出國報告(出國類別:進修)

赴新加坡進行研習結核病國際指標 接軌以及WHO後2015防治策略討論

服務機關:衛生福利部疾病管制署

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派赴國家:新加坡

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摘要

新加坡自 1997 年實施「新加坡結核病根除計畫」(Singapore Tuberculosis Elimination Programme, STEP),結核病發生率自 56 例(每 10 萬人)下降至 2006 年 36 例(每 10 萬人),成果卓著、在國際結核病防治經驗上享有盛譽。然該國對於外籍人士、多重抗藥性結核病等挑戰,仍積極調整國家政策因應。

本次研習行程共計參訪新加坡衛生部、結核病防治部門(TBCU)與中心參考實驗室。新加坡透過實施都治計畫、落實結核病治療追蹤與強化接觸者檢查與預防性治療來達到良好結核病防治成績。藉由與醫院及實驗室資訊系統銜接,得詳實掌握個案通報與定期返診情形。對於境外移民結核病與 MDR TB 病患通報亦進行密切監控。且透過就醫津貼補助,鼓勵病患至指定醫院接受標準化抗結核藥物治療,提升疾病完治率與降低抗藥比率。

接觸者檢查與LTBI預防性治療部分,新加坡依治療者機構特性與發病風險, 提供合適治療處方。另近年亦積極投注經費、增聘人力以建立更精緻之個案疫調 與接觸者檢查策略。新加坡對於防疫積極野心與策略值得我國作為參考。

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壹、目的

結核病十年減半為全球重點防治工作,我國目前亦致力推行各項結核病 防治工作,近年來國內不論在結核病發生率或死亡率上,雖有逐年下降的趨 勢,但仍面臨諸多防治的挑戰。

WHO 後 2015 年全球結核病防治策略指出,除了在治療與疫苗之研發至為重要以外,良好的國家監測指標、重點族群監測以及個案管理,更是達成 2035 年消除結核病之重要關鍵。

新加坡自 1997 年實施「新加坡結核病根除計畫」(Singapore Tuberculosis Elimination Programme, STEP),結核病發生率自 56 例(每 10 萬人)下降至 2006 年 36 例(每 10 萬人),成果卓著、在國際結核病防治經驗上享有盛譽。然而在近年人口老化、HIV合併感染、外籍人士以及多重抗藥性結核病等挑戰下,發生率降幅已漸趨緩,該國亦積極調整國家政策因應。

藉由本次參訪,與新加坡國家 STEP 負責同仁、結核病防治部門主管共同研商討論,瞭解該國面對 WHO 後 2015 年防治策略及進展,作為我國 2035 消除結核病計畫參考,並積極參與國際指標接軌之評估依據。

貳、行程

貝/ 11/1王	T	
日期	研習內容	地點及指導者
2014/12/14	臺北-新加坡	抵達新加坡
2014/12/15	• presentation of STEP	TB Control Unit,
	STEP Registry:Contact	Singapore/ Prof. Yee-Tang
	Investigations	Wang, Director TBCU
	Contact Investigations in the	
	Elderly	
	Contact Clinic	
2014/12/16	STEP Registry: Case notifications	TB Control Unit,
	and surveillance	Singapore/ Dr. Khin
	STEP Registry: MD117	Mar, Head, STEP Registry
	surveillance module and defaulters	
	TB in foreigners	
	Polyclinic DOT: case monitoring,	
	defaulters	
2014/12/17	Central TB Lab, Singapore General	Singapore General
	Hospital	Hospital/ Dr. Sng Li-Hwei,
	Communicable Diseases Division,	Head, CTBL
	Ministry of Health	Ministry of Health/ Jayne
		Lim, Assistant Director,
		Communicable Diseases
		Division
2014/12/18	新加坡-臺北	返抵臺北

參、參訪過程

Day 1

一、結核病流病概況:

(一)結核病通報數與發生率:

2013 年新加坡總計通報 2962 名結核病個案,其中 2028 人為結核病新案且身分別為新加坡居民(公民、永久居留者)或長期停留者,新案發生率為 37.6 例/每 10 萬人。就長期趨勢而言,新案發生率相較於 10 年前(2002 年)降幅約 8% (表一)。

表一、新加坡居民及長期居留移民結核病新案發生率

	New Cases			Incidence rate	Index		
Year	Pulmonary ¹	Extra pulmonary	Total	Pulmonary ¹	Extra pulmonary	Total	(base 2002)
2002	1,494	208	1,702	35.8	5.0	40.8	100.0
2013	1,750	278	2,028	32.4	5.1	37.6	92.2

(二)結核病個案年齡與性別分佈

在 2013 年所通報新案之中,43.6%個案年齡大於(含)50 歲,個案年齡中位數約 50 歲;男性佔 62.9%。各年齡層與性別發生率詳可參見表二。

表二、新加坡居民依年齡別結核病發生率

				Incidence ra	ate per 100,000	population*
Age (Yrs)	Male	Female	Total (%)	Male	Female	Total
0 – 4	1	0	1 (0.1)	1.1	0.0	0.5
5 – 9	1	1	2 (0.2)	1.0	1.0	1.0
10 – 14	3	1	4 (0.3)	2.6	0.9	1.8
15 – 19	17	19	36 (2.5)	13.1	15.2	14.1
20 – 29	57	64	121(8.5)	22.1	24.2	23.2
30 – 39	87	78	165 (11.6)	30.1	24.9	27.4
40 – 49	169	68	237 (16.7)	54.3	21.4	37.7
50 - 59	247	56	303 (21.3)	82.7	19.0	51.0
60 - 69	178	58	236 (16.6)	98.5	31.0	64.1
70 – 79	149	44	193 (13.6)	186.7	45.6	109.4
+ 08	77	45	122 (8.6)	252.5	86.9	148.3
Total	986	434	1,420 (100.0)	52.1	22.2	36.9

(三)結核病與愛滋共病情形

依據 2010 年統計資料,身分別為新加坡居民之結核病患,約

73%可取得 HIV 檢驗資料,HIV 陽性率約 4.5%。而非新加坡居民之結核病患,能掌握 HIV 檢驗比率則約為 70% (如圖一)。Dr. Wang另補充說明,在 TBCU 接受治療的病人,則有逾九成可掌握其 HIV 狀態。

