出國報告（出國類別：其他會議）

赴開普敦參加第八屆流感防治年會
(Options for Influenza Control VIII)

服務機關：行政院衛生福利部疾病管制署

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派赴國家：南非

出國期間：102 年 9 月 3 日至 9 月 11 日

報告日期：102 年 10 月 1 日

摘　　要

每三到四年召開一次的流感防治年會（Options for the Control of Influenza）為流感領域中最重要的國際會議，今年為第八屆，全球所有流感相關之政府代表與學者專家等均齊聚一堂，分享流感最新研發成果及防治策略。此次會議除了基本科學外，還討論了近來令人關注的一些流感相關議題，例如中國發生的 H7N9 流感群突發、流感病毒的基礎研究與疫苗研發的最新成果、流感病人的臨床照護和目前最新的季節性流感相關訊息，還有針對低收入和中等收入國家提高疫苗生產的相關議題。此外，鑑於今年 H7N9 流感在中國的出現的例子，還特別討論了人類與動物介面(Animal-human interface)這個重要的課題，會議的內容相當豐富。

我國自 2005 年起開始執行「因應流感大流行整備計畫」，到 2013 年已經進入第二期計畫，投注了大量人力物力來進行準備工作，並及時擷取應用國際各項新知，相關的重點目標亦都有納入執行。不過，基於流感的多變性及國際間交通往來的便利性，我們不能對此掉以輕心，仍須持續且積極的相關研究並進行準備，以期能保障國人的健康與生命。

此次參加會議一方面是可以了解國際最新流感資訊，掌握流行趨勢及現況，增進專業職能，以便作為日後釐定流感大流行整備計畫之參考；另一方面也發表我國在流感防治工作的成果，提供給其他國家參考，藉由參與此次會議，在學術上與未來防治政策的規劃上均有很大的收穫。

目　　次

壹、背景說明與開會目的

流感防治年會（Options for the Control of Influenza）為流感領域中最重要的國際會議，每三至四年始召開一次，此會議研討的範圍從基礎科學到醫療保健政策及流感大流行的整備規劃。此會議的專家委員會和學院成員包括了目前世界上流感領域第一線的專家與領袖。全球所有相關之政府及國際組織（包括 WHO）官員、學者專家(如公共衛生、醫療與獸醫相關等)、藥廠代表等均會共襄盛舉，一起來討論此重要議題。

這是流感防治年會第一次在非洲舉行，此次會議除了基本科學外，還將討論近來令人關注的一些流感相關議題，例如 H7N9 流感群突發、免疫功能低下的患者和慢性病患者的流感，流感與懷孕（包括臨床的影響，致病機轉，對母親和胎兒的影響）和目前最新的季節性流感相關訊息，還有針對低收入和中等收入國家提高疫苗生產的相關議題。此外，鑑於今年 H7N9 在中國的出現的例子，說明了人類與動物介面(Animal-human interface)這個重要的課題，此次會議也特別在星期六(9/7)規畫了這個專題討論。此次會議中並安排了一場有關獲得功能試驗(gain of function research)的倫理相關議題的辯論，此系列的研究曾被應用於 H5N1 禽流感，目前亦有專家將之應用於新的 H7N9 禽流感實驗計劃。

為了解國際最新國際流感研究新進展，掌握流行趨勢及現況，增進專業職能，並且與各國代表交換流感防治相關經驗與策略，藉此檢視並修訂我國之流感防治相關政策，以期能應變瞬息萬變之流感疫情。由本人代表疾病管制署參加本次在南非開普敦市舉辦的第八屆流感防治年會，並代表疾病管制署新興傳染病整備組發表四篇海報論文。

貳、行程表

日期	工作日誌	地　　點	行　程　內　容
102/09/03 102/09/04	啟程	台北→香港 香港→約翰尼斯堡 約翰尼斯堡→開普敦	路程（香港、約翰尼斯堡轉機）； 抵達
102/09/04	報到	開普敦	赴大會報到
102/09/05 102/09/09	開會	開普敦	參加會議並發表海報論文
102/09/10 102/09/11	返程	開普敦→約翰尼斯堡 約翰尼斯堡→香港 香港→台北	路程（香港、約翰尼斯堡轉機）
102/09/11	抵達	台北	抵達

