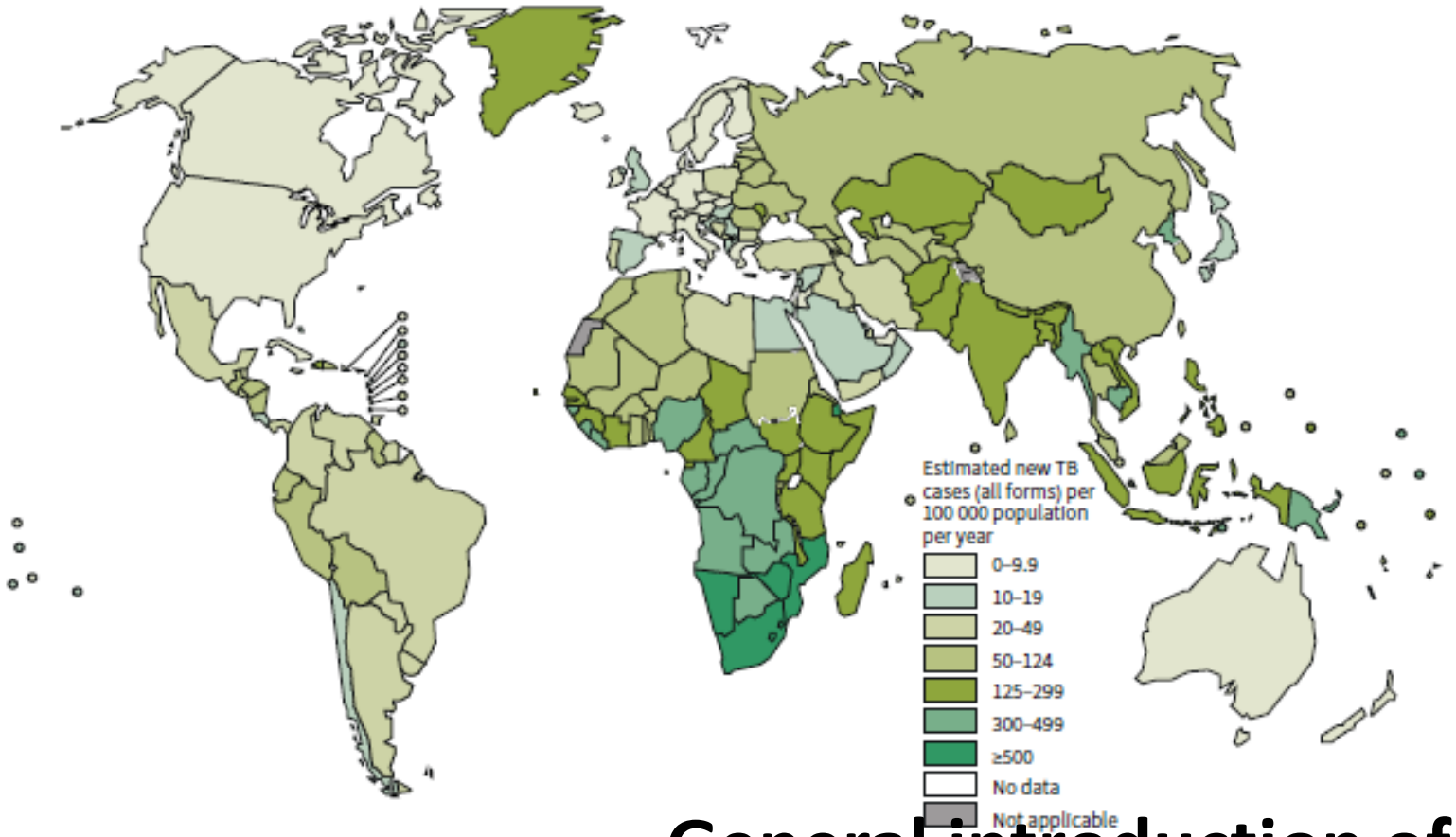
FIGURE 2.5

Estimated TB incidence rates, 2013



General introduction of the

QuantiFERON Gold In-Tube

Introduction of TB

- **Tuberculosis (TB)** remains one of the world's deadliest communicable diseases. In 2013, an estimated 9.0 million people developed TB and 1.5 million died from the disease.
- TB is slowly declining each year and it is estimated that 37 million lives were saved between 2000 and 2013.
- Death toll from the disease is still unacceptably high and efforts to combat it must be accelerated if 2015 global targets, set within the context of the Millennium Development Goals (MDGs), are to be met.