HIV and TB

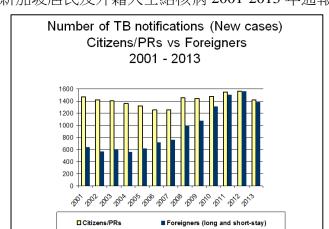
2010 data from TB Notification Registry:

Citizens / PRs: 73% of TB cases had known HIV status Of these, 4.5% were HIV co-infected Non-citizens / PRs: 70% of TB cases had known HIV status Of these, 2.0% were HIV co-infected Non-citizens / PRs: 70% of TB cases had known HIV status Of these, 2.0% were HIV co-infected Non-citizens / PRs: 70% of TB cases had known HIV status Of these, 2.0% were HIV co-infected

▲圖一、新加坡歷年結核病個案 HIV 陽性率

(四)結核病個案國籍組成

新加坡族群組成多元,除了新加坡居民(公民或具有永久居留身分者)(約384萬人口),還有一大部分外籍住民為持停留簽證於新加坡內工作、求學或依親(約155萬人口)。當新加坡居民通報結核病個案數近年逐步下降,外籍結核個案通報數却急遽上升。2013年統計資料指出兩者個案數已幾乎相當(如圖二)。

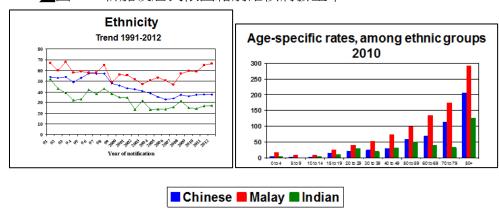


▲圖二、新加坡居民及外籍人士結核病 2001-2013 年通報數比較

除了多元移民來源的特色以外,新加坡居民自身亦是由多種民

族組成,華人佔 74.2%為主要族群,馬來人為第二大族群佔 13.3%, 其餘尚有印度人(9.2%)與其他族群(3.3%)。分析不同民族的結核病 發生率,華人約 35 例(每 10 萬人口)、馬來人約 65 例(每 10 萬人口)、 印度人約 30 例(每 10 萬人口)(如圖三)。綜合而言,馬來裔的結核病 患具有較嚴重的傳染力、共病與經濟弱勢問題。有關不同民族或外 來移民的疾病情形將於第二天研習進行更詳細說明。

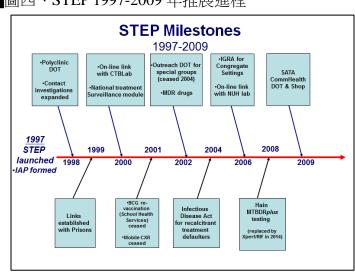
▲圖三、新加坡居民依國籍別結核病發生率



二、新加坡結核病根除計畫(STEP)

(一)緣起與主軸

1987年至1996年期間,新加坡的結核病發生率長期停滯於56例(每10萬人口),該國政府決定自1997年開始採行結核病根除計畫STEP(比我國推行十年減半計畫早了10年),推展步驟詳如圖四。



▲圖四、STEP 1997-2009 年推展進程

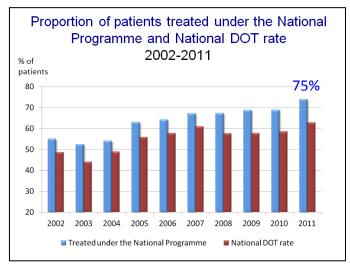
STEP 防治主軸包含實施都治計畫、落實結核病監測與強化接觸者檢查與預防性治療:

1. 都治計畫:

該國 DOT 模式係由病人至全國 18 個綜合診療所 (polyclinc)或至 TBCU,由診所經驗豐富的護理人員提供抗結核藥物並評估服藥情形。

目前全國約 75%病人於 TBCU 治療,這些病人都治執行率 80%,剩餘 20%則因身體虛弱無法親自到點服藥。(如圖五)

▲圖五、新加坡病患於 TBCU 治療比率與 DOT 執行率



2. 落實結核病監測:

新加坡的結核病監測體系包含公立實驗室系統與結核病治療成效監測系統(Treatment Surveillance Module)。

新加坡的結核病培養與鑑定應全數送至兩家公立醫院執行,新加坡中央醫院(Singapore general hospital)與國立大學醫院(National university hospital)。TBCU可直接取得上述兩間實驗室檢驗結果,當TBCU發現有細菌學陽性但診療醫師未通報的情形,會立即致函請醫師說明原因。透過該監測機制,每年約發現20至30例未即時通報案例。

另對於病人歷次返診情形,診療醫師均須填寫制式表格回

覆予 TBCU。該表格上亦會載明醫囑病人下次返診日期。倘逾返診日期未更新病人治療進度,TBCU亦立即致函提醒醫師。

3. 強化接觸者檢查與預防性治療:

針對家戶、職場與密集機構(護理之家、矯正機關、精神病院) 之密切接觸者進行 TST 篩檢,並針對全年齡層進行 LTBI 治療。 有關接觸者檢查與預防性治療將於後續課程進行更詳細說 明。

(二)近期新規劃

TBCU於 2013 年自衛生部取得額外資金補助,以規劃進一步防治策略,包含重新啟動 DOT 外展服務(送藥至行動不便病患家中)、增設病患至 TBCU治療補助津貼、建立結核菌菌株分子分型資料庫、於接觸者檢查廣泛運用 IGRA。

(三)目前瓶頸

STEP 推動迄今,最初十年成效極佳,由 1996 年 56 例(每 10 萬人), 2006 年已降至 36 例(每 10 萬人),但近 10 年再度面臨發生率停滯 不前的瓶頸。Dr. Wang 表示延遲診斷或延遲通報可能是主因之一。 病人通報時都會請醫師協助評估臨床症狀開始時間,並紀錄於通報 表格。先前分析發現,50%病人於通報前已超過 4 週有咳嗽症狀。

三、接觸者檢查與 LTBI 治療:

(一)接觸者檢查概況

以新加坡每年約 3000 例通報病患,其中約 2000 例為 MTB 培養陽性之指標個案;這些有傳染力個案約有 8000 名接觸者(平均每位指標個案約有 4 名接觸者)。對於接觸者疫調模式,係由 TBCU工作人員以書信通知指標個案至 TBCU contact clinic 接受訪問以釐清接觸者名單。對於不合作之傳染性個案,倘其工作可能接觸結核病易感族群(如個案職業別為教師、醫護工作者等),則將進一步依新加坡傳染病防治法要求其提供接觸者資訊。

