Detection of latent tuberculosis infection in hemodialysis patients: Comparison between the quantiferon-tuberculosis gold test and the tuberculin skin test

Mona T. Hussein[a], Laila M. Yousef[b], Ali T. Ali[c]

Background Tuberculosis (TB) remains an important cause of morbidity and mortality in hemodialysis (HD) patients. A gold standard for the diagnosis of latent tuberculosis infection (LTBI) is lacking.

Objective The aim of this study was to compare the diagnostic utility of the QuantiFERON-Tuberculosis Gold (QFT-G) test with the tuberculin skin test (TST) in identifying LTBI in patients with end-stage renal disease (ESRD) on HD.

Study design The present study had a prospective design.

Patients and methods A total of 74 patients with ESRD on HD without active TB and other immunosuppressive conditions were tested for LTBI by the QFT-G test and the TST.

Results LTBI, as estimated by the QFT-G test and TST, was detected in 35.1 and 13.5% of the HD patients, respectively; 37.8% of patients were positive for the QFT-G test and/or the TST. There was a poor agreement between QFT-G test and TST results in patients with ESRD on HD (QFT-G test vs. TST: κ=0.25, 95% confidence interval=0.12–0.37). TST was positive in 2.7% of patients when the QFT-G test was negative, and it was negative in 24.3% of patients when the QFT-G test was positive. There was no significant difference in duration of HD or creatinine levels between QFT-G-positive and QFT-G-negative patients (P=0.08 and 0.2, respectively). TST-positive patients had a significantly shorter duration of HD and lower creatinine levels than TST-negative patients (P=0.001 and 0.01, respectively).

Conclusion In patients with ESRD and on HD, LTBI cannot be simply ruled out with a negative TST result, but rather a QFT-G test is recommended. Screening and treatment of LTBI should be carried in dialysis patients, aiming to prevent progression to active TB and secondary infection of others.

Egypt J Bronchol 2017 11:255–259

Egyptian Journal of Bronchology 2017 11:255–259

Keywords: dialysis, interferon-γ release assays, latent tuberculosis infection, QuantiFERON-Tuberculosis Gold test, tuberculin skin test

Departments of, [a]Chest Diseases and Tuberculosis, [b]Clinical Pathology, [c]Internal Medicine, Faculty of Medicine, Sohag University, Sohag, Egypt

Correspondence to Mona T. Hussein, MD, Department of Chest Diseases and Tuberculosis, Faculty of Medicine, Sohag University, Sohag, Egypt; Tel: +20932329242 Mobile: +201028068879; fax: +20932329242; e-mail: monatahah@gmail.com

Received 21 February 2017 **Accepted** 24 March 2017

Introduction

In Egypt, tuberculosis (TB) is an important health problem. Egypt is ranked among the mid-level incidence countries [1]. The reported prevalence of chronic renal failure is 225 patients per million in Egypt [2]. Individuals with latent tuberculosis infection (LTBI) are assumed to have viable TB bacilli in their body. These bacilli are dormant, but have the potential to reactivate and cause disease [3]. According to the WHO, ~2–3 billion people in the world have LTBI, and 5–15% of them will suffer from reactivation of TB during their life. Therefore, the treatment for LTBI influences the future global prevention of TB infection [4].

Patients with end-stage renal disease (ESRD) and on dialysis are 6–25 times more likely to develop TB than the general population, mainly because of the impaired cellular immunity associated with this condition [5]. The mortality rate of TB in dialysis patients is high in comparison with the general population, ranging from 17 to 75% [6]. In these patients, the diagnosis of TB is often difficult because of nonspecific symptoms and prevailing extrapulmonary involvement [4,7–9]. Diagnosis of LTBI mainly depends on the immune reaction of the host rather than that of the bacterium itself, because the amount of *Mycobacterium tuberculosis* is small in LTBI individuals. A gold standard for the diagnosis of the LTBI is lacking. At present, there are two screening tests for LTBI: the tuberculin skin test (TST) and interferon-γ release assays (IGRAs, including the QuantiFERON-Tuberculosis Gold (QFT-G) and the T-SPOT.TB test) [9].

Aim

The aim of the present study was to compare the diagnostic utility of QFT-G test with the TST in identifying LTBI in patients with ESRD on hemodialysis (HD).

