出國報告（出國類別：開會）

參加「49th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)」出國報告

服務機關　：　衛生署疾病管制局

姓名職稱　：　楊靖慧　組長

派赴國家　：　美國舊金山

出國期間　：　98 年 9 月 10 日至 9 月 16 日

報告日期　：　98 年 10 月 16 日

摘　　要

第49屆抗微生物製劑與藥物治療跨領域年會「Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)」於2009年9月12日至9月15日於美國舊金山市之Moscone會議中心舉行。今年的主軸是「面對尚未結束的傳染病議程，On the Unfinished Agenda of Infectious Diseases」，說明新興傳染病對人類的影響。大會總計安排了102場的學術討論會，會議的主題包括院內感染控制、抗藥性細菌、新研發的抗微生物藥物、疫苗等等。而在傳染病上，愛滋病（HIV）囊括近1/3的討論會，此外結核病(TB)、流感、肝炎等均有相關的討論會。本人代表疾病管制局參加本次會議，同時報名參加前一天會前會的HIV研習會，並發表兩篇論文。

在愛滋病研究方面，抗 HIV 病毒藥物的血中濃度是此次的熱門話題之一，監測 HIV 感染者血中抗病毒藥物濃度有助於臨床治療，是我國未來可以考慮發展的項目。而在臨床治療上，包括起始治療時機、慢性代謝性併發症如糖尿病與心血管疾病、HIV 對中樞神經系統、肺臟與肝臟的傷害等等議題。此外有關潛伏性結核診斷與治療的討論會與 H1N1 新流感相關議題是本次大會的熱門焦點之一，其他還有一些重要議題，如性傳染病、細菌抗藥性與抗生素管制與院內感染相關等，均有眾多的討論會與論文發表。大會亦邀請多位專家分享了今年度感染症最重要的一些文獻回顧，經過討論的過程，點出一些未來需要繼續研究的主題。

本人此次代表本局參加此國際性會議，在會議中得以參與討論許多現今熱門感染症相關的研究，在與國際專家交流的過程有很多的收穫，尤其是與承辦業務相關的愛滋病與結核病防治議題，將把這些經驗與國內專家與同仁分享，作爲未來政策制定與研究發展的參考。

目　　次

壹、背景說明與開會目的

第 49 屆抗微生物製劑與藥物治療跨領域年會「Interscience Conference on Antimicrobial Agents and Chemotherapy，以下簡稱 ICAAC」於 2009 年 9 月 12 日至 9 月 15 日於美國舊金山市之 Moscone 會議中心舉行，為期 4 天。此會議主要是由美國微生物學會(American Society for Microbiology)所主辦，內容涵蓋感染性疾病與抗微生物製劑，是感染症相關領域極為重要的國際會議，全球各國的實驗室微生物專家與臨床感染症專家均會參與。

今年的主軸是「面對尚未結束的傳染病議程，On the Unfinished Agenda of Infectious Diseases」，說明新興傳染病對人類的影響。大會總計安排了 102 場的學術討論會，包括 Keynote session；2 場 ICAAC 演講；30 場專家座談會(Meet-the Experts session)；62 場教學討論會(didactic symposia)與 7 場互動式討論會(interactive symposia)。從接受的 1600 篇的論文投稿，規劃出 116 個海報論文展示會與 26 個口頭論文展示。特別的是為了因應 H1N1 新型流感的新疫情，接受了超過 70 篇的最新論文投稿(Late-breaker abstracts)，讓與會專家皆能得知感染症的最新研究成果。會議的主題包括院內感染控制、抗藥性細菌、新研發的抗微生物藥物、疫苗等等。而在傳染病上，愛滋病(HIV)囊括近 1/3 的討論會，此外結核病(TB)、流感、肝炎等均有相關的討論會。本次會議吸引了全球近萬人參與，而台灣感染症相關領域的學者專家亦參與踴躍，共計 30 餘人參與。為了解國際最新傳染病資訊(包括愛滋病、結核病)，掌握流行趨勢及現況，增進專業職能，並作為日後釐定愛滋病與結核病防疫政策之參考，因此由本人代表疾病管制局參加本次在美國舊金山市舉辦的第 49 屆 ICAAC，同時報名參加前一天會前會的 HIV 研習會，並發表兩篇論文。

