient due to the high frequency of indeterminate results and an attenuated IFN-č response[13]

Shahrad Hakimian et al conducted a retrospective observational study in 107 patients with inflammatory bowel disease (IBD) and 89 with rheumatoid arthritis (RA) who were screened for latent TB ILTB infection using QuantiFERON-TB Gold In-Tube (QFT-GIT) prior to the onset of anti-TNF drugs.

The authors observed a higher proportion of patients with IBD with undetermined QFT-GIT result compared to patients with RA.

Besides, they found that the minority of patients with undetermined results was tested during an acute outbreak of IBD (88%) and during administration of corticosteroids. Of all patients receiving ≥ 20 mg of prednisone equivalent dose (n = 32), 63% resulted in undetermined QFT-GIT compared to only 6% undetermined tests in patients receiving <20 mg of prednisone equivalent dose (n = 164, P <0.001). There was no correlation between undetermined results and age, gender, duration or distribution of the disease or smoking status in each population.

They concluded that high doses of corticosteroids may affect the QFT-GIT results leading to a high proportion of undetermined results, and proposed that patients with IBD should be tested before starting corticosteroids to avoid ambiguous results and prevent possible delays in the onset of anti-TNF drugs.[14])

Bélard et al. evaluated the performance of QuantiFERON Gold In-Tube (QFT-IT) and Tuberculin Skin Test (TST) prior to the onset of anti-TNF therapy in 248 patients with ulcerative colitis (39), Crohn's disease (54), rheumatoid arthritis (111) and spondyloarthropathy (44). Treatment with prednisolone was strongly associated with negative PPD, and with an increased risk of undetermined QFT-IT results, whereas no negative effects were found for long-acting corticosteroids. Doses of ≥ 10 mg prednisolone were associated with a 27% risk of undetermined outcomes. The single use of azathioprine, methotrexate or 5-aminosalicylate (5-ASA) did not affect the test results.[15]

Limited data are available regarding the use of QFT-GIT to test for immunocompromised persons. In two studies with a total of 34 HIV-infected individuals with culture-active tuberculosis, QFT-GIT sensitivities were 81% and 88%. (16) In another study, QFT-GIT and TST sensitivities were similar (81% and 85%, respectively; p <0.99).[17] Sensitivity of QFT-GIT was not significantly different among people with HIV infection from among those without the infection (81% and 73%, respectivaly; p = 0.59). In another study in Zambia involving 112 people (59 were infected with HIV, 37 were not infected by HIV, and 16 were not tested) in which active tuberculosis was diagnosed based on sputum smear microscopy, QFT-GIT and TST were significantly less sensitive in people infected with HIV than in people not infected with HIV (76% compared to 97% for QFT-GIT, p = 0.02, and 55% compared to 81% for TST, p = 0.04). Among people with HIV infection, the sensitivity of QFT-GIT tended to be higher than the sensitivity of TST (76% and 55%, respectively, p = 0.06). However, in this study, reduced sensitivity to TT may have resulted from late reading of TTs, which was read 48-164 hours after PPD injection. Low CD4 counts were associated with increases in the results of false negative TSTs and undetermined and false negative QFT-GIT results.[18]

An interesting option was suggested by the Guidelines for Using Interferon Gamma Release Assays (CDC), which was the incorporation of a boundary category for the test, increasing accuracy by classifying results close to the cutoff point (in which minor variations may affect interpretation) as positive or negative. Another tactic to improve detection sensitivity is to use any positive result from various tests, as it is done with culture or nucleic acid amplification tests. Interpreting any positive results from multiple tests as evidence of infection typically increases detection sensitivity and decreases specificity. On the other hand, requiring positive results from two or more tests typically has the opposite effect, i.e., decreasing sensitivity and increasing specificity.[7]

Igra in the pediatric population

There is little performance data for QFT-GIT and T-Spot tests in children (especially for those <5 years). Because rates of progression from latent infection to active disease (including severe forms of disease such as meningitis, disseminated disease, or death as a result of M. tuberculosis) are higher in infants and young children, caution is warranted when IGRA is used in children <5 years old.[19]