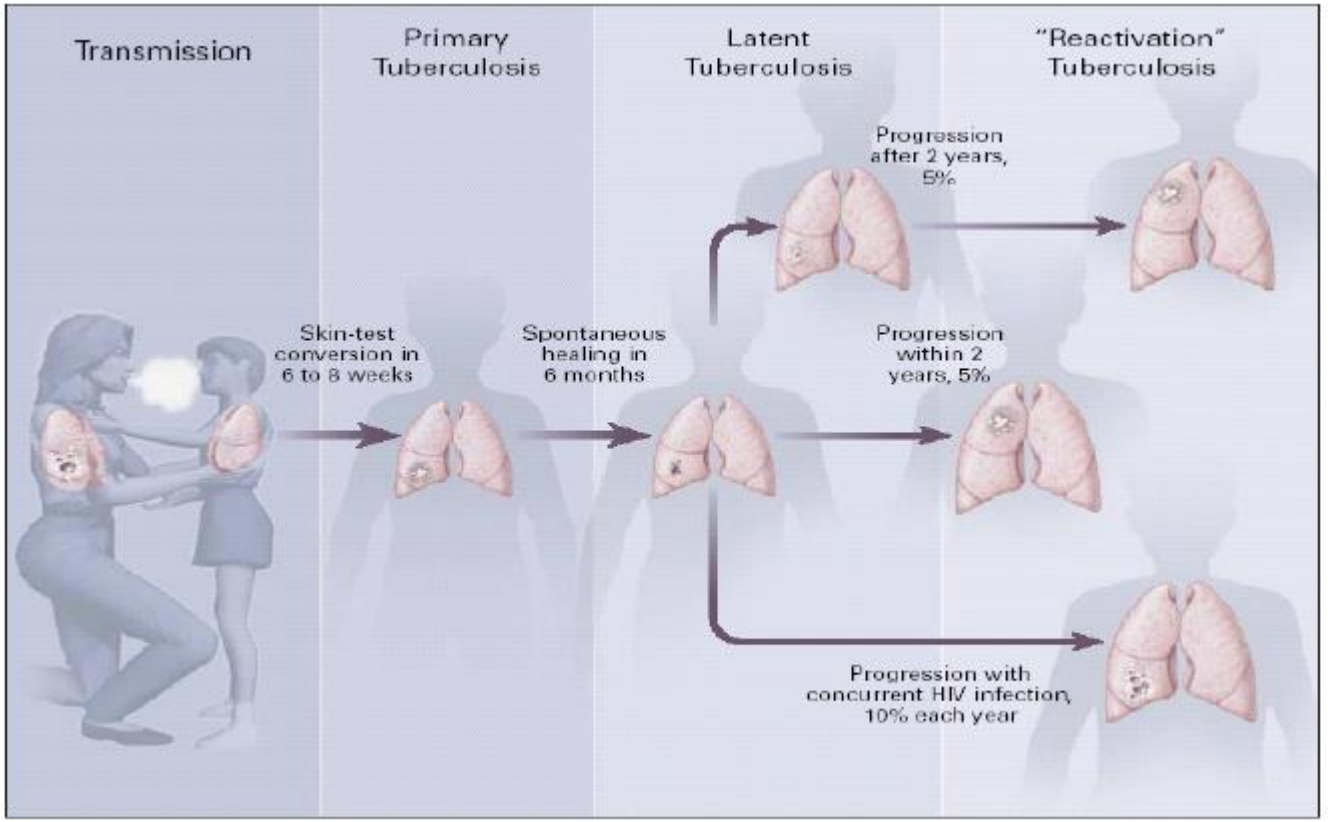


Figure 3. Transmission of Tuberculosis and Progression from Latent Infection to Reactivated Disease.

TB diagnostics

- Complete medical evaluation for TB must include a **medical history**, a **physical examination**, a **chest X-ray** and **microbiological examination** (of sputum or some other appropriate sample).
- It may also include a **tuberculin skin test(TST)**, other scans and surgical biopsy.
- The most common method for diagnosing TB worldwide is **sputum smear microscopy** (developed more than 100 years ago).