參、會議過程介紹

(一) 流感防治年會議程

Options VIII Programme

	Wed. 04 Sept	Thu. 05 Sept	Fri. 06 Sept
08.00	Registration 08.00-18.00		
09.00-09.40		**Opening Ceremony** *Welcome from Congress and* **IsIrv** *Chairs* *Wecome: The Honorable Aaron Motsoaledi Minister of Health-South Africa Cape Town, South Africa* *Opening Presentation: Robert Webster, St Jude's Children Research Hospital, Memphis, Tennessee, USA*	**Cross-Cutting Keynote:** **The interaction between influenza and lung co-pathogens** *Keith Klugman, Department of Global Health at the Rollins School of Public Health at Emory University, Atlanta, Georgia, USA*
09.40-11.00		**Morning plenary session 1—Virology** **vRNP structure and how does the polymerase work** *Speaker: Yoshihiro Kawaoka, University of Wisconsin, School of Veterinary Medicine, Madison, USA* **PA-x and PB1-N40** *Paul Digard, The Roslin Institute, University of Edinburgh, Scottland* **Importins and their role in host restriction of avian influenza viruses** *Gülsah Gabriel, Heinrich-Pette-Institute, Leibniz Institute for Experimental Virology, Hamburg, Germany*	**Morning plenary session 2—Epidemiology** **Maternal Influenza Immunization** *Saad Omer, Emory University, Schools of Public Health and Medicine, Atlanta, Georgia, USA* **Epidemiology of influenza in Africa** *Cheryl Cohen, NICD, Cape Town, South Africa* **Challenges to estimating influenza mortality/severity** *Anthony Mounts, Global Influenza Programme, Health Security & Environment Cluster, World Health Organization, Geneva, Switzerland*
11.00-11.30		Morning networking and refreshment	Morning networking and refreshment
11.30-13.00		**Mid-day plenary session 1—Pathogenesis** **Lung injury / ARDS** *Malik Peiris, University of Hong Kong, Hong Kong, SAR, China* **Overview of pathogenesis and transmission of swine influenza** *Juergan Richt, Kansas State University, College of Veterinary Medicine, Manhattan, Kansas, USA* **Experimental studies of influenza virus transmission in humans** *Speaker: Jonathan Van Tam, Health Protection & Influenza Research Group, Epidemiology and Public Health, University of Nottingham, Nottingham, United Kingdom*	**Mid-day plenary session 2—mmunology** **Mx Restriction of influenza viruses** *Otto Haller, University Hospital Freiburg, Freiburg, Germany* **T cells in the respiratory tract** *Thomas Braciale, University of Virginia, Charlottesville, Virginia, USA* **B cells and influenza** *Paul G. Thomas, Department of Immunology, St. Jude Children's Research Hospital, Memphis, Tennessee, USA*
13.00-14.00		Lunch - on own	13.00-15.00 Lunch - **Satellite Symposium** **Four Questions about Influenza Immunization, Sponsored by Sanofi Pasteur**
14.00-15.30		**Concurrent afternoon workshops** **1A: News and Views from the H7N9 Outbreak** State of the Art Presentation: H7N9 **1B: Epidemiology I** **1C: Policy and Risk Communication**	15.00-16.30 **Concurrent afternoon workshops** **3A: Evolution, Systems Biology & Genomics** **3B: Antiviral Drugs and Resistance** **3C: Disease Burden and Health Economics**
15.30-16.00		Afternoon networking and refreshment	16.30 – 17.00 Afternoon networking and refreshment
16.00-17.30		**Concurrent evening workshops** **2A: Virology and Viral Receptors** **2B: Epidemiology II** **2C: Models informing Public Health and Pandemic Mitigation**	17.00 – 18.30 **Concurrent evening workshops** **4A – Innate and Adaptive Immunity** **4B – Vaccines I** **4C – Transmission and Infection Control**
17.30-19.30		**Welcome reception** *(Options VIII exhibition hall 2)*	18.30-21.00 **Poster Reception** *Walkabout session #1* *(Options VIII exhibition hall 2)*