貳、行程表

日期	時間	內容
9/10(四)	下午	台北-舊金山
9/11(五)	全日 (8:30~16:30)	**49-11 HIV: A 2009 Update** 1. A clinical perspective : Importance of non-AIDS-associated morbidities in treated HIV infection 2. Role of immune activation and inflammation in non-AIDS-associated complications 3. HIV and neurocognitive dysfunction 4. HIV and cancer 5. HIV and cardiovascular disease
9/12(六)	全日 (7:00~18:00)	ID Fellows Program (7:00~9:00) Keynote lectures (9:30~11:30) Poster Sections (11:30~13:30) ID Literature (13:45–15:45) Symposia and Interactive Sections(16:00~18:00)
9/13(日)	全日 (7:00~18:45)	Meet-the-Experts Sections (7:00~8:15) Symposia and Interactive Sections(8:30~10:30) Poster Sections (11:15~13:15) Symposia and Interactive Sections(14:00~16:00)

		Meet-the-Experts Sections (17:30~18:45)
9/14(一)	全日 (7:00~18:30)	Meet-the-Experts Sections (7:00~8:15) Symposia and Interactive Sections(8:30~10:30) Poster Sections (11:15~13:15) Symposia and Interactive Sections(14:00~16:00) Meet-the-Experts Sections (17:30~18:45)
9/15(二)	上午 (7:00~11:00)	Meet-the-Experts Sections (7:00~8:15) Symposia and Interactive Sections(8:30~10:30) Poster Sections (10:00~11:00)
	下午	回程：舊金山-台北 (9/16 晚間抵達)

參、重要會議內容介紹

1. HIV workshop: HIV 感染者的非愛滋相關疾病

主持人 Peter W. Hunt 醫師在開場時就提到，自從有了高效能抗 HIV 病毒治療(Highly active antiretroviral therapy, HAART)後，HIV 感染成爲一種慢性疾病，在沒有 HAART 的時期(1995-1996)，只有一半左右的 HIV 感染者可以存活超過 30 歲，而引入 HAART 之後，HIV 感染者的壽命顯著延長，在早期 HAART 時期(1997-1999)，已有一半左右的 HIV 感染者可以存活超過 50 歲，到了晚期 HAART(2000-2005)，半數以上的感染者可以存活超過 65 歲以上。但是，即使在如此進步的治療下，HIV 感染者的平均壽命仍略低於未感染者，此外，隨著年齡的增加，HIV 感染者也開始發生非愛滋相關疾病，例如癌症、心血管疾病、代謝症候群等。HIV 感染者是否有較高機會產生這些疾病？是 HIV 本身亦或是治療藥物產生的結果？這些都是醫學上大家想要了解的問題，所以這一整天的座談會主要就是在討論這個議題。

座談會分成四個主題，第一階段是討論 HIV 感染者免疫重建的發炎反應與這些非愛滋相關疾病的關係。演講者 Michael Lederman 利用了兩種猴子來做例子，非洲黑猩猩(rhesus)若感染靈長類免疫缺乏病毒(SIV)，就會發生像人類感染 HIV 一樣的病程，免疫細胞被摧毀，發生伺機性感染而死亡。而另一種白鬢白眉猴(sooty mangabey)在感染 SIV 後，雖然體內亦可發現高濃度的病毒量，但是免疫細胞沒有被摧毀，亦不會發生伺機性感染，故不會因此而快速死亡。這兩類猴子的最大不同，是其對 SIV 的免疫活化程度有差異，前者有明顯免疫活化，故大量的免疫細胞被激發，並釋出大量細胞酵素，導致體內處於慢性發炎狀態，不停的有新的免疫細胞投入戰場，終於使之耗盡無法抵抗伺機性感染。而這種相似的免疫反應亦可在 HIV 感染者發現。至於讓體內持續免疫活化的可能原因，是來自腸道的細菌。腸道組織是人體中 CD4 淋巴球含量最多的器官，其數量是周邊血液的數百倍以上，當 HIV 剛入侵人體時會大量殺死腸道中的 CD4 淋巴球，病人的腸道免疫力下降，故移生於腸道中之格蘭氏陰性菌的外毒素(lipopolysaccharide, LPS)可能藉機進入循環系統而引起免疫系統活化，從 HIV 感

染者身上也測出較高濃度的 LPS 可以證實這個觀點。而這些慢性發炎反應可能與血管硬化等心血管疾病有關係。這些錯綜複雜的關係，使得在目前醫界對於到底該促進或抑制免疫活化仍未有定論。Dr. Lederman 以瞎子摸象的故事做結論，提出對 HIV 仍有許多等待研究的重要課題。