TBCU 定期監測接觸者執行情形。依據 2013 年統計,約 25% 塗陽指標個案通報後未曾被登錄任何接觸者(已較 2000 年 30% 改善), Dr. Wang 表示這部分將作為近年重點改進項目。資訊系統登錄在案的接觸者完成檢查比率約 98%。TST 或 IGRA 檢查陽性之接觸者,後續啟動 LTBI 治療比率約 93%、LTBI 完治率 75%。

(二)檢查工具

STEP 推行之初,接觸者檢查工具以 CXR 與 TST 為主(一般接觸者以 15 mm 為陽性判定基準、糖尿病及免疫低落等共病患者以 10 mm 為判定基準)

但近年亦逐步規劃於各類高危險族群結核病接觸者使用 IGRA 進行檢測。2007年由密集機構首先採用 IGRA、2009年納入 MDR TB 接觸者、2013年擴大至職場密切接觸者與校園師生接觸者、2014年再納入家戶內 5歲以上之密切接觸者(5歲以下仍維持以 TST 檢測)。對於免疫低弱者或洗腎病患接觸者則以 T-SPOT 替代 IGRA,以提升敏感度。在逐步擴大推動 IGRA 數年間,新加坡亦進行審慎評估,確認檢驗結果得與 TST 一致。

(三)檢查流程

TST(或 IGRA)操作時程依指標個案傳染力而異:

- 指標塗片陰性(可能培養 MTB 陽性):空窗期結束後(window period,與指標個案接觸後≥8週)結束後施測一次。
- 2. 指標塗片陽性:
 - (1) 應即刻施測。倘該次結果為陰性,則待空窗期結束後再施 測一次。
 - (2) 對於空窗期施測陰性個案,如符合以下條件則給予 prophylaxis: 5 歲以下接觸者或 HIV 陽性接觸者。
- 2. 對於 QFT 檢測結果為無法區分者(indeterminate),應釐清是否 為免疫低落者:

- (1) 免疫低落者應額外施測 T-SPOT
- (2) 倘無證據指出為免疫低落者,則待空窗期後再作檢測。
- (3) 倘該次 indeterminate 結果為空窗期後施測者,則以 CXR 確認該接觸者是否為活動性結核病患。

以下對象應接受 CXR 檢查:

- 1. 所有 TST 或 IGRA 陽性接觸者
- 2. 欲接受 prophylaxis 之接觸者
- 3. 以下對象無論 TST/IGRA 結果都應執行 CXR 檢查:具有疑似 結核病症狀之接觸者、MDR TB 指標接觸者、護理之家接觸者、 精神病患(因無法自述臨床症狀)、糖尿病患、HIV 陽性或免疫 低落接觸者、罹患腎疾病、塗陽指標之接觸者(且難以取得聯 繫)

(四)LTBI 治療處方

新加坡對於不同族群、考量其順服性高低,提供各種種類與期程處方:

- 1. 六個月 INH: 15 歲以上接觸者,且非 HIV 陽性、指標 MTB 菌株對 INH 敏感
- 2. 九個月 INH:
 - (1) 15 歲以下兒童接觸者;或
 - (2) 密集機構(矯正機關、護理之家、精神機構)內接受 DOPT 之接觸者;或
 - (3) HIV 陽性接觸者。
- 3. 四個月 RIF:
 - (1) 15 歲以上接觸者,指標 MTB 菌株對 INH 抗藥,但對 RIF 敏感;或
 - (2) 使用 INH 具副作用者(逐案特殊處理);或
 - (3) 矯正機關內接觸者、且預計於九個月內離開機構者;或

(4) 矯正機關內接觸者、且已知為 B 或 C 肝慢性帶原。

4. 六個月 RIF:

- (1) 15 歲以下兒童接觸者,指標 MTB 菌株對 INH 抗藥,但對 RIF 敏咸;或
- (2) 兒童接觸者使用 INH 具副作用者(逐案特殊處理);或
- (3) HIV 陽性接觸者,且指標 MTB 菌株對 INH 抗藥,但對 RIF 敏感。

(五)LTBI 治療副作用監測

我國自 2015 年 1 月推動全年齡層 LTBI 治療之試辦計畫,新加坡很早即有相關經驗,故我們特別就副作用監測請教該國作法。
TBCU 對於>35 歲接觸者、曾有肝病或酒精成癮史接觸者(不論年齡)、或懷孕接觸者(不論年齡)三類對象,皆會檢測治療前的 AST/ALT 基礎值。對於>60 歲接受 LTBI 治療者,另於開始治療後第 4 週與 16 週再次檢測肝功能。所有接觸者接受治療前皆會被給予用藥副作用衛教。

診療醫師依據 AST/ALT 情形將決定是否中斷 LTBI 治療,且標準比結核病治療更為嚴謹:

- 1. AST/ALT上升超過正常值二倍,則中斷治療。
- AST/ALT 上升值未超過二倍,須徵詢接觸者意願及說明接受 治療的益處。倘同意繼續治療,應每隔周持續監測肝功能兩個 月。如肝指數仍上升,則中斷治療。
- 一旦中斷治療即不再重新給藥。
 另外,倘個案出現疑似肝炎副作用,處置方式如下:
- 1. 暫停 LTBI 治療並檢測 AST/ ALT,並依據上述原則決定是否中 斷治療
- 2. 如果 AST/ ALT 檢驗值極度異常,應另檢測病毒性肝炎指標

Day 2

一、結核病個案通報與治療過程監測

(一) 通報表格(MD 532-92)

所有通報個案皆須完成 MD532-92 表格(參見相關表格章節)。 該表格內容與我國法定傳染病通報系統或中央傳染病追蹤管理系 統非常相近,另有幾點特色如下:

- 居留狀態:前面提及新加坡屬於移民多元的國家,故結核病個 案通報之初即密切掌握其居留身分
- 2. 共病狀態:該表格要求診療醫師應釐清個案是否有糖尿病、接 受類固醇治療、免疫低落相關疾病、HIV、末期腎臟病等共病
- 3. 通報前咳嗽史:診療醫師應釐清個案通報結核病前,何時開始 出現臨床症狀(該項資訊亦被作為監測病人是否被延遲診斷的 指標)