The higher rate of active tuberculosis and severe forms of the disease in infants and children aged <5 years compared to older children suggests that the immune response to M. tuberculosis infection differs in these groups.[20] Age-related immunological differences may explain the reported variations in IGRA test performance, including lower test sensitivity and lower IFN-γ production in response to mycobacterial and mitogen antigens (used as a positive control), among children <4 years of age with children aged 4 to 15 years, [20] increased mitogen response with increasing age,[21] and a higher proportion of indeterminate QFT-GIT results in children <5 years.[43] In contrast, a large study in an endemic scenario of tuberculosis found that infants and young children had robust IFN-γ responses to M. tuberculosis antigens, and that their responses were comparable to responses in adults and older children.

The use of IGRAs in children is subject to several limitations, especially since studies evaluating the performance of IGRA in children are scarce. In only a few studies separate results are provided for children, and even fewer studies divide the results by limited age categories.

Vallada et al. evaluated 195 children previously vaccinated with BCG, 184 healthy, without clinical or epidemiological evidence of M. tuberculosis infection, and 11 with infection, defined according to clinical, radiological and laboratory criteria. In the group of 184 uninfected children, 177 (96.2%) had a negative test result, six (3.2%) had an indeterminate result, and one (0.5%) had a positive result. In the group of 11 children with infection, two (18%) presented negative results.

The authors therefore observed a high negative predictive value of the test, a useful parameter for the exclusion of tuberculosis in clinical practice, thus reducing the prescription of unnecessary chemotherapy in children, and the surprisingly low percentage of undetermined results (3.2%). They concluded, however, that with the sensitivity of 81.8%, despite meeting the WHO criteria of at least 80%, QTF-G is not recommended as the only laboratory parameter to define tuberculosis in children.(23)

Gabriele et al. evaluated the performance of interferon (IFN)-γ Quantiferon®-TB Gold In-Tube for the detection of latent tuberculosis infection (TBL) in 79 children receiving antirheumatic treatment at a tertiary reference hospital in Norte Grécia. They concluded that Quantiferon may be a more reliable test than PPD for detecting TBL in children with rheumatic diseases receiving antirheumatic treatment. The pharmacological regimen may influence mitogen-induced secretion of IFN-γ, and the effect of TNF-α inhibitors may vary according to the specific agent administered.[24]

Many authors consider PPD to be preferred for testing children <5 years of age. The use of an IGRA along with PPD has been advocated by some specialists to increase diagnostic sensitivity in this age group. Recommendations on the use of IGRAs in children have also been published by the American Academy of Pediatrics.[25]

Lessons about the Igra test in patients with uveitis

La Distia Nora et al. evaluated the clinical manifestations of 77 patients with uveitis and scleritis of unknown origin and QuantiFERON Gold In-Tube positive test (quantiferon) in a non-endemic country for tuberculosis.

The ocular characteristics of patients with idiopathic uveitis and quantiferon positive were diverse, but retinal occlusive vasculitis and choroiditis serpiginosa were common. Quantiferon levels were generally very high, and 33% of patients exhibited lymphadenopathy, often suggesting the diagnosis of sarcoidosis.[26]

This finding regarding the possibility of sarcoidosis drew much attention. One-third of our patients exhibited mediastinal / hilar adenopathy, of which the majority of adenopathy was consistent with the diagnosis of sarcoidosis. The histological characteristics as well as the negative staining, culture and PCR results for M tuberculosis in 9 of 12 lymph node biopsies were considered consistent with the diagnosis of sarcoidosis. It was suggested by the authors that these diagnostic tests may not be sensitive enough to reveal mycobacteria nor it could be attributed to a sampling error, since the presence of mycobacteria in the lymph node tissue may be scarce. In contrast, these findings could also indicate that a specific type of sarcoid reaction could occur triggered by TB infection. These findings emphasized the possible relation between M. tuberculosis infection and the development of enlarged hilar and/or mediastinal lymph nodes, consistent with the diagnosis of sarcoidosis. The association between tuberculosis and sarcoidosis has been repeatedly reported, and several studies have suggested that mycobacterial antigens may represent the inciting agent in a proportion of patients with sarcoidosis. The results of Quantiferon also seem to be reliable in patients with sarcoidosis, in contrast to their anergy to the tuberculin skin test.

