
# PROSPECTIVE EVALUATION OF LATENT TUBERCULOSIS WITH INTERFERON-GAMMA RELEASE ASSAYS IN DRUG AND ALCOHOL ABUSERS



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# PROSPECTIVE EVALUATION OF LATENT TUBERCULOSIS WITH INTERFERON-GAMMA RELEASE ASSAYS IN DRUG AND ALCOHOL ABUSERS

**Running title:** Interferon-γ tests for diagnosis of latent TB

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**SUMMARY**

*In vitro* tests have been developed for the diagnosis of TB infection. The objective was to analyze latent TB infection in drug and alcohol abusers through two interferon-γ techniques. One hundred thirty nine patients were admitted between February 2006 and May 2007. Mean age was 39.8 years, HIV(+) 31%. The EIA and ELISPOT interferon-γ assays were positive in 34% of patients with a concordance of 83% (*kappa* 0.63). TST was positive in 29% of patients and the concordance of TST with EIA and ELISPOT interferon-γ assays was 85% (*k* 0.62) and 83% (*k* 0.57) respectively. Near 50% of patients with history of TB had a positive *in vitro* test. In conclusion, we observed a high prevalence of latent TB and good concordance between the new *in vitro* tests that otherwise may continue to be positive long after developing TB disease.

## INTRODUCTION

The rate of tuberculosis (TB) in Spain is amongst the highest of industrialised countries [1-3]. It is well known that drug addicts have a higher risk of TB and that alcoholism and intravenous drug use (IDU) are amongst the main factors associated with TB [4-6]. Moreover, IDU has been the main category of Human Immunodeficiency Virus (HIV) transmission in Spain [7], and the elevated incidence of TB in patients infected with HIV is also known, which raises the risk of developing tuberculosis up to 100 times [2,8,9].

The diagnosis and treatment of latent infection is very important in the control of TB. For more than 100 years the tuberculin skin test (TST) or Mantoux test has been the only method used in its detection [10]. The TST uses a protein purified derivate (PPD) that is a mixture of antigens, many of which are shared with *Mycobacterium tuberculosis*, *Mycobacterium bovis*, Bacille Calmette-Guérin (BCG), and other non-tuberculosis mycobacteria; the limitations of TST are well known: low specificity in individuals vaccinated with BCG or in those exposed to other mycobacteria; sensitivity may be lessened in immunocompromised patients. On the other hand a booster effect may be produced by the repeated use of TST and errors in the reading and interpretation of the results may occur. Another inconvenience is the need for a second visit for reading the results [11-12].

Immunodiagnostic methods for detecting TB infection are based on the *in vitro* quantification of the cellular immune response in response to specific *M tuberculosis* antigens [13-14].

In the first generation of *in vitro* test the same antigen was used as in the TST, which caused some limitations [13]. The new versions use antigens more specific to *M*

*tuberculosis* such as Early Secretory Antigen Target-6 (ESAT-6) Culture Filtrate Protein-10 (CFP-10) and TB7.7 antigen; the genes which encode ESAT-6 and CFP-10 are found in a segment named the Region of Difference 1 (RD 1) of the *M tuberculosis* genome and TB7.7 is encoded in RD11 which are not present in the genome of *M bovis*, BCG or other non-tuberculosis mycobacteria such as *M avium* [14]. Other mycobacteria that have shown to induce T-cell responses to ESAT-6 and CFP-10 are *M marinum* and *M kansasii* [15].

There are two tests marketed for the *in vitro* diagnosis of TB based on *M tuberculosis*-specific antigens: QuantiFERON TB Gold In-Tube (Cellestis Ltd, Carnegie, Australia) which uses enzyme-immunoassay (EIA) techniques to measure the production of interferon-γ by the T-cells in whole blood in response to ESAT-6,CFP-10 and TB7.7 and T-SPOT-TB test (Oxford Immunotec Ltd, Oxford, United Kingdom) that uses the enzyme-immunospot (ELISPOT) technique to determine the T-cells that produce interferon-γ in response to the *M tuberculosis*-specific antigens ESAT-6 and CFP-10 [12]. The usefulness of the tests in identifying latent infection by *MT* has been established [16,17]; however, there exists little information in some populations such as immunocompromised patients and drug users.