Patients and methods

This prospective study included adult patients with ESRD on HD, who were recruited prospectively from the outpatient HD unit at the Sohag University Hospital, Sohag, Egypt, in the period between February and April 2016. All patients enrolled were required to provide their consent. The study was approved by the Ethics Committee at Sohag Faculty of Medicine. Exclusion criteria were presence of active TB disease and other immunosuppressive diseases such as HIV, diabetes mellitus, immunological disorders, long duration of corticosteroid treatment, and chronic liver diseases.

All patients were subjected to the following:

(1) Complete history taking and examination, including age, sex, comorbid conditions, duration of dialysis, and history of Bacille Calmette–Guérin (BCG) vaccination (visual inspection for BCG scar).
(2) Chest radiograph.
(3) Laboratory investigations included the following: erythrocytic sedimentation rate test, serum creatinine test, and sputum analysis for acid-fast bacillifor 3 successive days.
(4) TST was performed by injecting 0.1 ml of tuberculin purified protein derivative (PPD) (5 U) intradermally into the skin of the forearm. The test was then read 48–72 h later. On the basis of published guidelines, induration greater than or equal to 10 mm was considered a positive TST for ESRD patients on dialysis [3].

QFT-G test in-tube: 1 ml of blood was collected by venipuncture directly into each of the collection tubes for the QFT-G test. The QFT-G system uses three specialized blood-collection tubes that contain antigens representing certain *M. tuberculosis* proteins (ESAT-6, CFP-10, and TB 7.7) as well as positive (mitogen) and negative (nil) controls. The mitogen tube can be used with the QFT-G test as a positive control. This may be especially warranted where there is doubt regarding the individual's immune status, and therefore it is specially used in immunocompromised patients. The following steps were performed according to the package insert of QFT-G (in-tube method), manufactured by Cellestis Limited (Hilden, Germany) [10]. The concentration of interferon-γ (IFN-γ) was determined by enzyme-linked immunosorbent assay.

Statistical analysis

Statistical analyses were performed using SAS software (SAS Institute Inc., Cary, NC, USA). Values are reported as mean±SD. A *P* value (two-tailed) less than 0.05 was considered statistically significant. Agreement between the results of the QFT-G test and the results of TST was evaluated using κ statistics, where κ less than 0.4 represents poor agreement, κ values from 0.4 to 0.75 represent fair to good agreement, and κ greater than 0.75 represents an excellent agreement [11].

Results

According to inclusion and exclusion criteria, the study included 74 adult patients with ESRD on HD. The mean±SD age of the patients was 45±18 years. Forty-five (60.8%) participants were males and 29 (39.2%) were females. Forty-seven (63.5) patients were BCG vaccinated. The mean±SD duration of HD was 28±19 months, as shown in Table 1.

Of the 74 participants in the present study, 26 (35.1%) patients had a positive QFT-G test. There were no significant differences in duration of HD and creatinine levels between QFT-G-positive and QFT-G-negative patients (*P*=0.08 and 0.2, respectively), as shown in Table 2.

Of the 74 participants in the present study, 10 (13.5%) had positive TST results. Patients with positive TST results had a significantly shorter duration of HD and lower creatinine levels than patients with negative TST (*P*=0.001 and 0.01, respectively), as shown in Table 3.

Of the 74 participants, 28 (37.8%) patients had positive QFT-G and/or positive TST results. Twenty-six (35.1%) patients had positive QFT-G results, whereas 10 (13.5%) patients had positive TST results. There was

Table 1 Demographic data of the studied patients

Characteristics	Study group (*N*=74)
Age, range (mean±SD)	21–65 (45±18)
Male sex [*n* (%)]	45 (60.8)
BCG vaccination, yes [*n* (%)]	47 (63.5)
Duration of HD (m) [range (mean±SD)]	4–52 (28±19)

BCG, Bacille Calmette–Guérin; HD, hemodialysis.

Table 2 Relationship between QuantiFERON-Tuberculosis Gold results and duration of hemodialysis and creatinine levels in the studied patients

	Positive QFT-G patients (*n*=26)	Negative QFT-G patients (*n*=48)	*P* value
Duration of HD (months) (mean±SD)	25±15	36±20	0.08
Creatinine level (mg/dl)	9.8±2.8	10.9±2.3	0.2

HD, hemodialysis; QFT-G, QuantiFERON-Tuberculosis Gold.

a poor agreement between QFT-G and TST results in patients with ESRD on HD (QFT-G vs. TST: κ=0.25, 95% confidence interval=0.12–0.37). TST results were positive in two (2.7%) patients when QFT-G results were negative, and the results were negative in 18 (24.3%) patients when QFT-G results were positive, as shown in Table 4.