(二) 結核病治療與都治

由於在新加坡就醫非常昂貴,例如一般門診加上驗痰就須花費約 130 新幣(約 3000 台幣)。政府對新加坡居民(公民或具永久居留身分者)雖已提供相關補助,但就醫費用仍不容小覷。為增進病患就醫意願並鼓勵至 TBCU 接受標準結核病治療,TBCU 自 2014 年4 月開始提供來就醫之新加坡居民更多就醫津貼:新加坡公民每次就醫僅須支付 10 元新幣(約 240 新幣)、具永久居留身分者則僅須支付 15 元新幣(約 360 新幣)。

DOT 藥物與 MDR TB 治療為免費以外,非政府組織 SATA (Singapore Anti-Tuberculosis Association)對經濟弱勢病患額外提供每月 40 元新幣購物券、完治時再提供 100 元新幣購物券補助(完整療程約可領到 300 元新幣,合約 7000 元台幣),對經濟弱勢者確為重要誘因。

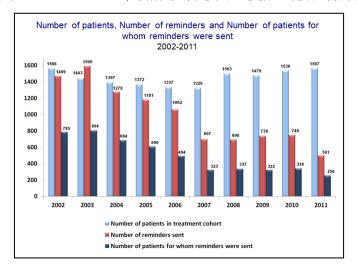
(三) 病人追蹤機制(MD 117):

為確保病患接受標準化抗結核藥物治療,每次病患回診後,診療醫師應即刻將該次診療情形回報 TBCU,尤其每次都應提供病患下次返診日期。倘逾返診日期超過兩周未更新病人治療進度,

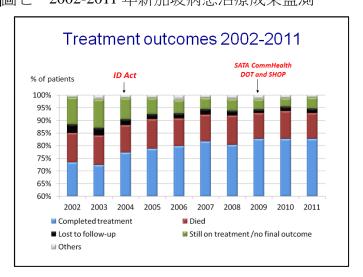
TBCU 則立即致函提醒醫師(我國中央傳染病追蹤管理系統亦有相關機制,但由地段護士逕行至系統下載相關名單)。

統計資料指出,自 2002 年開始該措施以來,提醒函發送數已顯著下降(如圖六);另一方面,治療成功比率亦逐年提升(如圖七)。

圖六、2002-2011 年新加坡病患回診提醒函發送數統計



▲圖七、2002-2011 年新加坡病患治療成果監測



二、外籍人士結核病情形

(一) 通報數

外籍人士通報結核病人數於 2002-2013 年期間大幅增加,2002年通報數約 560人,2013年已增加至 1380人(同期間新加坡居民通報數大約 1400人),其中持短期與居留(工作、依親、學生等)簽證者比例各半(詳細簽證分類如表三所示),國籍別則以印尼、菲律賓居多。外國籍通報個案平均年齡約 35歲,較新加坡居民病患年輕。

表三、新加坡外籍人士依入境簽證別統計

Distribution of non-residents with new tuberculosis by pass category/status, 2009 – 2013

Page estagon, l'atatua		No. o	f new TB cases	notified				
Pass category / status	2009	2010	2011	2012	2013			
Long-Term Immigration Pass Holders Residing in Singapore								
Work Permit Holders	403	403	442	458	434			
Employment Pass Holder	32	41	47	53	52			
Other Pass Holders *	89	106	104	132	122			
Sub-total	524	550	593	643	608			
Short Stay Foreigners								
Work Permit Applicants	218	329	462	528	389			
Visitors **	220	253	237	238	216			
Others ***	113	181	207	151	168			
Sub-total	551	763	906	917	773			
Total	1,075	1,313	1,499	1,560	1,381			

Professional pass holder, dependent pass holder, long-term social visit pass holder and student pass holder and S pass holder

(二) 體檢作業與結核病治療:

新加坡對於申請居留簽證者須辦理健康檢查(包含胸部 X 光檢查)。不合格者則依身分別得選擇是否留在新加坡治療。我們將體檢對象與治療方式整理如表四。

▲表四、外籍人士各居留原因別體檢要求與結核病治療

居留類別	X光檢查	結核病治療方式
work permit	是	遣返
student pass	是	遣返
S pass	是	TBCU 治療或遣返
dependent pass	是	TBCU 治療或遣返
employment pass	否	不限制

由於新加坡有許多外籍工作者,依月薪低至高可區分為 work permit(低階技術人員)、S pass (中階技術人員)、emplyment pass (高

^{**} Short term social visitor

^{***} Professional visit pass applicant, dependent pass applicant, long-term social visit pass applicant, student pass applicant, employment pass applicant, S pass applicant and illegal immigrant

階技術人員),後兩者居留滿一定期限後可申請成為永久居民(PR)。 對於持有 S pass 或依親居留者,倘取得雇主或親屬支持、並加入 DOT 服藥者,方得留於新加坡治療,且必須於 TBCU 就醫。這方 面政策與我國相近。外籍學生則一律遣返。

對於須遣返者,一般結核個案須治療至塗片陰轉、MDR TB 個案須治療至有連續兩次痰液陰轉,亦與我國政策相近。

新加坡提供 MDR TB 免費治療,包含外籍人士。但一般結核個案倘為外籍人士,須全額自費、無任何政府經費補助。故(未公開)統計資料指出,外籍人士結核病有約 20%以上未能獲得痰塗片與培養資料,係目前結核病防治難題之一。

另新加坡自 2013 年開始監測結核菌陽性菌株資料,迄今尚無 任何由外籍人士傳染給新加坡居民的聚集事件案例。

(三) 跨國轉介作業

我們另詢問新加坡對於遣返或離境的結核病患,是否會將疾病資料轉介予病患母國公衛體系。由於新加坡鄰近國家本身多為TB/MDRTB高負擔國家,故新加坡對於一般結核個案並不會特別辦理轉介作業,僅建議回國後應自行求醫;但對於MDRTB病患,因屬於較嚴重公衛議題,故除協助個案於母國尋得合適診療醫師,另透過IHR國際窗口通知母國,以掌握個案資訊。

Day 3

一、結核病患門診、接觸者門診與陳篤生醫院參訪

TBCU 的結核病患門診於 2013 年竣工。由於結核病是空氣傳播疾病,故所有診間均大量採用自然通風。另接觸者檢查是新加坡接續重點業務,接觸者門診目前正重新翻修;但與診間工作人員訪談時,得知TBCU 近年陸續增聘多位護理人員,以提供更高品質的接觸者調查。