The objective of this study is to analyze TB infection rates in patients at high risk of infection using 2 interferon-γ techniques based on TB-specific antigens.

## MATERIAL AND METHODS:

### Study population

Patients admitted to a detoxification unit in a tertiary hospital between February 2006 and May 2007 was included in the study. The patients came from different outpatient centres for the treatment of alcohol and drug abuse in metropolitan Barcelona. All subjects gave their consent to participation in the study.

### Methods

Socio-demographic characteristics, as well as information on the history of alcohol and drug abuse were collected from all patients. For medical history patients were asked about previous TB disease or TB infection. Upon admission blood samples were taken for HIV serology (EIA and WB), RNA-HIV, CD4 lymphocytes and interferon-γ tests.

TST was carried out by means of intradermal administration of 2U of PPD-RT23 in the forearm, except where the subject had a history of culture proven previous TB disease or previous positive TST; the reading of TST was performed 48 hours later and was considered positive if the induration was ≥ 5 mm in HIV positive subjects and ≥ 10 mm in HIV negative subjects. During admission active TB was ruled out in all cases by means of a chest x-ray and 3 sputum samples which were analysed using the Ziehl-Neelsen stain and Lowenstein-Jensen culture. If subjects presented with fever and/or constitutional symptoms, extrapulmonary localisation of TB was also excluded.

The participants were assessed for TB infection with two interferon-γ techniques based on *M tuberculosis*-specific antigens, (EIA) QuantiFERON-TB Gold In-Tube (Cellestis Limited, Carnegie, Victoria, Australia) and ELISPOT (T-SPOT.TB) (Oxford Immunotec, Abingdon, UK).

QuantiFERON-TB Gold In-Tube

Three mL. of blood were distributed in 3 test tubes with anticoagulant, one of which was contained ESAT-6, CFP-10 and TB7.7 specific antigens, another with saline solution (negative control) and the third with phytohemagglutinin (positive control). These were left to incubate at 37º C overnight. After incubation the plasma was separated by centrifugation and was kept frozen (-20º) until used.

The production of interferon-γ, expressed in IU/ml, was determined by ELISA (Enzyme-Linked ImmunoSorbent Assay) and analysis software from QuantiFERON was used to obtain the results. The value obtained was deduced in the negative control from the values obtained in the test tubes stimulated with mitogen and with the specific TB antigens. Values above 0.35 IU/ml were considered positive in the sample stimulated with TB antigens. The result of the test was considered indeterminate if the production of interferon-γ after stimulation with phytohemagglutinin was below 0.5 IU/mL as well as if the sample stimulated with TB antigen was also below 0.35 IU/mL.

T-SPOT. TB

The mononuclear cells were separated by density gradient centrifugation from a sample of 8 ml of peripheral venous blood, and after cell washing and counting were distributed in wells with ESAT6 and CFP10 specific antigens as well as phytohemagglutinin as positive control and cells only as negative control ($2.5x10^5$ cells per well) on a plate covered with anti-interferon-γ antibodies which were left to incubate overnight. After

washing the plate a conjugate was added against the antibodies used as well as an enzyme substrate.

The number of spots was determined with an automatic reader (AID ELISPOT, AIDSystem, Strassberg, Germany) as well as with visual assistance. The result was considered positive if the number of spots in any well with antigen was equal to or greater than 6 after subtracting the number of spots from the negative control.

Negative results with ESAT 6 and CFP10 antigens and phytohemagglutinin were considered indeterminate.

Statistical analysis

The descriptive statistics were expressed as mean ± standard deviation for the quantitative variables and absolute frequencies and percentages for the qualitative variables.

The comparisons were made by means of the Chi-square test and the Student's t-test.