Options VIII Programme

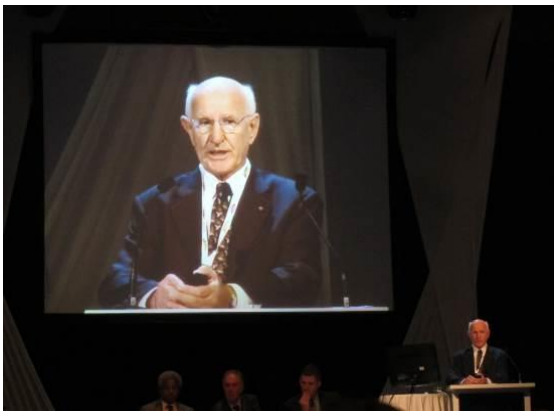
	Sat. 07 Sept	Sun. 08 Sept	Mon. 09 Sept
08.00	**Feature Cornerstone Session: Animal-Human Interface** **Mammalian adaptation of influenza viruses: what we know and what we don't** *Terrence Tumpey, Immunology and Pathogenesis Branch, Influenza Division, Centers for Disease Control and Prevention, Atlanta, Georgia, USA* **Ecology, evolution, and human health risks from emerging swine influenza viruses** *Richard Webby, Infectious Diseases, St Jude Children's Research Hospital, Memphis, Tennessee, USA*		
09.00-09.40		**Cross-Cutting Keynote:** **Universal epitopes, their application to vaccines and therapy and importance in influenza epidemiology** *Speaker: Peter Palese, Icahn School of Medicine at Mount Sinai, New York, New York, USA*	**Cross-Cutting Keynote:** **Host genetics of human influenza** *Paul Kellam, Wellcome Trust Sanger Institute, Hinxton, Cambridge, United Kingdom*
09.40-11.00	**Risk assessing animal viruses for pandemic threat** *Nancy Cox, WHO Collaborating Center for Surveillance Epidemiology and Control of Influenza, National Center for Immunization and Respiratory Diseases, Coordinating Center for Infectious Disease, Influenza Division, Centers for Disease Control and Prevention, Atlanta, Georgia, USA* **Human H5N1 and H7N9 Disease or Human Disease with Avian Viruses (H5, H7, H9, even H6)** *Peter Horby, Oxford University Clinical Research Unit, - Wellcome Trust Major Overseas Programme, Hanoi, Vietnam; Singapore Infectious Diseases Initiative, Singapore* **The pros and cons of GOF studies** • *Yoshihiro Kawaoka* • *Charles Russell* • *Adolfo Garcia-Sastre* • *Michael Osterholm* • *Marc Lipsitch* • *Jessica Bloom*	**Morning plenary session 3—Diagnostics** **Real-time PCR** *Stephen Lindstrom, National Center for Immunization for Respiratory Diseases, CDC, Atlanta, Georgia, USA* **Influenza whole genome analysis and its role in diagnostics, patient care and public health** *Monica Galiano, Health Protection Agency, London, United Kingdom* **Clinical relevance of influenza viral load measurement** *Nelson Lee, Stanley Ho Center for Emerging Infectious Diseases, The Chinese University of Hong Kong, Hong Kong, SAR, China*	**Morning plenary session 4—Therapeutic Interventions** **Overview of existing therapies/clinical experience with neuraminidase inhibitors** *Michael Ison, Northwestern University, Evanston, Illinois, USA* **Overview of the role of immunmodulation, cellular factors and proteases** *Béatrice Riteau, Faculte de Medecine de Laennec, Unité VirPathFrance Lyon, France* **Polymerase inhibitors** *Martin Schwemmle, University Hospital Freiburg, Freiburg, Germany*