第二個主題是由 Scott Letendre 醫師講授 HIV 相關的神經認知疾病，此主要是討論抗病毒藥物進入中樞神經系統的濃度與神經認知疾病的相關性。近年來有多篇國外文獻討論 HIV 感染相關的神經系統與精神科相關的疾病，不過在台灣的相關研究較少，未來值得進一步探討。

第三個主題是由 Kaiser 研究機構的 Michael J. Silverberg 博士對加州 HIV 感染者與非感染者發生癌症的研究，收集的參與者包括 20,277 個 HIV 感染者，對照組爲 202,313 個非感染者，研究時間爲 1996 到 2007 年間，講者把癌症區分爲: 非感染相關或感染相關癌症，後者包括子宮頸癌與肛門癌(HPV)、肝癌(HBV、HCV)、淋巴癌(EB 病毒)與卡波西氏肉瘤(HHV-8)。HIV 感染者發生感染相關癌症明顯高於非 HIV 感染者，以肛門癌爲例，其相對風險高達 101.6 倍。這突顯了針對 HIV 感染者對於可以預防的感染如 HPV 疫苗、B 型肝炎疫苗等的重要性。而在非感染相關癌症中，僅有肺癌發生風險較高，HIV 感染者是非感染者的 1.9 倍，但因爲沒有校正抽菸情況，故仍無法下定論。第四個主題是由 Judith S. Currier 醫師討論 HIV 感染者發生心血管疾病的原因探討，除了藥物、HIV 感染本身引起外，HIV 感染者的年齡老化與生活型態亦都是重要的因素。

經過一整天熱烈的討論，大家對於 HIV 感染的慢性病化都有深刻的了解，最後的結論是，爲了因應未來這群年齡日增的 HIV 感染者，相關疾病的研究、預防措施與治療對策都是需要投入經費去事先準備。

2. HIV 致病機轉與疫苗發展

在開會第一天的 keynote speech 請到 Françoise Barré-Sinoussi 博士針對「HIV 致病機轉與 HIV 疫苗研究發展」做演講，Barré-Sinoussi 博士是法國病毒研究團

隊的主持人，她從 1970 年起致力於反轉錄病毒的研究，在 1983 年發現 HIV 並命名，並且成為 2008 年醫學類諾貝爾獎得主。她的演講先回顧 HIV 疫苗的發展，從 1987 年 8 月第一個 phase 1 的臨床試驗後，之後陸續有將近 95 個 phase 1 與 phase 2 的臨床試驗進行，但都宣告失敗，到目前只剩下 2 個仍在進行中。基於目前在 HIV 治療與防治上遭遇的一些困難，人類迫切需要一個全新的 HIV 疫苗，而發展的方向應回頭從基礎醫學找起，試著從另一種思考方向，例如如何讓人類與 HIV 病毒能共存。Barré-Sinoussi 博士簡單介紹了 HIV 以及 SIV 的致病機轉，並且以兩種不同的靈長類(非洲黑猩猩與白鬢白眉猴)作例子，說明與 SIV 和平共處的白鬢白眉猴並不會產生疾病。她的團隊 ANRS EP36 cohort collaborative network 針對一群長期未發病之 HIV 感染者的研究(elite controller，定義為感染超過 10 年，未服用抗病毒藥物，血液中測不到病毒 RNA 且細胞中測不到病毒 DNA 的人，這只發現於 HIV 感染族群的 1%)，發現這類病人體內的發炎反應較低，CD8 淋巴球數目亦較低等，初步與動物實驗的結果相仿，但是，如何將此應用到 HIV 疫苗的發展，仍有許多需要釐清的問題，需要科學家、臨床醫師與病人間的緊密合作，才能找出最好的答案。

3. HIV 臨床治療相關議題

抗 HIV 病毒藥物的血中濃度是此次的熱門話題之一，由紐約 Buffalo 大學 Fatai Fehintola 醫師團隊發表，HIV 感染者若抽菸或大麻等成癮性精神藥物，會降低血中抗病毒藥物濃度，甚至有可能導致治療失敗。此外還有論文提到肥胖病人會降低血中抗病毒藥物濃度，以及抗病毒藥物與抗結核藥物之交互作用等。這些文章都認為監測 HIV 感染者血中抗病毒藥物濃度是很重要的。目前我國並無可以進行此類檢測的實驗室，是未來應考慮發展的項目。