Kappa statistics were used to evaluate the concordance between the diagnostic tests. Values from $p < 0.05$ were considered statistically significant. The data analyses were performed with SPSS 11.5 (SPSS, Chicago, IL, USA).

## RESULTS

One hundred and thirty nine patients were admitted to detoxification between February 2006 and May 2007; the results of the IGRAs were not valid in 4 cases. The mean age of the 135 patients analysed was 39.8 years (± 8.0 SD) and 83.7% were males. The main drug abused was alcohol for 59 patients (45%), cocaine for 46 (35.1%) and opiates for 26 (19.9%). Sixty-one patients (45.2%) were current IDU; 42 patients (31.1%) tested positive for HIV infection upon admission; the characteristics of the patients with and without HIV infection are shown in Table 1. In HIV positive patients the RNA-HIV was ≥ 400 cp/ml in 38.1% of cases; 18 patients (42.9%) were undergoing antiretroviral treatment.

In terms of history of TB, 13 patients (9.6%) had had TB disease before admission and 20 (14.8%) had history of positive TST before admission. TST was performed on 100 patients and was positive in 29 patients globally (29%). Chest x-rays were performed in 113 patients and was normal in 96 (85%); 8 patients (7.1%) presented with residual lesions and 9 (7.9%) with findings attributable to chronic obstructive pulmonary disease.

Fifty-seven (42.2%) patients tested positive in at least one of the interferon-γ tests. With EIA, 46 patients (34.1%) tested positive, two were indeterminate (1.5%), and one was positive with ELISPOT and the other negative. ELISPOT was positive in 46 patients (34.1%) and indeterminate in one case, which was positive with EIA. The concordance between EIA and ELISPOT was 83%, (*kappa* 0.63, CI 95% 0.50-0.76).

Prevalences of interferon-γ tests and TST in HIV-negative patients and HIV- positive patients with CD4 ≥ 350 cells and <350 cells are shown in Table 2; there were no statistically significant associations between HIV serostatus and *in vitro* or *in vivo* tests.

Amongst the 100 patients given the TST test upon admission, the concordance between TST and EIA was 85% (*kappa* 0.62, CI 95% 0.45-0.80) and was 83% between TST and ELISPOT (*kappa* 0.57, CI 95% 0.39-0.75). Figure 1 shows the frequency distribution of the results from the 2 *in vitro* tests according to TST. Amongst the 29 patients who tested positive with TST, 20.7% (6 cases) had negative results with IGRAs. Of the 71 patients who tested negative with TST, 15.6% (11) tested positive with IGRAs, 4 of which were HIV positive.

Table 3 shows the results of the interferon-γ tests in those patients with a history of TB disease. With EIA, positive results were obtained in 6 of 13 patients (46.1%) and 6 cases (46.1%) were also positive with ELISPOT with a concordance of 85%. Amongst those whose IGRA tests were positive, the time between TB disease and the interferon-γ test was 8.8 years for EIA and 9.8 years for ELISPOT compared to 14.7 years and 13.8 years for those whose EIA and ELISPOT interferon-γ results were negative.

In the univariate analysis, age, sex, HIV infection, Hepatitis C virus infection, previous imprisonment, being IDU, nor the main type of drug were associated with positive results with the IGRA tests.





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## DISCUSSION

The results from this cross-sectional study show an elevated prevalence of latent TB in current alcohol and drug abusers independently of the *in vitro* method used. This fact is not surprising since the level of TB rates in Spain has been high until recent years. In drug users, studies developed with the first generation of interferon-γ techniques that used stimulation with PPD found more than double the positive results in the *in vitro* test than in the skin test [13,18]. Another study in patients receiving methadone, showed a 17% prevalence of first generation interferon-γ test [19]. Only one study in drug addicts has used new interferon-γ assays with antigens specific to TB [20]. To our knowledge this is the first study using IGRA tests in alcohol and drug abusers from Spain. The results described in a setting characterized by high prevalence of drug abuse and TB infection will permit to better estimate the burden of latent infection when using the new in vitro techniques. The observed concordance between the 2 *in vitro* techniques is good ($k$=0.63) and coincides with that which has been observed in other populations [21].