11.00-11.30		Morning networking and refreshment	Morning networking and refreshment
11.30-13.00	Scholarship awards ceremony	**Mid-day plenary session 3—Clinical** **Brave and ISARIC: New Paradigms for responding to global respiratory threats** *Nahoko Shindo, World Health Organization, Geneva, Switzerland* **Influenza and pregnancy** *Shigeru Saito, Department of Obstetrics and Gynecology, Graduate School of Medicine and Pharmaceutical Science for Research, University of Toyama, Toyama Prefecture, Japan* **The many faces of influenza** *Fred Hayden, University of Virginia, School of Medicine, Charlottesville, Virginia, USA*	**Mid-day plenary session 4—Vaccines** **Overview of vaccine effectiveness issues and controversies** *Alain Moren, EpiConcept, Paris France* **Next generation of influenza vaccines** *Rick Bright, HHS/OS/ASPRA BARDA, Washington, District of Columbia, USA* **Clinical aspects in the development and licensing of the Russian-based live attenuated influenza vaccines for pandemic influenza preparedness in developing countries** *Larisa Rudenko, Institute of Experimental Medicine of the NorthWest Branch of the Russian Academy of Medical Sciences, St Petersburg, Russia*
	12.00-13.00 **isirv** annual general meeting (AGM)		
13.00-14.00		Lunch - on own	Lunch - on own
14.00-15.30		**Concurrent afternoon workshops** **5A: Animal-Human Interface** **5B: Vaccines II** **5C: Diagnostics**	**Concurrent afternoon workshops** **7A: Late Breaking Abstracts** **7B: Surveillance II** **7C: Novel Therapeutics**
15.30-16.00		Afternoon networking and refreshment	Afternoon networking and refreshment
16.00-17.30		**Concurrent evening workshops** **6A: Animal Influenza and Models** **6B: Surveillance I** **6C: Clinical Management** **Poster Reception** *Walkabout session #2* *(Options VIII exhibition hall 2)*	**Closing plenary session** **Public Health** **Usefulness of modeling for decision making on influenza** *Guy Walker Department of Health, London, United Kingdom* **Non-pharmaceutical interventions-effectiveness and consequences** *Benjamin Cowling, University of Hong Kong, Hong Kong, SAR, China* **Update on global vaccine policy** *Marie-Paule Kieny, World Health Organization, Geneva, Switzerland*
17.30-19.30			