Discussion

The TST is the classic method for the diagnosis of LTBI, which is based on cell-mediated immune response induced by LTBI. It measures the delayed-type hypersensitivity response to intradermal inoculation of tuberculin PPD [3,12]. QFT-G is another diagnostic method for the diagnosis of TB. This test uses two proteins encoded by a unique genomic segment termed 'Region of Difference 1', which is present in *M. tuberculosis* but is absent from all strains of BCG, most nontuberculous mycobacteria, and *Mycobacterium bovis* [13]. These proteins are major targets of T-helper type 1 cells in infected individuals with *M. tuberculosis*. Therefore, a T cell response to these antigens could serve as a specific marker of *M. tuberculosis* infection, avoiding the antigenic cross-reactivity of PPD, the main cause of poor specificity of the TST [14].

In our study, 35.1% of patients with ESRD on HD were positive for QFT-G. There was no significant difference in the duration of HD or creatinine levels between QFT-G-positive and QFT-G-negative patients. These results are in agreement with those of Abdel-Nabia *et al.* [15]. In addition, Ates *et al.* [16] and Hoffmann *et al.* [17] recorded that there was no difference between QFT-G-positive and QFT-G-negative patients regarding HD duration, and suggested that patients with ESRD on HD were still able to produce IFN-γ. However, Inoue *et al.* [18] recorded a significant increase in indeterminate QFT-G results with increased duration of dialysis.

Table 3 Relationship between tuberculin skin test results and duration of hemodialysis and creatinine levels in the studied patients

	Positive TST patients (n=10)	Negative TST patients (n=64)	P value
Duration of HD (months) (mean±SD)	19±13	39±14	0.001
Creatinine level (mg/dl)	8.1±2.3	10.7±2.1	0.01

HD, hemodialysis; TST, tuberculin skin test.

Table 4 Agreement between the results of QuantiFERON-Tuberculosis Gold with the results of tuberculin skin test

	TST		
	Negative	Positive	Total
QFT-G [*N* (%)]			
Negative	46 (62.2)	2 (2.7)	48 (64.9)
Positive	18 (24.3)	8 (10.8)	26 (35.1)
Total	64 (86.5)	10 (13.5)	74 (100)
κ Value		0.25	

QFT-G vs. TST: κ=0.25, 95% CI=0.12–0.37. CI, confidence interval; QFT-G, QuantiFERON-Tuberculosis Gold; TST, tuberculin skin test..

We found that 13.5% of ESRD patients on HD were positive for TST. TST-positive patients had a significantly shorter duration of HD and lower creatinine levels than TST-negative patients. These results are in agreement with those of Abdel-Nabia *et al.* [15], but in disagreement with those of Sagheb *et al.* [19] and Ates *et al.* [16], who found that there was no significant relationship between TST results and duration of HD.

In our study, 37.8% of HD patients had LTBI, and they were positive for the QFT-G test and/or TST; 35.1% of the patients were positive for QFT-G, whereas 13.5% of patients were positive for TST. Lee *et al.* [20] studied LTBI in patients with ESRD on dialysis, and reported that 62.5% of patients were positive with TST, and 40% of the patients were positive with the QFT-G test. In addition, Lee *et al.* [21] studied LTBI in patients with ESRD on HD, and found that 34.4% of patients were positive by the QFT-G test and 10.8% were indeterminate, whereas by using the TST 53.9% of patents were positive. Abdel-Nabia *et al.* [15] reported that 25% of the HD patients were positive for the QFT-G test and/or TST, 20% were QFT-G positive, and 15% were TST positive. Dialysis patients are not only at higher risk for reactivation of TB disease but also at higher risk for nosocomial transmission of TB within dialysis centers [22].

In our study, there was a poor agreement between the results of the QFT-G test and the results of the TST in patients with ESRD on HD (QFT-G vs. TST: κ=0.25, 95% confidence interval=0.12–0.37). In previous studies, the QFT-G and T-SPOT.TB tests were used for detecting LTBI in HD patients. The agreement between the two tests has been found to be fair or moderate (κ=0.27–0.60), whereas the agreement between TST and IGRAs was only poor or fair (κ=0.16–0.27 for QFT-G and 0.16–0.32 for T-SPOT.TB) [20,23,24]. On the other hand,

Winthrop *et al.* [25] found that the concordance between results was better, ranging from 71% (TST vs. T-SPOT.TB) to 79% (TST vs. QFT-G) to 87% (QFT-G vs. T-SPOT.TB). Lee *et al.* [21] recorded a poor correlation between TST and QFT-G for any TST cutoff criteria in patients with ESRD on HD. Abdel-Nabia *et al.* [15] found 85% concordance between QFT-G and TST results in HD patients. The poor agreement between QFT-G results and TST results could be explained by multiple limitations affecting the role of TST in the diagnosis of LTBI and active TB in patients with ESRD and on dialysis.