The interferon-γ techniques that used TB-specific antigens have shown an elevated specificity (98% with EIA and 92% with ELISPOT) [14,22] in low risk populations; in terms of sensitivity, the results are controversial: while some studies find better sensitivity than in patients with TB disease [21-23], in others, the sensitivity of EIA is less than that of TST for the diagnosis of TB [24]. In immunocompromised subjects, ELISPOT has been associated with higher sensitivity than TST [14,16,22,25].




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In this study the agreement between TST and EIA and the agreement between TST and ELISPOT was 85% (k=0.62) and 83% (k=0.57), respectively. The discordance between IGRAs and TST in the cases where TST was positive and IGRA negative could be ascribed to previous BCG vaccination, to environmental mycobacteria or an increased sensitivity of TST with respect to IGRAs. The cases where TST was negative and IGRAs positive suggest higher sensitivity with new in vitro tests. However, the absence of a reference test for latent TB makes the evaluation of the sensitivity and specificity difficult to determine with IGRAs

The frequency of an IGRA test with indeterminate results is lower than observed in previous studies [21,26]. It is well known that indeterminate results are associated with immunodepression [16,27] and the association between the number of CD4 cells and indeterminate results [26]. The mean of CD4 cells in HIV-positive patients in this study was above 500 cel/$\mu L$ and only 2 of the 42 HIV+ patients presented with CD4 counts below 100 cel/$\mu L$, which would explain the low (with EIA) or null (with ELISPOT) number of indeterminate results. CD4 cell counts above 500 cel/$\mu L$ in HIV-positive patients could probably also explain the fact that no significant differences were observed for EIA and ELISPOT according to HIV serostatus at admission.

The results of the interferon-γ tests were positive in more than 50% of patients previously diagnosed and treated for TB disease. The same number of positive IGRA results (6/13) was obtained with the 2 tests in the subgroup that had TB disease before admission and the concordance between them was good. The duration of an IGRA test positive after TB disease, an average of 9 years in the EIA positive cases and 10 years in the ELISPOT positive cases, is even longer than that described in other studies [26]. In this sense, it is

not well defined when interferon-γ tests turn out negative after treatment for TB; our results indicate that IGRAs test can remain positive for years after the illness which could limit its usefulness in differentiating current or past infection and should be an indication to do additional tests for active TB.

We found no associations between a positive IGRA test and HIV infection, age, sex, substance of abuse, intravenous drug use or antecedent of imprisonment. Other studies in wider populations are necessary to assess the risk factors for TB infection when using new *in vitro* tests.

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## REFERENCES

1. Euro TB and the national coordinators for tuberculosis in the WHO European Region. Surveillance of tuberculosis in Europe. Report on tuberculosis cases notified in 2005. Institut de veille sanitaire. Saint Maurice, France. March 2007. Available in :http://www.eurotb.org , Accessed January 14, 2008.

2. Díez M., *et al*. Tuberculosis in Spain: epidemiological pattern and clinical practice. *The International Journal of Tuberculosis and Lung Disease* 2002; 6:295-300 .

3. Caminero J., *et al*. Evaluation of tuberculosis trends in Spain, 1991-1999. *The International Journal of Tuberculosis and Lung Disease* 2003;7:236-242.

4. Friedman L., *et al*. Tuberculosis, AIDS and death among substance abusers on welfare in New York City. *The New England Journal of Medicine* 1996;334:828-833.

5. Altet-Gomez M.N., *et al.* Clinical and epidemiological aspects of smoking and tuberculosis: a study of 13.083 cases. *The International Journal of Tuberculosis and Lung Disease* 2005;4:430-436.

6. Moreno S., *et al*. Risk for developing tuberculosis among anergic patients infected with HIV. *Annals of Internal Medicine* 1993;119:194-198.