另於參訪陳篤生醫院的病房時,我們發現該院對於病房訪客管理極為嚴謹。所有訪客皆須於櫃檯登記身分資料,且進入建物前皆須刷卡登

錄。Dr. Wang 表示,作為 SARS 期間指定治療醫院,該項管控措施係為提供完善接觸者追蹤紀錄;並且類似登記設施已於新加坡公立醫院廣泛採用。

二、中央參考實驗室參訪

第一天研習曾提及,新加坡境內的結核病培養與鑑定應全數送至兩家公立醫院執行,新加坡中央醫院(Singapore general hospital, SGH)與國立大學醫院(National university hospital, NUH)。TBCU可直接取得上述兩間實驗室檢驗結果並進行監測。其中新加坡中央醫院是新加坡第一大醫院,規模大於陳篤生醫院,負責新加坡約80%結核病檢體量。我們第三日即至該醫院拜會結核病實驗室負責人Dr. Sng。

SGH 每年結核病檢體量約 40,000 件,其中約 3,000 件(7.5%)檢出 MTBC。我們首先注意到,實驗室為處理大量檢體(包含結核病與其他 各式疾病或院內檢體),發展出極完善的輸送管道(如照片所示)以將檢體 分送至各疾病實驗室。

我們首先請教 Dr. Sng 有關結核病檢驗報告時效, AFS 為 24 小時、培養為 21 天、菌種鑑定加藥敏約 28 天, 與我國對認可實驗室要求相近。

結核菌中央實驗室除積極參予國際品質認證與協助國內實驗室 AFS 進行品質管理,另亦廣泛採納各國先進檢測儀器,詳可參見該院所 出版年報資料(Department of Pathology Annual Report 2013)。

三、新加坡衛生部參訪

我們接續拜會衛生部傳染病防治組(Communicable Diseases Division)負責結核病防疫政策規劃的 Ms. Lim。Ms. Lim 除仔細為我們講解新加坡公衛體系與分工以外,亦針對我們所請教外籍人士結核病情形,提供國家政策觀點的建議。

從相關數據,我們看到外籍人士確為新加坡結核病防治重點。2013年抗藥分析顯示,新案 INH 抗藥比率於新加坡出生國人為 2.9%、境外出生者(含國人與非新加坡居民)約為 7%;新案 MDR 抗藥比率於新加坡

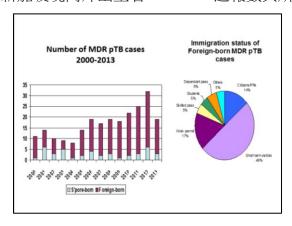
出生國人為 0.3%、境外出生者約為 2.6%; 再治 MDR 抗藥比率於新加坡出生國人為 1.6%、境外出生者約為 19% (詳如表五)。

表五、新加坡居民(含本地出生與外裔)與外籍人士抗藥性分析

	S	Sigapore-born		Forei	Foreign-born		Non-residents	
		reside	ents	resi	dents			
Sensitivity result		20	13	2	013	2013		
of sputum examination *		No.	%	No.	%	No.	%	
New cases								
**Sensitive to: Streptomycin, Isoniazid, Rifampicin		666	93.4	126	88.1	341	87.0	
Resistant to:								
Single drug		38	5.3	12	8.4	32	8.2	
More than 1 drug		9	1.3	5	3.5	19	4.8	
Total examined		713	100.0	143	100.0	392	100.0	
***Resistant to Isoniazid		21	2.9	10	7.0	27	6.9	
Resistant to Rifampicin 8 Isoniazid	k	2	0.3	0	0.0	¥ 12	3.1	
Relapsed cases								
Sensitive to: Streptomycin, Isoniazid, Rifampicin		57	93.4	6	100.0	15	75.0	
Resistant to:								
Single drug		3	5.0	0	0.0	1	5.0	
More than 1 drug		1	1.6	0	0.0	4	20.0	
Total examined		61	100.0	6	100.0	20	100.0	
Resistant to Isoniazid		1	1.6	0	0.0	1	5.0	
Resistant to Rifampicin & Isoniazid	k	¥ 1	1.6	0	0.0	4	20.0	

MDR TB 個案數自 2000 年以來,境外出生國人為或非新加坡居民 通報數已遠勝於新加坡本地出生國人(2013 年為 16 例:3 例)。外籍 MDR TB 另一隱憂為倘個案未於公立醫院接受標準化抗結核藥物治療,可能 造成更嚴重抗藥問題。例如,新加坡每年統計約有 49% MDR TB 病人係 持短期旅遊簽證往返國門於私人門診就醫(如圖八)。

▲圖八、新加坡境內外出生者 MDR TB 通報數與所持簽證統計

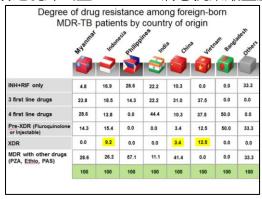


進一步將境外出生者(含國人與非新加坡居民)依出生地區分,可發現緬甸與印尼出生者具有較高 MDR TB 比例(如表六)。另印尼、中國與越南出生者有較高比例之 MDR TB 個案罹患 XDR TB(如表七)。Ms. Lim表示,印尼籍病患常見自行於母國藥局買藥服用情形,故 MDR/ XDR TB 比例偏高。

表六、各國籍別之境外出生 MDR TB 比例分析

	country of birth	, 2000-2010	
Country of birth	New cases MDR / Total cases (%)	Previously treated MDR/Total cases (%)	Overall % of MDRTB
Indonesia	30/1438 (2.2)	28/84 (33.3)	3.8
Myanmar	25/311 (8.0)	5/28 (17.9)	8.8
China	18/798 (2.3)	3/130 (2.3)	2.2
Philippines	6/420 (1.4)	1/9 (11.1)	1.6
Vietnam	3/68 (4.4)	1/2 (50.0)	5.7
India	3/427 (0.7)	1/6 (16.7)	0.9
Bangladesh	1/136 (0.7)	1/3 (33.3)	1.4
Malaysia	3/980 (0.3)	1/76 (1.3)	0.4
Singapore	16/8050 (0.2)	14/1110 (1.3)	0.3

▲表七、各國籍別之境外出生 MDR TB 病患抗藥嚴重度分析



肆、心得與建議

我們從本次參訪發現新加坡防治成績已經極佳,但衛生單位仍持續精益 求精,除衛生部挹注更龐大經費於結核病防治、加上 TBCU 同仁人力擴增 與逐步落實政策規劃。參訪數日期間,我們充分感受到該國對於防治工作的 積極野心。

