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.\textsuperscript{CDC}
- Alternative criteria include increases of 6, 12, 15 or 18 mm.\textsuperscript{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

CONTENTS

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**
QTF Analysis

QFT results are interpreted using the following criteria:

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

* For Mitogen minus Nil, ≥ 0.5 indicates positivity; < 0.5 indicates negativity.
<table>
<thead>
<tr>
<th>Sample Id</th>
<th>Nil</th>
<th>TB Ag</th>
<th>Mitogen</th>
<th>TB Ag - Nil</th>
<th>Mitogen - Nil</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>4070703471</td>
<td>0.046</td>
<td>0.032</td>
<td>1.411</td>
<td>-0.014</td>
<td>1.365</td>
<td>Negative</td>
</tr>
<tr>
<td>4070704019</td>
<td>0.042</td>
<td>0.036</td>
<td>0.399</td>
<td>-0.006</td>
<td>0.358</td>
<td>Indeterminate - Low Mitogen</td>
</tr>
<tr>
<td>4070704020</td>
<td>0.031</td>
<td>0.038</td>
<td>3.521</td>
<td>0.006</td>
<td>3.490</td>
<td>Negative</td>
</tr>
<tr>
<td>4070801958</td>
<td>0.073</td>
<td>4.191</td>
<td>0.028</td>
<td>4.118</td>
<td>-0.045</td>
<td>Positive</td>
</tr>
<tr>
<td>4070801909</td>
<td>0.036</td>
<td>0.052</td>
<td>0.741</td>
<td>0.016</td>
<td>0.705</td>
<td>Negative</td>
</tr>
<tr>
<td>4070805559</td>
<td>0.044</td>
<td>0.049</td>
<td>0.201</td>
<td>0.006</td>
<td>0.157</td>
<td>Indeterminate - Low Mitogen</td>
</tr>
<tr>
<td>4070805693</td>
<td>0.026</td>
<td>0.025</td>
<td>0.270</td>
<td>-0.001</td>
<td>0.244</td>
<td>Indeterminate - Low Mitogen</td>
</tr>
<tr>
<td>4070902441</td>
<td>0.029</td>
<td>0.028</td>
<td>0.657</td>
<td>-0.001</td>
<td>0.628</td>
<td>Negative</td>
</tr>
<tr>
<td>4070904694</td>
<td>0.088</td>
<td>0.057</td>
<td>0.206</td>
<td>-0.031</td>
<td>0.118</td>
<td>Indeterminate - Low Mitogen</td>
</tr>
<tr>
<td>4070905779</td>
<td>0.070</td>
<td>0.631</td>
<td>0.418</td>
<td>0.560</td>
<td>0.348</td>
<td>Positive</td>
</tr>
<tr>
<td>4070905911</td>
<td>0.042</td>
<td>0.058</td>
<td>4.466</td>
<td>0.016</td>
<td>4.424</td>
<td>Negative</td>
</tr>
<tr>
<td>4070905912</td>
<td>0.059</td>
<td>0.032</td>
<td>4.568</td>
<td>-0.027</td>
<td>4.509</td>
<td>Negative</td>
</tr>
</tbody>
</table>
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 children aged <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
2. Progression Management of tuberculosis in the United States, NEJM 2001/07/19

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
### 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

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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.