Whole-blood interferon-gamma release assay in the diagnosis of active tuberculosis infection in HIV infected and HIV non-infected individuals: a five year review of data

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Background

- Role of IGRAs in latent TB infection clearly defined.
- Role in active disease less clear.
- HPA (2008)[1]: "**IGRA should currently not be used as a routine diagnostic tool for active TB**…"
- BHIVA (2010 unpublished)[2]: "… **IGRA tests should not be used as the means by which the diagnosis is confirmed or refuted**…"

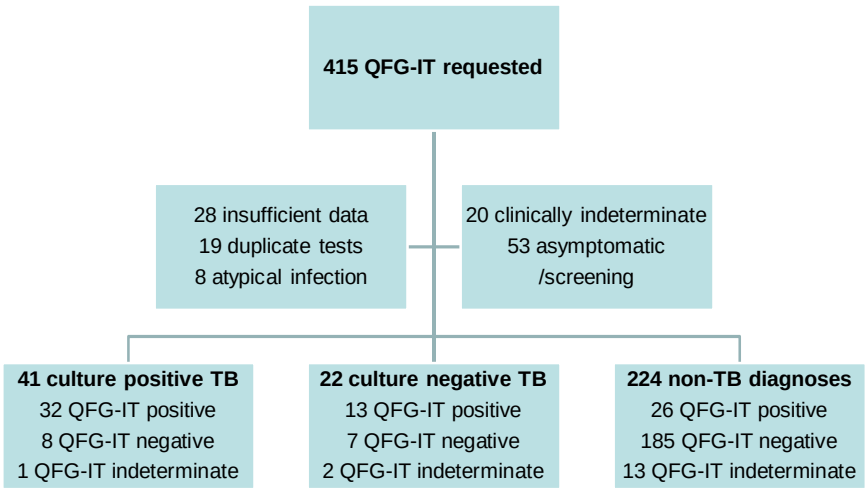
[1]Health Protection Agency position statement on the use of Interferon Gamma Release Assay (IGRA) tests for tuberculosis (TB)
[2]British HIV Association guidelines for the treatment of TB/HIV coinfection 2010 (in consultation).

Study aims

- To determine the usefulness of QGF-IT in diagnosing active TB infection
  - UK *v.* non-UK
  - PTB *v.* EPTB
  - HIV positive *v.* negative
- To review the use of QFG-IT in our unit

Methods

- 415 QFG-IT requested through ID between 29/06/05-28/10/10
- Data collected: presenting symptoms, final diagnosis, TB smear, culture and site of infection, sex, age, nationality, HIV status, and CD4 count if HIV positive.
- Cases assigned into 5 categories:
  1. culture confirmed TB
  2. culture negative TB
  3. clinically indeterminate cases
  4. active TB excluded
  5. screening/asymptomatic latent disease
- Excluded: duplicate tests, insufficient data, atypical mycobacterial infection, category 3 and 5 patients



Demographic and clinical characteristics

	All	Active TB	Non-TB diagnosis
Total	287	63	224
Male sex (%)	150 (52)	39 (62)	111 (50)
Age, median yrs (range)	40 (16-90)	33 (17-90)	42 (16-80)
Origin (%)			
UK	165 (57)	14 (22)	151 (67)
Other European	3 (1)		3 (1)
Indian subcontinent	52 (18)	22 (35)	30 (13)
Middle East	8 (3)	4 (6)	4 (2)
Other Asia	7 (2)	3 (5)	4 (2)
Africa	52 (18)	20 (32)	32 (14)
HIV +ve (%)	48 (17)	14 (22)*	34 (15)
Median CD4 (range)	329 (28-1060)	261 (93-891)	350 (28-1060)

* 15 (24%) no record of HIV test

Site of TB infection

	All	QFG-IT		
		Positive	Negative	Indeterm
Disease site (%)				
PTB	9 (14)	6 (67)	2 (22)	1 (11)
EPTB	47 (75)	32 (68)	13 (28)	2 (4)
PTB and EPTB	6 (10)	6 (100)		
Miliary	1 (2)	1 (100)		

Overall analysis

	TB	Non-TB	Sensitivity (95% CI)	Specificity (95% CI)	NPV (95% CI)
All patients	63	224	71.4% (59.3-81.1)	82.6% (77.1-87.0)	92.5% (88.0-95.4)
Positive	45	26			
Negative	15	185			
Indeterminate	3	13			
Culture positive	41	-	78.0% (63.3-88.0)	-	-
Positive	32	-			
Negative	8	-			
Indeterminate	1	-			
PTB	9	-	66.7% (35.4-87.9)	-	-
Positive	6	-			
Negative	2	-			
Indeterminate	1				
EPTB	47	-	68.1% (53.8-79.6)	-	-
Positive	32	-			
Negative	13	-			
Indeterminate	2				
UK born	14	145	57.1% (32.6-78.6)	91.0% (85.3-94.7)	97.1% (92.3-98.9)
Positive	8	6			
Negative	4	132			
Indeterminate	2	7			
Non-UK born	49	79	75.5% (61.9-85.4)	67.1% (56.2-76.5)	82.8% (71.8-90.1)
Positive	37	20			
Negative	11	53			
Indeterminate	1	6			

HIV data

	TB	Non-TB	Sensitivity (95% CI)	Specificity (95% CI)	NPV (95% CI)
All patients	63	224	71.4% (59.3-81.1)	82.6% (77.1-87.0)	92.5% (88.0-95.4)
Positive	45	26			
Negative	15	185			
Indeterminate	3	13			
All HIV	14	34	71.4% (45.4-88.3)	85.3% (69.9-93.6)	90.6% (75.8-96.8)
Positive	10	3			
Negative	3	29			
Indeterminate	1	2			
CD4 <200	6	7	83.3% (43.7-97.0)	85.7% (48.7-97.4)	85.7% (48.7-97.4)
Positive	5	0			
Negative	1	6*			
Indeterminate	0	1			

* Including 2 CD4 <50

Discussion

- Potential role in low risk (UK-born) groups.
- Limited role in higher risk groups.
- HIV status does not appear to influence results irrespective of CD4 count.
- Clinical, microbiological, radiological and histological diagnosis remains key.

Limitations

- Retrospective study with potential for observer bias.
- Assumption that request of QFG-IT in symptomatic patient suggests TB as a diagnosis suspected.
- High NPV influenced by significant number of tests in patients unlikely to have TB.

Acknowledgements

- Dr Ed Ong
- Prof John Magee
- Anne Barrett
- Deborah Osbourne
- Dr Matthias Schmid
- Dr Ashley Price
- Dr Uli Schwab