7. Carlos III Health Institute. National Epidemiology Center. Secretariat of the National Plan of AIDS. HIV/AIDS epidemiological surveillance in Spain . National register of AIDS cases. Updated to December 2006. Semester Report nº 2, Year 2006

8. Muga R., *et al.* Changes in the incidence of tuberculosis in a cohort of HIV-seroconverters before and after the introduction of HAART. *AIDS* 2007;21:2521-2527.

9. Selwyn P.A., *et al*. A prospective study of the risk of tuberculosis among intravenous drug users with human immunodeficiency virus infection. *The New England Journal of Medicine* 1989; 320:545-550.

10. Horsburgh C. Priorities for the treatment of latent tuberculosis infection in the United States. *The New England Journal of Medicine* 2004;350:2060-2067.

11. Duncan L.E., *et al.* Tuberculin sensitivity and HIV-1 status of patients attending a sexually transmitted diseases clinic in Lusaka, Zambia: a cross-sectional study. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1995;89:37-40.

12. Richeldi L. An update on the diagnosis of tuberculosis infection. *American Journal of Respiratory and Critical Care Medicine* 2006;174:736-742.

13. Converse P.J., *et al.* Comparison of a tuberculin Interferon-gamma assay with the tuberculin skin test in high-risk adults: effect of human immunodeficiency virus infection. *The Journal of Infectious Diseases* 1997;176:144-150.

14. Pai M., Riley L.W., Colford J.M. Interferon gamma assays in the immunodiagnosis of tuberculosis: a systematic review. *The Lancet Infectious Diseases* 2004; 4:761-776.

15. Arend S.M., *et al*. Tuberculin Skin Testing and in vitro T cell responses to ESAT-6 and culture filtrate protein 10 after Infection with *Mycobacterium marinum* or *M. kansasii. The Journal of Infectious Diseases* 2002;186:1797-1807.

16. Menzies D., Pai M., Comstock G. Meta-analysis: new tests for the diagnosis of latent tuberculosis infection: areas of uncertainty and recommendations for research. *Annals of Internal Medicine* 2007;146:340-354.

17. Lalvani A., *et al.* Enumeration of T cells specific for RDI-encoded antigens suggest a high prevalence of latent *Mycobacterium tuberculosis* infection in healthy urban Indians. *The Journal of Infectious Diseases* 2001;183:469-477.

18. Kimura M., *et al.* Comparison between a whole blood interferon-γ release assay and tuberculin skin testing for the detection of tuberculosis infection among patients at risk for tuberculosis exposure. *The Journal of Infectious Diseases* 1999;179:1297-1300.

19. Dewan P.K., *et al.* Feasibility, acceptability, and cost of tuberculosis testing by whole-blood interferon-gamma assay. *BMC Infectious Diseases* 2006; 6:47.

20. Grimes C.Z., *et al.* Tuberculosis infection in drug users: interferon-gamma release assay performance. *The International Journal of Tuberculosis and Lung Disease* 2007; 11:1183-1189.

21. Ferrara G., *et al.* Use in routine clinical practice of two commercial blood tests for diagnosis of infection with *Mycobacterium tuberculosis*: a prospective study. Lancet 2006;367:1328-1334.

22. Liebeschuetz S., *et al.* Diagnosis of tuberculosis in South African children with a T-cell-based assay: a prospective cohort study. Lancet 2004;364:2196-2203.

23. Taggart E.W., *et al.* Evaluation of an *In Vitro* assay for Interferon gamma production in response to the *Mycobacterium tuberculosis*-synthesized peptide antigens ESAT-6 and CFP-10 and the PPD skin test. *American Journal of Clinical Pathology* 2006;125:467-473.

24. Tsiouris S.J., *et al.* Sensitivity analysis and potential uses of a novel gamma interferon release assay for diagnosis of tuberculosis. *Journal of Clinical Microbiology* 2006;44:2844-2850.

25. Chapman A.L., *et al*. Rapid detection of active and latent tuberculosis infection in HIV positive individuals by enumeration of *Mycobacterium tuberculosis*-specific T cells. AIDS 2002;16:2285-2293.