Introduction of TST

- TST known as the Mantoux screening test, tuberculin sensitivity test, Pirquet test, or PPD test for purified protein derivative.
- The person's medical risk factors determine at which increment (5 mm, 10 mm, or 15 mm) of induration the result is considered positive.[CDC]
- Alternative criteria include increases of 6, 12, 15 or 18 mm.[ROC]

IFN-γ release assay(IGRA)

- QuantiFERON-TB Gold (Liquid antigen version)
  - Liquid antigen version
  - Specific antigen : ESAT-6, CFP-10
  - FDA, Japanese MHLW, CE Marking, CDC and JST guidelines
- **QuantiFERON-TB Gold In Tube**
  - In Tube version
  - Specific antigen : ESAT-6, CFP-10, TB7.7
  - Replaces the liquid antigen version. FDA and Japan approved, Canadian approved….., CE Marked, US and European guidelines
- **T Spot TB**
  - Liquid antigen
  - Specific antigen : ESAT-6, CFP-10
  - Canadian approved, CE Marked, European guidelines, FDA approved.

QuantiFERON® TB Gold In-Tube

Blood Collection Tubes

Nil control —negative control

TB antigen —ESAT-6, CFP-10, TB7.7

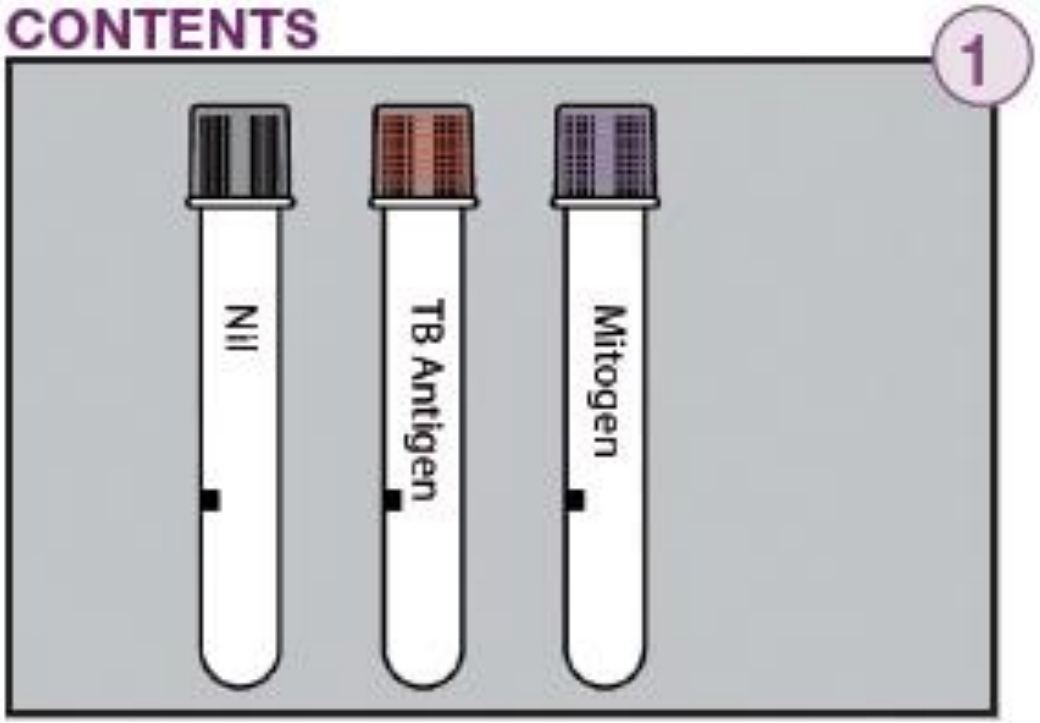
ex. M. kansasii, M. szulgai and M. marinum

Mitogen —especially warranted to the individual's immune status.