對於新加坡目前面臨外籍人士重大防疫難題,值得我國做為借鏡。臺灣境內外籍人士(外籍勞工、新住民與外籍學生)約100萬,每年結核病例數約700人。從新加坡報告中,我們看到印尼與越南籍外勞有較嚴重抗藥性問題,其中印尼為我國外勞主要來源國家,應密切留意其結核病情形。而我國自2014年起開放外籍勞工在臺治療,可預防結核病患遣返母國後接受非標準抗結核藥物治療所致抗藥性問題;再配合我國健保就醫補助,可解決其就醫困難。另一方面,我國防治作為亦有新加坡稱羨之處,例如我國DOT實施到家送藥或指定地點送藥關懷服務,執行率均達96%以上。新加坡則於2013年取得相關經費,重新啟動都治外展服務。

綜合而言,幾點建議作為我國結核病防治工作參考:

一、外裔結核病患防治:

我國 2014 年約 80 名外勞結核病人留臺治療,預計人數將逐年上升。留臺治療者須密切追蹤都治執行品質與治療結果。另外,署內先前研究指出新住民在入境臺灣後第 1-2 年仍有較高結核病發生率,且本類人士多擔任家庭之幼童或老年人主要照顧者,但在移民申請程序中,這段時期並無體檢相關要求,故建議可利用衛教管道加強其對於疑似結核症狀警覺心,避免延遲診斷情形。

二、引進新興 LTBI 治療處方增進治療順服性與完治率:

新加坡依據接觸者結核病發病風險或所在機構類別,提供不同期程或藥物處方。我國目前以9個月 INH 為標準處方,另國內尚有短期處方於相關研究計畫試辦中。倘未來能引進新興 LTBI 治療處方,縮短治療期程或提供醫師選擇個案最適之治療組合,可提供 LTBI 治療意願與完治

機率。

三、選派優秀結核病防治人員參與國際會議訓練促進交流:

藉由深度國際交流得掌握各國結核病防治方向,除有助檢視我國政策有否待調整處;另一方面,可以培育我國防治人員專業素養以及對結核病防治工作責任心。

結核病通報格式(MD 532-92)

Notification date (dd/mm/yy) Singapore 1. Notification date (dd/mm/yy) Singapore 142 M Singapore 144 M Singa	n form must be completed promptly for the Tuberculosis, Completed form is to be d to: Director, TB Control Unit
2. Name (as in NRIC/Passport/other document) 3. NRIC/Passport/Foreign Identification No. 4. Gender Male Female 5. Ethnic group (or stick patient label here)	STEP REGISTRY Moulmein Road japore 308087 : 6258-4369 : 6252-4051
3. NRIC/Passport/Foreign Identification No. 4. Gender Male Female 5. Ethnic group (or stick patient label here) 6. Date of birth (dd/mm/yy) / (if unknown please specify age)	
9. Residence Name (If place of residence is long-term care facility)	7. Marital Status Single Widowed Married Divorced Separated Unknown 8. Occupation
House / Bilk no.	
# - (H) (Pg/HP)	10. Housing type HDB 182 rm
House / Blk no. Unit no. # - Contact no. Ext.	HDB 3 m
Street name Postal Code	HDB 5 rm & above
Street name Postal Code	HUDC Private condominium/apartmen
Singapore citizen (pink NRIC)	Landed property Others (specify)
DIAGNOSIS 17a. Patient category* New case Relapse (state year previously treated) Reinstatement Uncertain 17b. If transferred from overseas, tick here "Please specify "DIAGNOSIS 18. Case diagnosed through Symptoms of disease Incide Screening of contacts Mobile Pass application/renewal Others "Please specify	d in Singapore gapore) care facility (if applicable) ad/aged sick
17a. Patient category* New case Relapse (state year previously treated) Reinstatement Uncertain 17b. If transferred from overseas, tick here *Please specify *DEFINITIONS Patient category New: Patient who never previously received treatment for more than 1 month. Relapse: Patient who previously completed treatment or was treated and declared cured prior to developing active TI Reinstatement: Patient who previously had not completed treatment and now returns after one year of last being on	
New case Relapse (state year previously treated) Reinstatement Uncertain **Please specify **DEFINITIONS Patient category New: Patient who never previously received treatment for more than 1 month. Relapse: Patient who previously completed treatment or was treated and declared cured prior to developing active TI Reinstatement: Patient who previously had not completed treatment and now returns after one year of last being on	10a Status at diais
*DEFINITIONS Patient category New: Patient who never previously received treatment for more than 1 month. Relapse: Patient who previously completed treatment or was treated and declared cured prior to developing active TI Reinstatement: Patient who previously had not completed treatment and now returns after one year of last being on	iental finding Alive Dead
Patient category. New: Patient who never previously received treatment for more than 1 month. Relapse: Patient who previously completed treatment or was treated and declared cured prior to developing active TI Reinstatement: Patient who previously had not completed treatment and now returns after one year of last being on	
DOT: Directly Observed Treatment, ie. a health care worker watches as the patient swallows each dose of TB medical Polyclinic DOT: DOT carried out by the nurses at the government polyclinics. Institutionalised DOT: DOT carried out by health care workers at hospitals, nursing or community homes or correctic Outreach DOT: DOT carried out by a health care workers at the patient's home. Other DOT: e.g. DOT carried out by a health care workers at general practitioner clinic, school, army camp. SAT: Self Administered Treatment.	n medication. ation.