26. Brock I., *et al*. Latent tuberculosis in HIV positive, diagnosed by the *M. Tuberculosis* specific Interferon Gamma test. *Respiratory Research* 2006;7:56.

27. Rangaka M.X., *et al.* Effect of HIV-infection on T-cell-based and skin test detection of tuberculosis infection. *American Journal of Respiratory and Critical Care Medicine* 2007; 175:514-520.

Table 1. Characteristics of the study population according to HIV serostatus.

| | HIV- n / N (%) | HIV+ n / N (%) |
|---|---|---|
| **Male** | 80 / 93 (86.0) | 33 / 42 (78.6) |
| **Age (mean ± SD)** | 40.3 ± 8.9 | 38.9 ± 5.6 |
| **Current or past IDU** | 23 / 93 (24.7) | 38 / 42 (90.5) |
| **Duration of drug use (months) (mean ± SD)** | 157.5 ±111.2 | 161.4 ± 107.3 |
| **Previous imprisonment** | 14 / 73 (19.2) | 16 / 25 (64.0) |
| **Hepatitis C virus infection** | 28 / 89 (31.5) | 39 / 40 (97.5) |
| **CD4 cell count, (mean ± SD) (n=125)** | 1144 ± 465.8 | 536.5 ± 347.9 |
| **Hemoglobin (gr/dL) (mean ± SD) (n=111)** | 14.7± 1.6 | 13.9 ±1.5 |
| **Body Mass Index (mean ± SD) (n=101)** | 25 ± 4.7 | 22.5 ± 3.1 |
| **History of TST(+)** | 10 / 93 (10.8) | 10 / 42 (23.8) |
| **History of TB disease** | 6 / 93 (6.5) | 7 / 42 (16.7) |

Table 2: Prevalence of *in vitro* and *in vivo* tests for the diagnosis of latent tuberculosis according to HIV infection and CD4 cell count.

| | **HIV (-)** | **HIV (+) CD4 ≥ 350** | **HIV (+) CD4 < 350** |
|---|---|---|---|
| | **n / N (%)** | **n / N (%)** | **n / N (%)** |
| **EIA (+)** | 33 / 93(35.5) | 11 / 28 (39.3) | 1 / 10 (10.0) |
| **ELISPOT (+)** | 35 / 93 (37.6) | 8 / 28 (28.6) | 2 / 10 (20.0) |
| **EIA (+) or ELISPOT (+)** | 41 / 93 (44.1) | 13 / 28 (46.4) | 2 / 10 (20.0) |
| **TST (+)*** | 27 / 77 (35.1) | 2 / 15 (13.3) | 0 / 5 (0.0) |
| **EIA (+) or TST (+)** | 31 / 77 (40.3) | 4 / 15 (26.7) | 0 / 5 (0.0) |
| **ELISPOT (+) or TST (+)** | 32 / 77 (41.6) | 5 / 15 (33.3) | 0 / 5 (0.0) |

* ≥ 5mm in HIV+ patients; ≥ 10 mm in HIV (-) patients





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Table 3. Characteristics of patients with previous tuberculosis disease and results of IGRA tests.

| Sex | Age (yrs.) | HIV | CD4 cells | Years between TB disease and an IGRA test | EIA | ELISPOT |
|---|---|---|---|---|---|---|
| M | 43 | - | 796 | 8 | - | - |
| M | 55 | - | 716 | 30 | - | - |
| H | 41 | - | 668 | 9 | + | - |
| H | 43 | - | 1061 | 13 | + | + |
| H | 41 | - | 974 | 8 | + | + |
| H | 45 | - | 1129 | 9 | + | + |
| M | 38 | + | 185 | 13 | - | - |
| H | 43 | + | 667 | 15 | - | - |
| H | 43 | + | 602 | 11 | - | - |
| H | 43 | + | 694 | 11 | - | - |
| M | 43 | + | 217 | 15 | - | + |
| H | 43 | + | 1014 | 10 | + | + |
| H | 42 | + | 150 | 4 | + | + |





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Figure 1: Concordance of two IGRA tests with tuberculin skin test at admission.