此外，有一些新的抗 HIV 病毒藥物的臨床試驗結果發表，目前除了已上市的核苷酸反轉錄酶抑制劑、非核苷酸反轉錄酶抑制劑、蛋白酶抑制劑、HIV 酶結合抑制劑(integrase inhibitor)、CCR5 接受器抑制劑外，沒有更新類型的藥物。不過同類型中仍有一些新的試驗結果發表，有些藥物已產生抗藥性，有些則有不錯之治療效果。HIV

抗藥性的監測資料亦是重要議題之一，有一些新的檢驗試劑發表。

在 HIV 的臨床治療上，起始治療時機、慢性代謝性併發症如糖尿病與心血管疾病、HIV 對中樞神經系統、肺臟與肝臟的傷害等等，亦是熱門話題之一。最新的治療指引已建議將起始治療的 CD4 淋巴球數目臨界點提高到 500 cells/ L，但是仍需持續追蹤相關服藥順從性與長期併發症的問題。

4. 潛伏性結核診斷與治療相關議題

在第一天下午有一場潛伏性結核診斷與治療的討論會，由Timothy R. Sterling醫師與Madhukr Pai醫師主持。首先由Pai醫師介紹「卡介苗接種族群的潛伏性結核診斷」，BCG會干擾TST診斷LTBI的能力。在 2006 的一篇文獻中發現，如果只有新生兒時期接種一劑卡介苗，TST的僞陽性約 6%；但若在新生兒之後有接種卡介苗，例如日本，TST僞陽性可達 40%。所以要增進TST的判讀，可行的方式有三種：加強皮膚結核菌素測試(Tuberculin skin test, TST)的判讀、加強TST的特異性與用體外測試的方法如干擾素-γ釋放檢驗(Interferin-γrelease assay, IGRA)來取代TST。第一步必須先了解各國的卡介苗接種政策，Pai醫師團隊建立了一個網站http://www.bcgatlas.org/，讓醫師可以輕易查詢各國的卡介苗接種政策，決定TST的可靠性。第二個方法是使用更具特異性的TB抗原來做皮膚測試，例如使用ESAT-6 抗原，此試驗已有上市商品，蘇聯已開始使用，可以等待進一步的結果報告。第三種方法是目前很熱門的研究主題，但其在免疫力低下族群的使用仍未知，截至現今的報告顯示其對未來TB的發病率上僅有中度預測度，所以各國對TST與IGRA的使用建議分歧，像德國，決定用IGRA取代TST，美國則覺得任一皆可，英國則認爲先使用TST，再使用IGRA。各國應該評估其結核病流病資料來決定其政策。

接者由 Sterling 醫師來介紹潛伏性結核的新治療方式。他開宗明義的說，其實沒有新的治療方式，目前現有的治療是安全且也有效的。9 個月的 isoniazid 治療已有超過 21 個臨床試驗發表結果，有超過 13 萬個受試者，結果顯示可以藉低 TB 的發生率達 60%，若在規則服藥完成的病人，其降低率更高達 90%。其次是 4 個月的 rifampicin 治療，目前臨床經驗較少，但看起來有效性與安全性均佳，但未有報導在 HIV 感染

者使用的經驗。其他還有 3 個月的 rifampicin 合併 isoniazid 治療、3 個月的一週一次的 isoniazid 合併 rifapentine 治療等，臨床研究較少，仍無較好之結論可參考。而 TB 疫苗的發展、短程或間斷式的結核病治療等均無較新的結果。第三位講者 Matto Zighol 醫師討論重點爲 isoniazid 抗藥性結核菌的全球性流行病學。最後一位講者 Stephen D. Lawn 醫師之討論重點爲 HIV 病人潛伏性結核診斷與治療的挑戰。這場討論會有很多深入的討論，與會者均覺得受益良多。

5. H1N1 新流感相關議題

H1N1 新流感相關議題是本次大會的熱門焦點之一，有許多篇論文發表，包括重症病例的流病與危險因子調查、墨西哥 H1N1 新流感的流行病學調查、H1N1 新流感群突發調查等，下面列出幾篇較受注目的論文。

(1) H1N1 流感病毒持續排出時間：有兩篇論文均發現可以從症狀開始一週後的病人身上分離出活的 H1N1 流感病毒。香港 David Lye 醫師追蹤 73 位病人，若只用 PCR 檢驗，到第 10 天仍有 10%的病人呈陽性反應。而加拿大 De Serres 醫師追蹤 44 位病人，在症狀後第 8 天仍有 19%的病人有存活的 H1N1 病毒，到第 10 天才檢驗不出來。可以表示病人 H1N1 流感病毒排出時間比一般季節性流感病毒長。但是其傳染性是否亦是如此長期，從臨床資料看不出來。