結核病通報格式(MD 532-92) (續)

NRIC/Passport/Foreign Identification No.	21	. No.	BCG scars		23. CXR
20. Concurrent medical conditions (Tick all that a	noly	Г	0 1 1 2	Unknown	Date:
	_	. Cou	-		Scar (old TB)
Diabetes mellitus Steroid therapy End stage renal Impaired immunity other			ign		Active TB (with cavitation)
failure Impaired immunity of than HIV	tner		☐ No		Active TB (without cavitation)
Cancer Others (please speci	fy)		Yes (state duration	an)	Milliary TB
HIV test done: Yes/No			i res istate duratio	A0	Not done
If Yes, result of latest test: Reactive/Non-react	ive		V	weeks	
Date of test	_		22-22-38		Others (Specify)
24. Site(s) of disease (Tick all that apply)	25	. Res	sults of initial smear#	Lab no.	Date Result
Pulmonary Extrapulmonary			Pulmonary		
Laryngeal			(specify specimen type,		
Pleura			eg. sputum)		
Lymphatic system			Extra-pulmonary		
Skeletal system			Pleural fluid / tissue		
Genitourinary system			Lymph node		
Central nervous system			Urine	-	
Disseminated			Endometrium		
Gastro-intestinal system			503 NUMBER		
(including mesenteric			Spinal fluid		
glands & peritoneum			Others:		
Others (please specify)		1170		20.0	
(i)			Please use the following of done = 1	codes: = + 3 = +	
(ii)				=++ 4=+	
(1)	_	N	ote: Results of initial sme	ear MUST be provi	ided if done.
16a. Date started (dd/mm/yy) 16b. Treatment centre TBCU SATA TTSH Polyclinic	-		Patient red	ferred to other trea called for treatmen sle for treatment du	tment centre (complete item 27b, c, t (complete item 27d) the to medical contraindication
NUH General practitioner (ple	ase specit	fy)	000000000	99999	
SGH Private hospital/specialis	st (please	spec	(fv) Others (pl	lease specify)	
AH					
26c. Intended duration			27b. Name of I	hospital/centre/clin	nic referred to
6 months 18-24 months Other	s	n	nonths		
			97e Nome -1	physician referred	10
16d. Intended regimen (e.g. 2HRZ/4H ₃ R ₃)			Z/C. Name of (physician referred t	
Tick if Fixed Dose Combination used		_			
26e. Treatment delivery mode*			27d. Appointm	nent date (dd/mm)	(yy)
Polyclinic DOT SAT	·ox				1 6 7
Polyclinic DOT SAT Outreach DOT Institutionalised I	тоот				
Outreach DOT Institutionalised I		JLA	RS OF NOTIFYING	DOCTOR	
Outreach DOT Institutionalised I		JLA		DOCTOR	itution:
Outreach DOT Institutionalised I		JLA	30. Name of c	linic/hospital/inst	
Outreach DOT Institutionalised to 8. Name & Signature of Notifying Doctor:		JLA	30. Name of cl	linic/hospital/inst	able) :
Outreach DOT Institutionalised [JLA	30. Name of cl	linic/hospital/inst	able) :

結核病治療追蹤格式(MD 117)

Ministry of Health Singapore	1. Date (dd/mm/yy):	Completed form is to be posted or faxed monthly to: The Director, TB Control Unit clo STEP REGISTRY 142 Moulmein Road Singapore 308087 Tel: 6258-4369 Fax: 6252-4051
A. Patient Particulars 2. Name		4. Name and Signature of Attending Doctor:
B. NRIC/Passport/FIN no.		5. MCR No.
3. Treatment Centre i. Current treatment centre	re Name & Addres	ss of Treatment Centre ([#] please specify)
SGH NUH	SATA Others # Department/Wa	ard Telephone Fax
. Treatment Progres f patient data not available, letails of arrangements for e.g. if admitted to hospital	please state reason and give follow-up of TB treatment	
. Is patient compliant*? Yes No		If from SAT to DOT Others
	agement Decision	Date (dd/mm/yy): 13. Transfer Centre - Follow Up If patient is transferred to another treatment centre for TB
Drugs	prescribed at this visit o state drugs)	treatment, please indicate: a. Appointment date (dd/mm/yy) b. Treatment centre/hospital: TBCU TTSH CGH AH SGH NUH SATA Others # (# please specify) c. Name and Address
0. Treatment delivery mod	de (each visit) *	Telephone Fax
Polyclinic DOT Outreach DOT	SAT Institutionalised DOT	14. Final Outcome
1. Temporarily cease trea Reason: Drug reaction Refusal of trea Others (specification)	tment	Completed treatment* Cured *? Yes No Final regiman used (e.g. 2HRZ/4H _g R _g) Drug reaction, decided no further action Left country Diagnosis revised (not TB, specify diagnosis)
2. Duration to next TCU:	1	Lost to follow-up after refusing treatment Lost to follow-up after starting treatment (Defaulted) Died of TB Other Cause (specify): Others (specify)

結核病治療追蹤格式(MD 117)(續)

*DEFINITIONS

Compliant to Treatment

Patient who has consumed at least 80% of prescribed medications in the judgement of the attending physician.

Completed Treatment

Patient who has been compliant with at least 80% of medications for the total length of treatment, in the judgement of the attending physician.

Cured

Sputum smear or culture positive patient who has completed treatment, and who had at least 2 negative sputum smears and/or cultures during the continuation phase, one of which was at the end of treatment.

Treatment delivery mode:

DOT: Directly Observed Treatment, ie. a health care worker watches as the patient swallows each dose of TB medication.

Polyclinic DOT: DOT carried out by the nurses at the government polyclinics.

Institutionalised DOT: DOT carried out by health care workers at hospitals, nursing or community homes or correctional facilities.

Outreach DOT: DOT carried out by STEP designated health care workers at the patient's home or workplace.

SAT: Self Administered Treatment.



SINGAPORE TUBERCULOSIS ELIMINATION PROGRAMME MINISTRY OF HEALTH

Dear Sir/Madam,

The National Tuberculosis Registry has been informed that you were recently diagnosed with Tuberculosis (TB).

TB is an infectious disease caused by germs which spread through the air. When a person ill with TB coughs or sneezes, the expelled TB germs may be breathed in by healthy persons who are in close contact with him or her, and infect their lungs. Persons infected with TB germs may still look and feel well, with symptoms only appearing later when the germs actually cause disease.

The TB Control Unit does TB screening to determine whether exposed persons or "contacts" of the TB patient have become infected. If so, it is possible to administer treatment which *prevents* infection from developing into disease. We therefore request that you help us identify persons whom you have been in close and prolonged contact with. An interview of approximately 1 hour is necessary for our nurses to identify all your contacts. All persons living in your household are contacts and should go for TB screening at the TB Control Unit (Contact Clinic) at the address below. Contacts who turn up will be screened for TB on the same day, and may be required to return for further testing on another day.

Please come to the TB Control Unit (Contact Clinic) at the address below, and bring this letter, together with your original NRIC / passport / work permit / birth certificate (if under 15 years of age) within 1 week on receiving this letter. We hope that you will cooperate with us in minimising the possible risk to your contacts.

Please note that if you fail to provide us with the necessary information, you may be compelled under the Infectious Diseases Act by the Ministry of Health to provide the necessary information.