There are multiple limitations to the use of TST in the diagnosis of LTBI or active TB in patients with ESRD. The first limitation is the poor sensitivity of TST in patients with ESRD. There is a higher prevalence of anergy to TST in patients with ESRD than in the general population (44 vs. 16%) [26]. The second limitation of TST is its low specificity. Individuals vaccinated with BCG but not infected with *M. tuberculosis* can show false-positive results with TST [27]. Farhat *et al.* [28] found that the effect of BCG on TST received in infancy is minimal, especially greater than or equal to 10 years after vaccination.

In a comparative study between using the QFT-G test and the TST for the diagnosis of *M. tuberculosis* infection, the authors reported that the QFT-G test has excellent sensitivity and specificity and is unaffected by BCG vaccination. The specificity of the TST is high in non-BCG-vaccinated populations, but low and variable in BCG-vaccinated populations. In addition, they found that there was a good agreement between the clinical findings and the QFT-G test results [29].

Helmya *et al.* [30] studied the value of QFT-G assays in monitoring the efficacy of antituberculosis therapy, and recorded that there was a correlation between treatment outcome and changes in IFN-γ response to *M. tuberculosis*-specific antigens. The low sensitivity and specificity of the TST may explain the reported poor correlation of its results with history, chest radiograph, and QFT-G in the diagnosis of TB in HD patients [8].

Multiple authors studied LTBI in immuno-compromised populations and found the superiority of IGRAs in the diagnosis of LTBI in comparison with the TST, which has low sensitivity in these settings [31–34].

Other advantages of the IGRAs compared with the TST include the shorter time required for obtaining results (16–24 vs. 48–72 h), no need for return visits, objective (instrument-based) interpretation of the test, and lack of boosting effect in repeated tests. Higher sensitivity of IGRAs would identify more infected persons among those with a false-negative TST result. On the other hand, higher specificity will reduce false-positive test results, thus avoiding unnecessary chemoprophylaxis. More true-positive results in infected individuals would increase the rate of diagnosis and treatment of LTBI before progression to active TB [35]. Two meta-analyses have been previously conducted, and both of them reported little value for the prediction of active TB with either IGRAs or TST [36,37].

Limitations of the IGRAs include lack of distinction between LTBI and active TB, and another important issue is the limited availability of IGRAs (in contrast with the worldwide accessible TST). However, the important disadvantage of IGRAs is their high cost [38]. In patients with ESRD and on dialysis, active TB or LTBI cannot be simply ruled out with a negative TST result, but rather IGRA tests and more invasive investigations are recommended [4]. In several reports and guidelines, screening and prophylaxis of LTBI in ESRD patients are recommended [4,39,40].

There are multiple limitations to our study. First, a small number of ESRD patients were included in our study. Second, our study was not a follow-up study to record values for the prediction of active TB with either the QFT-G test or the TST. Further studies are recommended including larger number of patients with ESRD with a good follow-up period to record values for predicting active TB with either the QFT-G test or the TST.

Conclusion

In patients with ESRD and on HD, LTBI cannot be simply ruled out with a negative TST result, but rather IGRA tests (QFT-G) are recommended. Screening and treatment for LTBI should be carried in dialysis patients, aiming to prevent progression to active TB and secondary infection of others.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 National TB Control Program. *Guidelines on management of tuberculosis for non-chest physicians*. Egypt: Ministry of Health and Population; 2008.

2 Shaheen FA, Al-Khader AA. Preventive strategies of renal failure in the Arab world. *Kidney Int Suppl* 2005; **98**:S37–S40.

3 American Thoracic Society; Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. *Am J Respir Crit Care Med* 2000; **161**(Suppl):221–247

4 World Health Organization. *Global tuberculosis report 2015*. Geneva: WHO; 2015. Available at: http://www.who.int/tb/publications/global_report/en/. [Accessed 23 November 2015].