Reagent

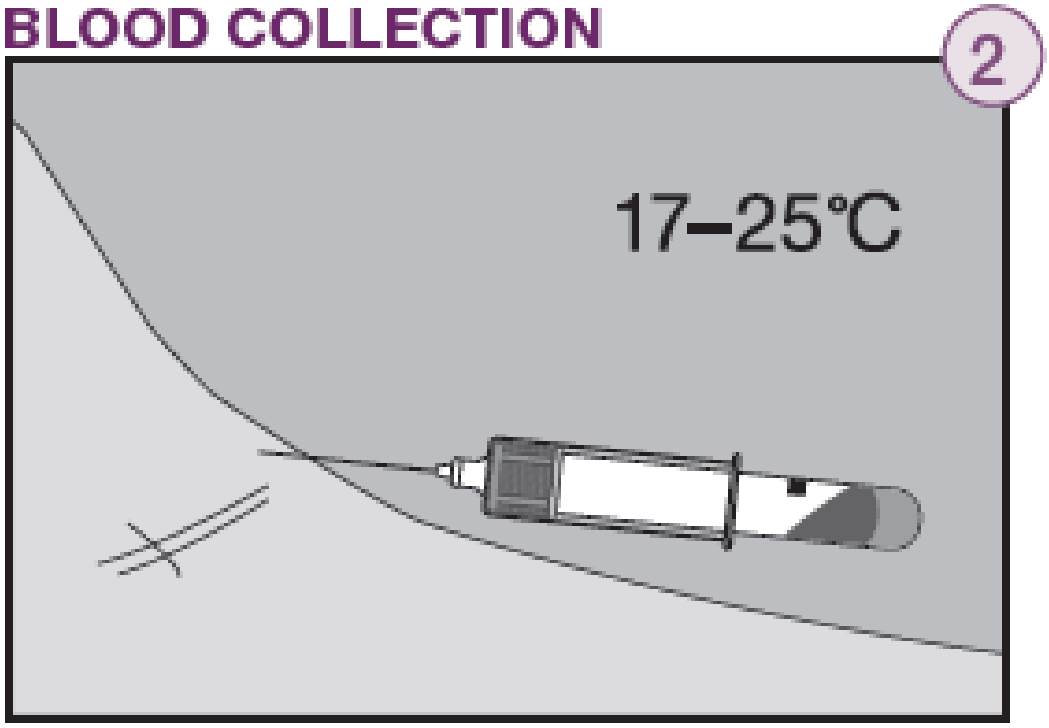
ELISA Kit —ELISA analysis

Sample collection



3x 1mL QFT blood collection tubes 1x Package Insert.

Sample collection

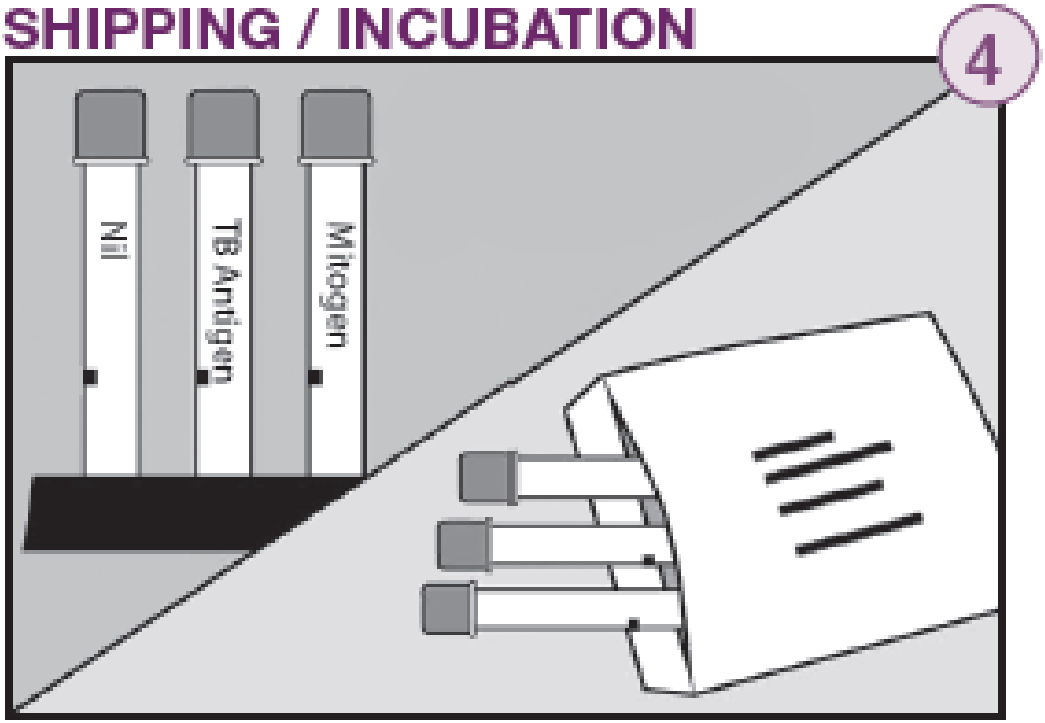


Collect **1mL** blood by venepuncture, up to the **black mark**.