For clarification, kindly contact our staff at the telephone number below. If you have already provided us with the necessary information, please ignore this letter.

Thank you.

Blk 201 Communicable Diseases Centre 2 7 Jalan Tan Tock Seng Singapore 308440 Tel: 6258-4430, Email: sock@ttsh.com.sg Consultation hours: Mon to Fri – 8 am to 12 noon, 2 pm to 4 pm Sat – 8 am to 12 noon (See map on reverse)

Director, Tuberculosis Control Unit for Director of Medical Services Ministry of Health This is a computer generated letter and requires no signature.



Tuberculosis Control Unit 142 Moulmein Road Singapore 308087

Version 020508

結核病患肝功能監測指引(2014.1 更新)

GUIDELINES FOR MONITORING FOR HEPATOTOXICITY IN PATIENTS ON TB TREATMENT AND CHEMOPROPHYLAXIS

A. PATIENTS ON TB TREATMENT

- All patients to have baseline AST / ALT performed prior to starting of anti-TB treatment. Liver enzymes / bilirubin are also to be performed at any time should the patient complain of symptoms suggestive of hepatitis, eg. nausea, loss of appetite.
- There is no need to monitor AST / ALTs routinely, during the course of TB
 treatment if baseline levels are normal, and if the patient has no history of
 chronic liver disease or alcohol abuse. However, elderly patients on PZA
 should have their liver enzymes monitored (see 3.)
- Monitoring of AST / ALT is advised (eg. 2 to 4 weekly) during the first 2 months of treatment in the following circumstances:
 - · if the baseline level is abnormal
 - if there is a history of chronic liver disease
 - if the patient is unable to abstain from alcohol during the course of TB treatment
 - if the patient is elderly (> 65 years old) and on PZA
- 4. For patients with abnormal transaminases:

If AST /ALT <3x upper limit of normal (ULN):

- If patient is asymptomatic, treatment may be continued, but may need to be modified (eg. dose reduction or less hepatotoxic regimen)
- Levels to be monitored at weekly intervals, to stop TB Rx if there is a rising trend.

If AST /ALT > 3x ULN, or if Bil raised and AST / ALT > 2x ULN:

- · Treatment to be stopped.
- Acute viral hepatitis markers (HepBsAg, anti-HAVlgM, anti-HepBcigM) and screening for Hep C status (anti-HepC IgG) to be done
- Advise hospitalization if patient is unwell, or if AST/ALT >10xULN.
- If managed as an outpatient, levels to be monitored weekly until AST/ALT <
 3x ULN, and Bil normal.
- Treatment may then be restarted with a less hepato-toxic regimen or with modification of drug dosage, with careful monitoring of liver enzymes (consider restarting treatment as an inpatient)

結核病患肝功能監測指引(2014.1 更新)(續)

9.11.09.; updated 2.1.14.

ADDENDUM TO TBCU GUIDELINES FOR MONITORING FOR HEPATOTOXICITY IN PATIENTS ON TB TREATMENT

Further to the above guidelines (in effect since year 2000), the following categories of TB patients are to have *routine* ALT/AST monitoring at each scheduled visit (ie. week 2, 5 and 8) during their intensive phase of treatment:

- 1. Hepatitis B or Hepatitis C carriers
- 2. Patients with other chronic liver diseases
- 3. Patients > 65 years of age
- 4. Patients who consume alcohol
- 5. Pregnant women
- 6. HIV-positive patients
- 7. Mentally incapacitated patients who are unable to verbalize their symptoms
- 8. Persons on statins or other potentially hepatotoxic drugs

The TBCU Guidelines of 2000 still otherwise apply – all patients are to have baseline AST/ALT; patients with elevated baseline transaminases should be managed according to the existing guidelines.

All patients on TB treatment should be asked specifically at every visit regarding symptoms of hepatotoxicity such as nausea, loss of appetite, abdominal discomfort, unexplained fatigue, tea-coloured urine. Where clinically indicated, AST/ALT and bilirubin levels should be performed. In patients with the above risk factors for TB drug hepatotoxicity, there should be a lower threshold for performing AST/ALT/Bil, and for temporary cessation of treatment while awaiting AST/ALT results

LTBI 治療對象肝功能監測指引(2006.12 更新)

B CONTACTS ON PREVENTIVE TREATMENT (PT) WITH ISONIAZID OR RIFAMPICIN

- Baseline serum AST/ALT to be done for the following contacts prior to starting PT:
 - >35 years old
 - · those with history of liver disease or alcohol abuse regardless of age
 - · pregnant regardless of age
- Prior to starting PT, all contacts should receive counselling regarding the
 potential side-effects of the medications. Staff should be alert at every visit to
 elicit the development of any symptom(s) which could suggest drug-induced
 hepatitis
- Wef 3.1.07, contacts> 60 years old are to have routine AST/ALT monitoring at the 2nd and 4th visit (ie. at 4 and 16 weeks after starting PT)
- 4. Action to be taken according to degree of elevation of AST/ALT:
 - AST / ALT> 2 x ULN, to discontinue treatment; and to offer referral for GE
 consult
 - AST / ALT < 2 x ULN, treatment may be continued if the contact is willing, after explanation of risk / benefit to contact, and need for monitoring. Liver enzymes to be monitored 2 weekly for 2 months -if rising trend, to stop treatment
- If the contact has symptoms suggestive of hepatitis anytime during the course of PT:
 - · treatment should be stopped
 - serum AST / ALT / bilirubin levels should be done, and if elevated, steps taken according to point 4 above
 - acute and chronic viral hepatitis markers should be done if there is derangement of liver enzymes
- 6. PT is generally not re-instituted after recovery from drug-induced hepatitis

25.4.00. Updated 20.4.02. Revised 26.12.06.

伍、研習相片





TBCU 緊鄰陳篤生醫院,包含行政大樓、病患門診與接觸者門診 3 棟建物。





與 TBCU 主任 Dr.Wang(左圖)以及護理長(右圖)合影。





TBCU 病患門診為 2013 年新落成建物,診間與候診室均採自然通風。





參訪新加坡中央醫院 TB central lab, 左圖中央為實驗室負責人 Dr. Sng; 右圖為檢體分流之運輸平台,新加坡全國及院內檢體皆會送至此處。





陳篤生醫院之訪客應先登記身分(左)並刷卡(右)方能進入病房大樓。