(2) 新抗流感病毒藥物：由 Shigeru Kohno 醫師發表的針劑型抗流感病毒藥物 Peramivir 第三期臨床試驗結果，此跨國試驗一共募集了 1,009 位流感快篩陽性病人(日本、香港與台灣)，隨機分配接受 Peramivir 300mg 一劑、600mg 一劑或克流感 75mg 一日兩次連續 5 天共三組治療方式，結果顯示臨床療效相似，且副作用比口服藥物低，此新的發現對未來不能使用口服或吸入型抗流感藥物的流感病人，提供了一個新的治療方式。另一個新的治療藥物 DAS181 (Fludase®)，其作用機制與其他抗流感藥物不同，是作用在人體的流感病毒 sialic acid 接受器上，使病毒無法入侵細胞，所以理論上可以對抗所有類型的流感病毒，此次的兩篇論文報告是由華裔科學家余芒、房芳夫婦創辦 NexBio 生物科技公司與香港大學合作研究，在老鼠與體外人類肺部細胞的初步研究

結果，可以有效阻止流感病毒(包括 H5N1 病毒)入侵細胞，未來將繼續進行下一步的試驗。

(3) N95 口罩與外科口罩的在預防院內感染的比較：這是全球第一個比較口罩防護效益的隨機臨床試驗，由澳洲 Raina MacIntyre 博士在中國北京 24 家醫院進行的，選定 1,936 位在急診或呼吸道疾病病房工作的醫護人員，隨機分配成四組：配戴 N95 口罩並要進行口罩合適度試驗(fitting test)、N95 口罩但毋須進行口罩合適度試驗、外科口罩、不具保護效果的平面口罩(含布口罩)。在冬天時連續配戴追蹤四週，停止配戴後再追蹤一週。結果發現配戴外科口罩無法預防呼吸道疾病或流感，但是配戴 N95 口罩可以降低被傳染呼吸道疾病(60%)、流感(75%)、其他呼吸道病毒傳染病(56%)的機會。N95 口罩並合適度試驗並未增加保護效果。這篇論文引起廣泛的討論，對於未來預防院內感染的感染管制措施，提供一些支持的證據。

6. 其他公共衛生相關議題

其他還有一些重要議題，如性傳染病(包含全球淋病抗藥性調查、第一型與第二型之人類皰疹病毒感染、披衣菌感染等)；細菌抗藥性(包含金黃色葡萄球菌、格蘭是陰性菌等)；抗生素管制與院內感染相關等，均有眾多的討論會與論文發表。大會亦邀請多位專家分享了今年度感染症最重要的一些文獻回顧，經過討論的過程，點出一些未來需要繼續研究的主題。

肆、心得與建議

此次國際會議在感染症與愛滋病的議題上有充分的討論與新知發表，可惜的是，本局僅有一位代表前往，與其他單位比較稍微單薄，而且由於會議的設計，同一時段會有多種不同議題演講同時進行，常常顧此失彼，建議未來在經費許可下，可以增派人員參與此盛會，除了可以獲得專業知識外，也可進行國際衛生外交，拓展視野。

在愛滋病防治的議題方面，有幾個方向是我們可以考慮推行的：

1. 設置可以監測抗HIV病毒藥物血中濃度的實驗室，以便讓HIV感染者得到更好的治療效果。
2. 台灣自1997年引進高效能抗病毒治療藥物後，有效降低HIV感染者的死亡率，目前此有效的治療已經使HIV感染變成慢性病，HIV感染者的存活可以延長20年以上，爲了因應未來這群年齡日增的HIV感染者，相關代謝性疾病、心血管疾病的研究、預防措施與治療對策都是需要事先做好規劃。
3. 爲了使感染者得到完善的醫療照護，應依據新發表的研究報告，與相關醫學會合作，定期修訂台灣愛滋病檢驗及治療指引。

在結核病防治的議題方面，針對潛伏性結核的診斷與治療，台灣應該針對本國的卡介苗政策，訂定合適的追蹤與治療政策，以期能達到逐年降低結核病個案的目標。

本人此次代表本局參加此國際性會議，在會議中得以參與討論許多現今熱門感染症相關的研究，在與國際專家交流的過程有很多的收穫，尤其是與承辦業務相關的愛滋病與結核病防治議題，將把這些經驗與國內專家與同仁分享，作爲未來政策制定與研究發展的參考。

Epidemiology of Human Immunodeficiency Virus Testing Among Tuberculosis Patients in Taiwan

H-234

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Abstract

Introduction. Human immunodeficiency virus (HIV) testing is recommended for all patients with tuberculosis (TB). This study assessed the frequency and results of HIV testing among patients diagnosed with TB in Taiwan from 2004 to 2007.