5 Passalent L, Khan K, Richardson R, Wang J, Dedier H, Gardam M. Detecting latent tuberculosis infection in hemodialysis patients: a head-to-head comparison of the T-SPOT. TB test, tuberculin skin test, and an expert physician panel. *Clin J Am Soc Nephrol* 2007; **2**:68–73.

6 Hussein MM, Mooij JM, Roujouleh H. Tuberculosis and chronic renal disease. *Semin Dial.* 2003; **16**:38–44.

7 Abdelrahman M, Sinha AK, Karkar A. Tuberculosis in end-stage renal disease patients on hemodialysis. *Hemodial Int* 2006; **10**:360–364.

8 Segall L, Covic A. Diagnosis of tuberculosis in dialysis patients: current strategy. *Clin J Am Soc Nephrol* 2010; **5**:1114–1122.

9 Ai JW, Ruan QL, Liu QH, Zhang WH. Updates on the risk factors for latent tuberculosis reactivation and their managements. *Emerg Microbes Infect* 2016; **5**:e10.

10 Gerogianni I, Papala M, Klapsa D, Zinzaras E, Petinaki E, Gourgoulianis KI. Whole-blood interferon-gamma assay for the diagnosis of tuberculosis infection in an unselected Greek population. *Respirology* 2008; **13**: 270–274.

11 Kraemer HC. Measurement of reliability for categorical data in medical research. *Stat Methods Med Res* 1992; **1**:183–199.

12 Bloch AB. Screening for tuberculosis and tuberculosis infection in high-risk populations recommendations of the advisory council for the elimination of tuberculosis. *MMWR* 1995; **44**:19–34.

13 Andersen P, Munk ME, Pollock JM, Doherty TM. Specific immune-based diagnosis of tuberculosis. *Lancet* 2000; **356**:1099–1104.

14 Lalvani A, Pathan AA, McShane H, Wilkinson RJ, Latif M, Conlon CP, *et al.* Rapid detection of *Mycobacterium tuberculosis* infection by enumeration of antigen-specific T cells. *Am J Respir Crit Care Med* 2001; **163**:824–828.

15 Abdel-Nabia EA, Eissaa SA, Solimana YMA, Amin WA. Quantiferon vs. tuberculin testing in detection of latent tuberculous infection among chronic renal failure patients. *Egypt J Chest Dis Tuberc* 2014; **63**:161–165.

16 Ates G, Ozekinci T, Yildiz T, Danis R. Comparison of interferon-gamma release assay versus tuberculin skin test for latent tuberculosis screening in hemodialysis patients. *Biotechnol Biotechnol Equip* 2009; **23**: 1242–1246.

17 Hoffmann M, Tsinalis D, Vernazza P, Fierz W, Binet I. Assessment of an interferon-gamma release assay for the diagnosis of latent tuberculosis infection in haemodialysis patient. *Swiss Med Wkly* 2010; **140**:286–292.

18 Inoue T, Nakamura T, Katsuma A, Masumoto S, Minami E, Katagiri D, *et al.* Value of QuantiFERON TB-Gold in the diagnosis of tuberculosis among dialysis patients. *Nephrol Dial Transplant* 2009; **24**:2252–2257.

19 Sagheb MM, Goodarzi M, Roozbeh J. The booster phenomenon of tuberculin skin testing in patients receiving hemodialysis. *Iran J Immunol* 2008; **5**:212–216.

20 Lee SS, Chou KJ, Su IJ, Chen YS, Fang HC, Huang TS, *et al.* High prevalence of latent tuberculosis infection in patients in end-stage renal disease on hemodialysis: comparison of QuantiFERON-TB GOLD, ELISPOT, and tuberculin skin test. *Infection* 2009; **37**:96–102.

21 Lee SS-J, Chou K-J, Dou H-Y, Huang T-S, Ni Y-Y, Fang H-C, *et al.* High prevalence of latent tuberculosis infection in dialysis patients using the interferon-γ release assay and tuberculin skin test. *Clin J Am Soc Nephrol* 2010; **5**:1451–1457.

22 Centers for Disease Control and Prevention. Tuberculosis transmission in a Renal Dialysis Center – Nevada, 2003. *MMWR* **2004**; 53:873–875.

23 Triverio PA, Bridevaux PO, Roux-Lombard P, Niksic L, Rochat T, Martin PY, *et al.* Interferon-gamma release assays versus tuberculin skin testing for detection of latent tuberculosis in chronic haemodialysis patients. *Nephrol Dial Transplant* 2009; **24**:1952–1956.