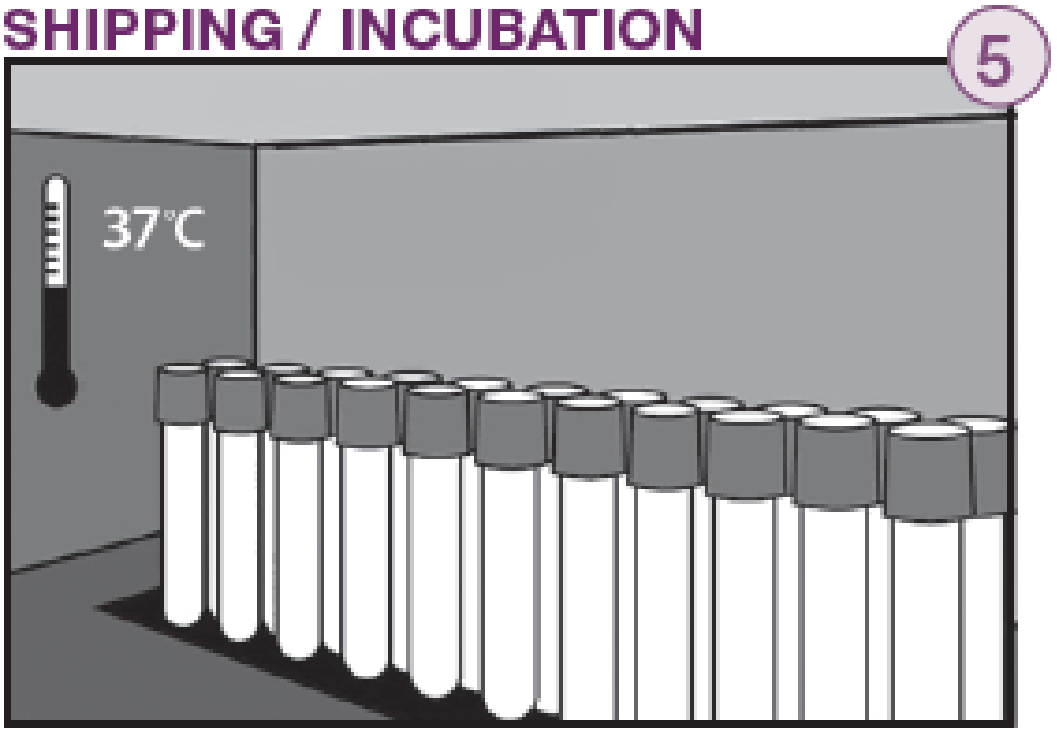
Sample collection

Immediately after filling tubes, shake them **ten (10) times**.