Methods. Data were obtained from the Taiwan CDC national surveillance register of all patients notified with TB (all forms) and HIV, linked with the HIV testing practices data from National Health Insurance of Taiwan (NHI) claims data. The HIV testing was enrolled for study when testing date was after TB diagnosis date or within 90 days before TB diagnosis date.

Results. Of the total 63,114 TB patients, 11,254 (17.8%) had HIV testing data reported through NHI system and 341 (2.9%) among them were positive. The annual HIV testing rate and positive rate of TB patients remained stable during study period. Compared with the TB patients to whom HIV testing was not performed, the TB patients who performed testing were more likely to be younger, male and had extrapulmonary involvement. The positive rate was highest in the age group 20-39 years, which was the sexual active age group. But even in this group, the rate of providing HIV testing was only up to 28.7%. The proportion of new identified HIV infection among TB cases was also higher among TB cases with extrapulmonary involvement and male gender.

Conclusions. HIV testing among TB patients remained low in Taiwan. Patients in higher-risk groups were more likely to be tested and more likely to be HIV positive. Health care providers should offer HIV testing to all TB patients, especially for high risk group such as young males.

Introductions

Human immunodeficiency virus(HIV) infection increases the risk of developing tuberculosis(TB) through activating latent infections and accelerating the progression. Early diagnosis of HIV infection among TB patients can combined anti-TB and antiretroviral therapy which can tremendously improve the prognosis of HIV-TB co-infected patients. According to WHO and the U.S. CDC recommendations, all TB patients should be offered HIV testing. Despite these recommendations, previous studies in different countries shown that only 22.9–71.9% of patients with TB were tested for HIV.

Taiwan had low HIV prevalence and median high TB prevalence. This study aimed to assess the frequency and results of HIV testing among patients diagnosed with TB in Taiwan from 2004 to 2007.

Methods

Data were obtained from the Taiwan CDC national surveillance register of all patients notified with TB (all forms) and HIV, linked with the HIV testing practices data from National Health Insurance of Taiwan (NHI) claims data from January 2000 to September 2008. When more than one HIV testing was performed, first choice is the nearest date which interval with TB diagnosis date is less than 30 days and the second choice is the nearest date after TB diagnosis. The HIV testing was enrolled for study when testing date was after TB diagnosis date or within 90 days before TB diagnosis date. Positive HIV testing was confirmed with Taiwan CDC HIV registry.

Results

The number of annual new report TB cases declined gradually from 16,784 cases in 2004 to 14,481 cases in 2007. Of the total 63,114 TB patients, 11,254 (17.8%) had HIV testing data reported through NHI system and 341 (2.9%) among them were positive. The annual HIV testing rate and positive rate of TB patients remained stable during study period. But only less than half of the TB patients received HIV testing within 30 days after TB diagnosis, some cases may delay HIV testing even years.

Compared with the TB patients to whom HIV testing was not performed, the TB patients who performed testing were more likely to be younger (mean age: 55.5 years vs. 61.6 years, p<0.001), male (18.1% vs.17.2%, p<0.005) and had extrapulmonary involvement (27.1% vs. 16.8%, p<0.001).

After linked with Taiwan HIV registry, we found 402 (0.6%) of reported TB patients had HIV infection and 225(56%) cases of them had HIV diagnosis after TB diagnosis. There were 20 patients who confirmed HIV infection didn't have HIV testing data in NHI system, means they were tested through other voluntary counseling HIV testing program. The rates of receiving HIV testing and positivity of HIV stratified by age groups were shown in Table 1. The positive rate was highest in the age group 20-39 years, which was the highest group receiving HIV testing. But even in this group, the rate of providing HIV testing was only up to 28.7%.

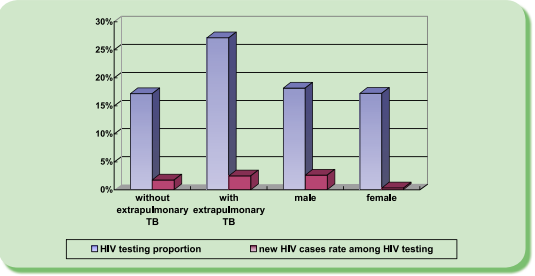
Table 1. The rates of receiving HIV testing and positivity of HIV stratified by age groups.

