Screening of Childhood Latent Tuberculosis Infection by an Interferon Gamma Release Assay

Thesis
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بسم الله الرحمن الرحيم

وقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ
ورَسُولُهُ والْمُؤْمِنُونَ

صدق الله العظيم

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Ahmed Reda M. Hassan

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List of Abbreviations

AAP	American Academy of Pediatrics
AIDS	Acquired immune deficiency syndrome
BCG	Bacilli –Calmette –Guerin
CFP-10	Culture filtrate protein
DOTS	Direct observed therapy
ELISA	Enzyme linked immune sorbent assay
EMB	Ethambutol
ESAT-6	Early secretory antigen target-6
ETH	Ethionamide
FK	Fructokinase
HEPA	High –efficiency particular air
HIV	Human immunodeficiency virus
HLA	Human leukocyte antigen
IGRA	Immunoglobulin release assay
IL2	Interleukin 2
INF-γ	Interferon –gamma
INH	Isoniazid
LTBI	Latent tuberculosis infection
MDR	Multidrug resistant
MHC	Major histocompatibility complex
MW	Molecular weight
NOS2	Nitric oxide synthase
NRAMP	Natural resistance –associated macrophage protein
PCR	Polymerase chain reaction
PPD	Protein purified derivative
PZA	Pyrazinamide
QFT	Quantiferon-test
QFT-G	Quantiferon –TB –gold
RD-1	Region of difference -1
RMP	Rifampicin
RNI	Reactive nitrogen intermediate
ROI	Reactive oxygen intermediate

List of Abbreviations (Cont.)

SM	Streptomycin
SODA	Superoxide dismutase A
TB	Tuberculosis
TGF	Transforming growth factor
TH	T –helper
TLR	Toll - like receptor
TNF	Tumor necrosis factor
TST	Tuberculin skin test
UK	United kingdom
WBC	White blood cells
WHO	World health organization

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Introduction

Tuberculosis (TB) remains a global public health problem, with an estimated 3 million deaths and 8 million new cases yearly. Most individuals infected with Mycobacterium tuberculosis control the bacilli and develop asymptomatic latent infection, a reservoir currently estimated to be one-third of the total human population (***Goswami et al., 2009).***

Latently infected individuals face a lifetime risk of reactivation with symptomatic TB disease depending upon their immune status. There is a dramatic increase in the risk of developing reactivation TB in Immunocompromised children or children with deficient immune system (patients receiving steroids for long periods) which had become increasingly common. So, there is an urgent need for more efficient ways of diagnosing latent TB (***Pai et al., 2008).***

The tuberculin skin test (TST) has long been used as a gold standard for the diagnosis of latent TB. TST is a measure of a delayed type hypersensitivity response to purified protein derivative (PPD). PPD is a mixture of mycobacterial antigens, some of which are shared between non tuberculous mycobacteria (NTM) and Mycobacterium bovis Bacille Calmette-Guerin (BCG) vaccine strains (***Van Zyl-Smit et al., 2009).***

As a result, the TST is not adequate for the diagnosis of latent TB in populations with high BCG coverage and/or high levels of NTM exposure (***Pai et al., 2008).***

The sensitivity also may be low in individuals with decreased immune function (i.e., AIDS and other immunosuppressive conditions, advanced TB, malnutrition). To increase the specificity of such tests, 2 M. tuberculosis-