Sample collection



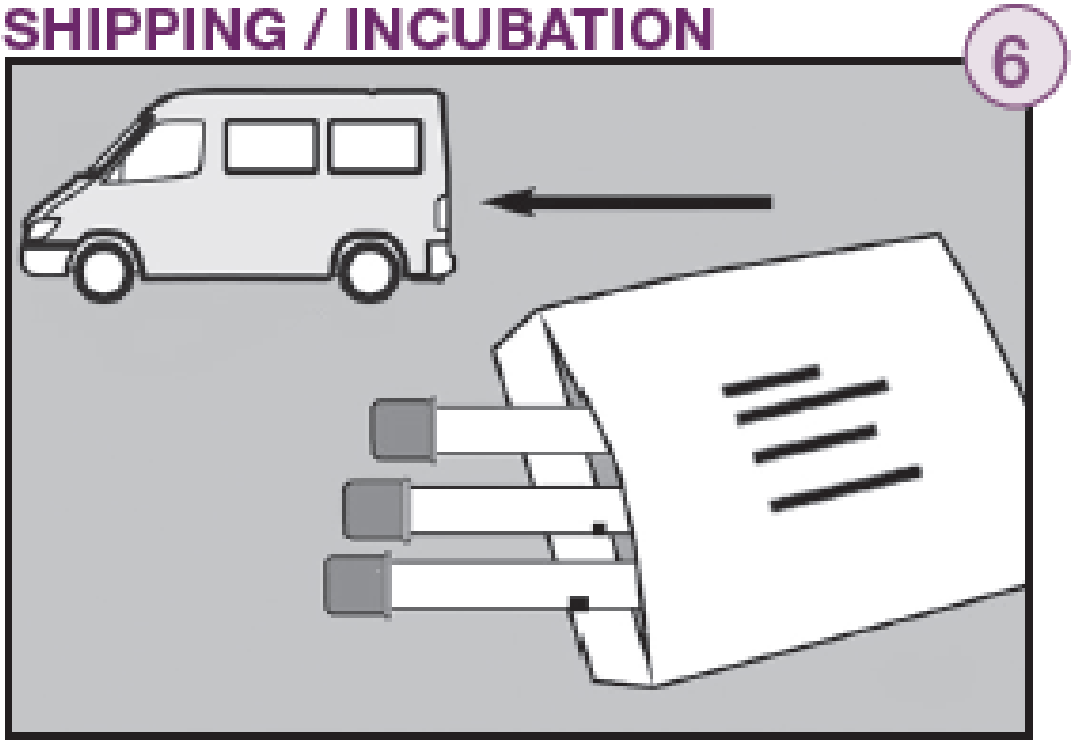
Sample collection



Blood must be incubated as soon as possible (and **within 16 hrs** of collection).

Incubate tubes upright at **37˚C for 16 – 24 hours**.

Sample collection



Ship incubated tubes to testing laboratory (within 3 days, if not centrifuged).

Centrifuge tubes for **15 minutes at 2000-3000g RCF**

中華民國風濕病醫學會

QFT採檢送檢建議2013.5.4

QTF Analysis

QFT results are interpreted using the following criteria:

Table 2. When Nil, TB Antigen, and Mitogen tubes are used

Nil (IU/ml)	TB Antigen minus Nil (IU/ml)	Mitogen minus Nil (IU/ml)*	QFT result	Report/Interpretation
≤8.0	< 0.35	≥ 0.5	Negative	*M. tuberculosis* infection NOT likely
	≥ 0.35 and < 25% of Nil value	≥ 0.5	Negative	*M. tuberculosis* infection NOT likely
	≥ 0.35 and ≥ 25% of Nil value	Any	Positive†	*M. tuberculosis* infection likely
	< 0.35	< 0.5	Indeterminate‡	Results are indeterminate for TB-Antigen responsiveness
	≥ 0.35 and < 25% of Nil value	< 0.5	Indeterminate‡	Results are indeterminate for TB-Antigen responsiveness
> 8.0§	Any	Any	Indeterminate‡	Results are indeterminate for TB-Antigen responsiveness

Assay: Cellestis QFT-4pt-read Q. C. Passed

Sample Id	Nil	TB Ag	Mitogen	TB Ag - Nil	Mitogen - Nil	Result
4070703471	0.046	0.032	1.411	-0.014	1.365	Negative
4070704019	0.042	0.036	0.399	-0.006	0.358	Indeterminate - Low Mitogen
4070704020	0.031	0.038	3.521	0.006	3.490	Negative
4070801908	0.073	4.191	0.028	4.118	-0.045	Positive
4070801909	0.036	0.052	0.741	0.015	0.705	Negative
4070805539	0.044	0.049	0.201	0.005	0.157	Indeterminate - Low Mitogen
4070805693	0.026	0.025	0.270	-0.001	0.244	Indeterminate - Low Mitogen
4070902441	0.029	0.028	0.657	-0.001	0.628	Negative
4070904694	0.088	0.057	0.206	-0.031	0.118	Indeterminate - Low Mitogen
4070905770	0.070	0.631	0.418	0.560	0.348	Positive
4070905911	0.042	0.058	4.466	0.016	4.424	Negative
4070905912	0.059	0.032	4.568	-0.027	4.509	Negative

Factors Associated with Indeterminate

- **Age**
  - The median age of the indeterminate group was 70.5 years.
- **Lymphocytopenia**
- **CRP elevation**
- **Hypoproteinemia**

CDC recommendations

Risk factors for *TB* infection

- Close contacts
- Foreign-born persons from areas or frequently visit areas that have a high incidence of active TB (e.g., Africa, Asia, Eastern Europe, Latin America, and Russia)
- Health-care workers
- Medical underserved, low-income populations
- Infants, children, and adolescents exposed to adults who are at increased risk for LTBI or active TB.