Age at TB diagnosis	TB reported case, N	Confirmed HIV infection, N(%)	Received HIV testing, N(%)	New HIV infection found among HIV testing#, N(%)
<20 years	1,952[3.1%]	0	301(15.4%)	0
20-39 years	9,390[14.9%]	223(2.4%)	2,697(28.7%)	112(4.3%)
40-59 years	15,543[14.6%]	149(0.95%)	3,125(20.1%)	79(2.6%)
≥60 years	36,226[57.4%]	30(0.08%)	5,131(14.2%)	23(0.4%)
Total	63,114[100%]	402(0.63%)	11,254(17.8%)	205(1.8%)

the denominator is the number of TB patients received HIV testing, exclude cases with known HIV infection.

The proportion of new identified HIV infection among TB cases was higher among TB cases with extrapulmonary involvement (2.5% vs.1.7%, p<0.05), and male gender (2.5% vs.0.3%, p<0.001) compared to female TB cases (Figure 1).

Figure 1. HIV testing rate and new HIV infection identified rate among different categories.



Discussions

This study reports population-based levels of HIV counseling and testing among TB patients. In Taiwan, more than half of the TB patients were aged over 60 years old. In such aged population, the proportion of HIV positive rate is extremely low and the cost-effective analysis is not so efficient. More data are required to establish the cost effectiveness of offering HIV testing to TB patients in a region of high TB and low HIV incidence and ageing TB population, such as Taiwan. However, it may be reasonable to identify risk factors associated with HIV infection among incident TB patients.

Conclusions

HIV testing among TB patients remained low in Taiwan from 2004 to 2007. Patients in higher-risk groups were more likely to be tested and more likely to be HIV positive, but even within the highest-risk groups, the testing rate was not good enough. HIV testing for TB patients is an essential entry point for public health, both in treatment and prevention aspects. HIV counseling and testing program should be expanded and offered to all TB patients, especially to high risk patients.

Isoniazid Preventive Therapy Related Hepatitis in a Population with High Prevalence of Hepatitis B and C

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Abstract

Introduction. The roles of chronic hepatitis B and C on isoniazid preventive therapy (IPT) related hepatitis are seldom discussed. A cohort study to evaluate the risk of chronic hepatitis B and C on IPT-induced hepatitis was conducted in a prison with 15% and 24% of hepatitis B and C carriers.

Methods. A patient who received IPT and subsequently had values of GPT >= 3 times of upper limit of normal value (40 U/L) met the criteria of IPT-hepatitis and GPT >= 5 times was defined as having moderate to severe IPT-hepatitis. The relationship between hepatitis carrier status and IPT-related hepatitis was analyzed by Fisher-exact test.

Results. Among the 163 male patients who received IPT (median age 41.2), 18 (10.8%) patients developed hepatitis. Carries of hepatitis B or C did not increase possibility of IPT-related hepatitis. Eight (4.9%) cases developed moderate to severe IPT-hepatitis. Among carriers of hepatitis B, 6 (15.8%) had IPT-related hepatitis, while 2 (1.6%) in non B carriers did (p=0.0022). Among carriers of hepatitis C, 2 (8%) had IPT-related hepatitis, while the rate non C carriers was 4.4% (p=0.3542). Overall, 12 cases discontinued the treatment and could not resume INH and the other 6 cases could resume and complete INH therapy. Categorized by hepatitis carrier status, hepatitis B carriers were more likely to discontinue treatment permanently (15.8%), than non-B carriers (4.8%) (p=0.0339). The difference between hepatitis C carriers (16%) and non-carriers (5.8%) did not reach statistical significance (p=0.0905).

Conclusions. The carrier of hepatitis B increased the likelihood to have moderate to severe IPT-hepatitis, while carrier of hepatitis C did not. The carrier of hepatitis B decreased the likelihood to complete the LTBI treatment. Serology tests for hepatitis B before the commencement of IPT were highly recommended. Providing routine liver function tests during IPT for carriers of hepatitis B is crucial to avoid permanent liver injury.