24 Chung WK, Zheng ZL, Sung JY, Kim S, Lee HH, Choi SJ, *et al.* Validity of interferon-γ-release assays for the diagnosis of latent tuberculosis in haemodialysis patients. *Clin Microbiol Infect* 2010; **16**:960–965.

25 Winthrop KL, Nyendak M, Calvet H, Oh P, Lo M, Swarbrick G, *et al.* Interferon-gamma release assays for diagnosing *Mycobacterium tuberculosis* infection in renal dialysis patients. *Clin J Am Soc Nephrol* 2008; **3**:1357–1363.

26 Shankar MS, Aravindan AN, Sohal PM, Kohli HS, Sud K, Gupta KL, *et al.* The prevalence of tuberculin sensitivity and anergy in chronic renal failure in an endemic area: tuberculin test and the risk of post-transplant tuberculosis. *Nephrol Dial Transplant* 2005; **20**:2720–2724.

27 Huebner RE, Schein MF, Bass JB Jr. The tuberculin skin test. *Clin Infect Dis* 1993; **17**:968–975.

28 Farhat M, Greenaway C, Pai M, Menzies D. False-positive tuberculin skin tests: what is the absolute effect of BCG and non-tuberculous mycobacteria? *Int J Tuberc Lung Dis* 2006; **10**:1192–1204.

29 Abdel-Samea SA, Ismail YM, Fayed SM, Mohammad AA. Comparative study between using QuantiFERON and tuberculin skin test in diagnosis of Mycobacterium tuberculosis infection. *Egypt J Chest Dis Tuberc* 2013; **62**:137–143.

30 Helmya N, Abdel latif S, Kamela MM, Ashoura W, El Kattana E. Role of Quantiferon TB gold assays in monitoring the efficacy of antituberculosis therapy. *Egypt J Chest Dis Tuberc* 2012; **61**:329–336.

31 Lalvani A, Pareek M. A 100 year update on diagnosis of tuberculosis infection. *Br Med Bull* 2010; **93**:69–84.

32 Stephan C, Wolf T, Goetsch U, Bellinger O, Nisius G, Oremek G, *et al.* Comparing QuantiFERON-tuberculosis gold, T-SPOT tuberculosis and tuberculin skin test in HIV-infected individuals from a low prevalence tuberculosis country. *AIDS* 2008; **22**:2471–2479.

33 Luetkemeyer AF, Charlebois ED, Flores LL, Bangsberg DR, Deeks SG, Martin JN, *et al.* Comparison of an interferon-gamma release assay with tuberculin skin testing in HIV-infected individuals. *Am J Respir Crit Care Med* 2007; **175**:737–742.

34 Raby E, Moyo M, Devendra A, Banda J, De Haas P, Ayles H, Godfrey-Faussett P. The effects of HIV on the sensitivity of a whole blood IFN-gamma release assay in Zambian adults with active tuberculosis. *PLoS One* 2008; **3**:e2489.

35 Richeldi L. An update on the diagnosis of tuberculosis infection. *Am J Respir Crit Care Med* 2006; **174**:736–742.

36 Metcalfe JZ, Everett CK, Steingart KR, Cattamanchi A, Huang L, Hopewell PC, *et al.* Interferon-γ release assays for active pulmonary tuberculosis diagnosis in adults in low- and middle-income countries: systematic review and meta-analysis. *J Infect Dis* 2011; **204**(Suppl 4): S1120–S1129.

37 Rangaka MX, Wilkinson KA, Glynn JR, Ling D, Menzies D, Mwansa-Kambafwile J, *et al.* Predictive value of interferon-γ release assays for incident active tuberculosis: a systematic review and meta-analysis. *Lancet Infect Dis* 2012; **12**:45–55.

38 Lagrange PH, Simonney N, Herrmann JL. New immunological tests in the diagnosis of tuberculosis. *Rev Mal Respir* 2007; **24**(Part 1): 453–472.

39 British Thoracic Society Standards of Care Committee, Joint Tuberculosis Committee, Milburn H, Ashman N, Davies P, Doffman S, Drobniewski F, Khoo S, *et al.* Guidelines for prevention and management of Mycobacterium tuberculosis infection and disease in adult patients with chronic kidney disease. *Thorax* 2010; **65**:557–570.

40 Prevention Committee of the Japanese Society for Tuberculosis, Treatment Committee of the Japanese Society for Tuberculosis. Treatment guidelines for latent tuberculosis infection. *Kekkaku* 2014; **89**:21–37.