Ocular inflammation reacted favorably to antituberculosis therapy, although only a small minority had documented previous tuberculosis.

Despite extensive investigation including IGRA, the diagnosis of intraocular tuberculosis (TB) is still challenging, and remains predominantly presumptive. According to the literature, it seems that the management of suspected ocular TB differs significantly based on whether patients come from areas of high prevalence of TB or from non-endemic countries for TB. The accuracy and final contribution of chest X-rays, tuberculin test and IGRA differ significantly according to areas of low or high endemic TB. Different guidelines should be established for the management of patients suspected of having ocular TB, first taking into account the relative prevalence of TB.[27]

The reported specificity of QFT for pulmonary and latent tuberculosis varies from 91% to 99%, but the reported sensitivity is somewhat lower (89% - 91%). As such, separating the true positives from the false positives and deciding when to start anti-TB treatment still requires a case-by-case analysis in patients with uveitis. A negative test effectively excludes tuberculosis, but a substantial number of positive tests are false-positive. The reasons for false-positive results may include cross-reactivity with pulmonary and ocular infection by Mycobacterium kansasii, or exposure to a limited number of other non-tuberculous mycobacteria. False positives have also been reported in connection with a non-specific defect in the test vial. In the case where the high suspicion of a false positive result develops, an option open to the clinician is to repeat the test. The untreated negative test was reported in patients with uveitis and a positive QFT result, and disease characteristics not suggestive of true mycobacterial infection.

Babu et al. showed the results for QuantiFERON TB Gold (QFT-G) in 82 patients with presumed ocular tuberculosis, and the effect of antitubercular therapy on the QFT-G result. They observed that there were no statistically significant differences in QFT-G results with age, gender, history of oral steroids, or type of uveitis. There was a statistically significant association between positive QFT-G and choroiditis serpiginous. Most patients had QFT positive, even after completion of therapy, but with a significant drop in the average values after treatment. The authors concluded that there was a significant association between positive QFT with choroiditis serpiginous and persistent positivity even after termination of therapy in most cases. However, the average values of QFT-G decreased after treatment.[30]

A curious finding also noted in another study was that ophthalmologists and rheumatologists use this Quantiferon TB Gold test more often than pulmonologists.

This is probably due to the fact that ophthalmologists and rheumatologists see more of latent tuberculosis in their practice, and depend on indirect evidence such as the Mantoux test and the Quantiferon TB Gold test for a diagnosis, whereas pulmonologists see active TB more frequently, and depend on direct evidence such as biopsy or culture for a diagnosis of TB, and therefore rarely use the Mantoux and Quantiferon TB Gold Test in their practices.[31]

Conclusion

Precise detection of latent tuberculosis infection is becoming increasingly important due to increased use of immunosuppressive drugs and human immunodeficiency epidemic, which increased the risk of reactivation to active tuberculosis (TB).

The IGRA QuantiFERON® TB Gold Test has advantages over the PPD test, for example, it requires a simple blood sample collection; there is no need for the patient to return to the laboratory for reading and interpretation of the results; the results are objective, do not require interpretation of the reader or interference of subjective criteria; it is an in vitro test, therefore there is no "booster effect" (potentiation of the tuberculin reaction); the test is not affected by prior vaccination by BCG or infection by other species of mycobacteria.

Although rare, some limitations are described, such as cross-reactions of this method with infections by some species of non-tuberculosis mycobacteria (including Mycobacterium kansasii, Mycobacterium szulgai and Mycobacterium marinum).

There is still little data on the IGRA test in certain populations, such as in children, immunocompromised patients, and pregnant women. In these groups, the interpretation of the test can be difficult, and more studies are needed.

Therefore, the IGRA test is more effective in detecting TB infection than PPD. Despite the higher cost, it has added value, and can be requested in addition to the PPD.

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