Keywords: isoniazid induced hepatitis, hepatitis B, IPT

Introductions

The roles of chronic hepatitis B and C on isoniazid preventive therapy (IPT) related hepatitis are seldom discussed. In August, 2008, a surveillance of latent TB infection (LTBI) was conducted in a prison with 3000 inmates. Inmates who signed informed consents could received tuberculin skin test (TST) and Interferone gamma release assay (IGRA). LTBI was diagnosed when the inmate had both TST>=10mm, IGRA positive and chest radiography without lesion compatible to TB. IPT for six months was provided to these patients with free charge. The prevalence of hepatitis B and C in this population was 15% and 24%, separately. A cohort study to evaluate the risk of chronic hepatitis B and C on IPT-induced hepatitis was conducted.

Methods

1.Serology tests for HBsAg and anti-HCV antibody to document their chronic carrier status were performed before he received IPT.

2.Liver function tests were performed at 30 days and 60 days after initiation of isoniazid.

3.A patient who received IPT with elevated Glutamic Pyruvic Transaminase (GPT) >= 3 times of upper limit of normal value (40 U/L) met the criteria of IPT-hepatitis.

4.A patient who received IPT with elevated Glutamic Pyruvic Transaminase (GPT) >= 5 times of upper limit of normal value (40 U/L) was defined as having moderate to severe IPT-hepatitis. The patient would discontinue isoniazid for 14 days and rechecked GPT if the patient met the criteria of IPT-hepatitis. Isoniazid was resumed when GPT checked revealed the value within 3 times of upper limit of normal value at 14th days.

6.A patient who received IPT and with GPT< 3 times met the criteria of control.

7.The cohort was followed-up until 2 months after IPT completion.

8.The relationship between hepatitis carrier status and IPT-related hepatitis was analyzed by Fisher-exact test.

Results

Among the 163 male patients who received IPT (age between 19.8 -75.7 years, median age 41.2), 18 (10.8%) patients developed hepatitis. Carries of hepatitis B or C did not increase possibility of IPT-related hepatitis. Eight (4.9%) cases developed moderate to severe IPT-hepatitis. Among carriers of hepatitis B, 6 (15.8%) had IPT-related hepatitis, while 2 (1.6%) in non B carriers did (p=0.0022). Among carriers of hepatitis C, 2 (8%) had IPT-related hepatitis, while the rate non C carriers was 4.4% (p=0.3542).

Overall, 12 cases discontinued the treatment and could not resume INH and the other 6 cases could resume and complete INH therapy. Categorized by hepatitis carrier status, hepatitis B carriers were more likely to discontinue treatment permanently (15.8%), than non-B carriers (4.8%) (p=0.0231). The difference between hepatitis C carriers (16%) and non-carriers (5.8%) did not reach statistical significance (p=0.0905). Figure 1 revealed the detailed information of above.

The relative risks for patients of either B or C carrier to non B non C carrier and for patients of dual B and C carrier to non dual B and C carrier were illustrated in the figure 2.

Figure 1. The relationship between hepatitis carrier status and IPT-related hepatitis, moderate to severe IPT-hepatitis, or discontinued IPT permanently.(B to non B Carrier/ C to non C carrier)

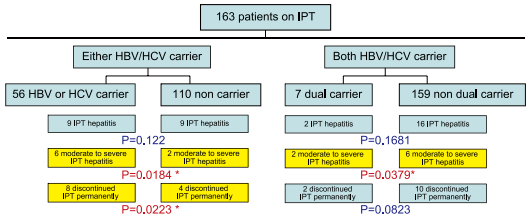
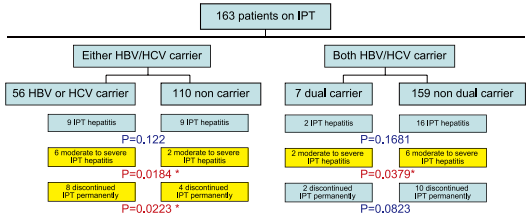


Figure 2. The relationship between hepatitis carrier status and IPT-related hepatitis, moderate to severe IPT-hepatitis, or discontinued IPT permanently
(either B or C carrier to non B non C carrier/ dual B and C carrier to non dual B and C carrier).



Conclusions

The carrier of hepatitis B increased the likelihood to have moderate to severe IPT-hepatitis, while carrier of hepatitis C did not. The carrier of hepatitis B decreased the likelihood to complete the LTBI treatment. Serology tests for hepatitis B before the commencement of IPT were highly recommended. Providing routine liver function tests during IPT for carriers of hepatitis B is crucial to avoid permanent liver injury.