CDC recommendations

Risk factors for progression of infection to active tuberculosis

–HIV infection

–Infants and childrenaged <5 years

–Persons who are receiving immunosuppressive therapy

–Persons who were recently infected with TB(within the past 2 years)

–Persons with a history of untreated or inadequately treated active TB

–Persons with silicosis, diabetes mellitus, chronic renal failure, leukemia, lymphoma, or cancer of the head, neck, or lung

–Persons who weigh <90% of their ideal body weight

–Cigarette smokers and persons who abuse drugs or alcohol

–Medical underserved or low-income populations

reference

1. Global tuberculosis report 2014. ISBN 978 92 4 156480 9
2. ProgressionManagement of tuberculosis in the United States, NEJM 2001/07/19
3. http://www.who.int/en/
4. http://www.cdc.gov.tw/professional/index.aspx
5. http://www.cdc.gov/

reference

1. Wang CS, Chen HC, Yang CJ, Wang WY, Chong IW, Hwang JJ, et al. The impact of age on the demographic, clinical, radiographic characteristics and treatment outcomes of pulmonary tuberculosis patients in Taiwan Infection. 2008;36:335-40.
2. Kiwon Cho, M.D., Eunha Cho, M.D., Soohoon Kwon, M.D., Sanghyuk Im, M.D., In Sohn, M.D., Sookhee Song, M.D., Hyeok Kim, Ph.D., Suhyun Kim, M.D. Factors Associated with Indeterminate and False Negative Results of QuantiFERON-TB Gold In-Tube Test in Active Tuberculosis. 2012;72:416-425.

The end

&

Thanks for your attention

Millennium Development Goals(MDGs)

Millennium Development Goals by 2015:

- To eradicate extreme poverty and hunger
- To achieve universal primary education
- To promote gender equality and empower women
- To reduce child mortality
- To improve maternal health
- To combat HIV/AIDS, malaria, and other diseases
- To ensure environmental sustainability
- To develop a global partnership for development

MDGs about TB

BOX 1.3

The *post-2015 global TB strategy* at a glance

VISION	A TB-free world — zero deaths, disease and suffering due to TB
GOAL	End the global tuberculosis epidemic
MILESTONES FOR 2025	— 75% reduction in TB deaths (compared with 2015)
	— 50% reduction in TB incidence rate (less than 55 TB cases per 100 000 population)
	— No affected families facing catastrophic costs due to TB
TARGETS FOR 2035	— 95% reduction in TB deaths (compared with 2015)
	— 90% reduction in TB incidence rate (less than 10 TB cases per 100 000 population)
	— No affected families facing catastrophic costs due to TB

PRINCIPLES

1. Government stewardship and accountability, with monitoring and evaluation
2. Strong coalition with civil society organizations and communities
3. Protection and promotion of human rights, ethics and equity
4. Adaptation of the strategy and targets at country level, with global collaboration

QTF Analysis

QFT results are interpreted using the following criteria:

Table 3. When only QuantiFERON Nil and TB Antigen tubes used

Nil (IU/ml)	TB Antigen minus Nil (IU/ml)	QFT result	Report/Interpretation
≤8.0	< 0.35	Negative	*M. tuberculosis* infection NOT likely
	≥0.35 and < 25% of Nil value	Negative	*M. tuberculosis* infection NOT likely
	≥ 0.35 and ≥ 25% of Nil value	Positive*	*M. tuberculosis* infection likely
> 8.0†	Any	Indeterminate‡	Results are indeterminate for TB-Antigen responsiveness

TST result

- 5 mm or more is positive in
  - An HIV-positive person
  - Persons with recent contacts with a TB patient
  - Persons with nodular or fibrotic changes on chest X-ray consistent with old healed TB
  - Patients with organ transplants, and other immunosuppressed patients
- 10 mm or more is positive in Recent arrivals (less than five years) from high-prevalence countries
  - Injection drug users
  - Residents and employees of high-risk congregate settings
  - Mycobacteriology lab personnel
  - Persons with clinical conditions that place them at high risk
  - Children less than four years of age, or children and adolescents exposed to adults in high-risk categories
- 15 mm or more is positive in
  - Persons with no known risk factors for TB

- The Food and Drug Administration (FDA) announced that QuantiFERON-TB GOLD test (QFT-G; Cellestis Ltd., Carnegie, Victoria, Australia) can be alternatively used for TB diagnosis.

- In previous study in Taiwan, elderly patients with pulmonary TB were more likely to present with negative sputum smears and had more pleural effusion but fewer cavity findings on chest radiography.