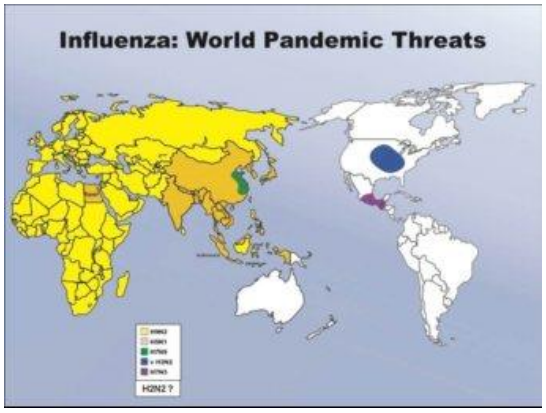
(二) 會議過程與重要演講內容摘錄

此次總計約有 900 人與多個國際媒體參加此一為期 5 天的重要國際會議，會議進行的模式是以早上 9 點至下午 1 點，均是安排不同主題的專題演講，午 2 點到晚上 7 點半則是安排兩場次的口頭論文發表，每個場次有三個主題同時進行。以下針對較重要的演講內容做介紹。

1. 開幕演講(9/5)：

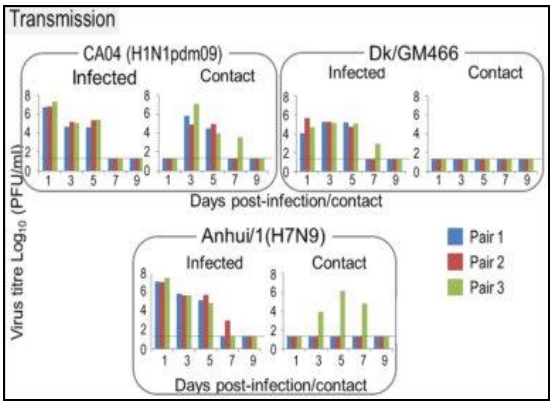
講者是禽流感權威、美國聖猶大兒童研究醫院 Robert G. Webster 教授。他簡介了他的對流感病毒的研究過程。他提到當年他與友人在海邊散步，看到大量的死鳥，他懷疑是否與禽流感病毒相關，故設計研究進一步採檢了數百隻鳥類來研究，後來經過更多的研究，終於發現禽流感病毒與人流感病毒間的相關性。他特別提到當年想要申請經費研究禽流感病毒時曾多次碰壁，而將成果發表成論文時還遭到退稿，藉此來勉勵年輕的學者們要堅持努力的方向，最終仍是可以得到好的成果。Robert G. Webster 教授分析在現階段全世界有大流行威脅性的流感病毒包括 H9N2、H5N1、H7N9、vH3N2、H7N3 與 H2N2 等。其中從燕雀(Brambling)分離出來的 H9N2，為歐亞地區家禽常見的禽流感病毒，其具有高度重組(reassortment)的潛力，目前已知的 H5N1 與 H7N9 禽流感病毒，其中六段基因均來自於 H9N2，因此其威脅不容小覷。而對於流感防治的問題有四大挑戰：是否病毒基因的分析足以預測未來可能的大流行病毒?而我們對於 H5N1 或 H7N9 流感病毒可能引起的大流行之準備是否足夠？廣效性流感疫苗(universal influenza vaccine)的安全性?第四點則是提醒各國應該要盡可能地降低流感病毒重組的風險。這位 81 歲知名禽流感病毒專家勉勵在場的與會者，針對流感防治要持續的研究，以降低流感大流行對人類的衝擊。





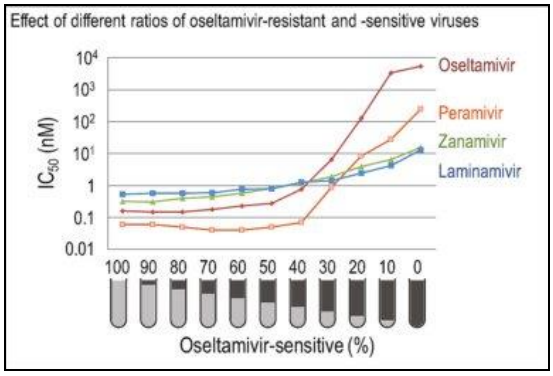
2. Morning Plenary Session 1—病毒學(9/5)：

一共有三位講者，其中來自美國威斯康辛州麥迪遜大學的 Yoshihiro Kawaoka 博士，特別討論了 H7N9 流感病毒的一些研究發現。首先是病毒的複製能力，實驗中發現 H7N9 流感病毒可以在多種哺乳類動物宿主的呼吸道上皮細胞中複製。而在受體結合與傳播模式試驗中，從之前的研究中得知，大多數的禽流感病毒會與α2-3 半乳糖苷唾液酶受體結合，而人流感病毒會與α2-6 半乳糖苷唾液酶受體結合。人類的α2-6 唾液酶受體主要分布在整個呼吸道系統，而α2-3 唾液酶受體則只占少部分，且存在於下呼道系統，這種受體類型和分佈的不同被認為是流感病毒在禽類和人類跨物種傳遞的主要障礙。而分離自中國的 H7N9 禽流感病毒中，有部分菌株在 HA(Hemagglutinin，血球凝集蛋白)的第 226 個胺基酸位置發生突變，使其具有結合α2-6 唾液酶受體的能力，此變異可能導致 H7N9 禽流感病毒具有微弱感染哺乳類動物包括人類上呼吸道細胞的能力，因而增加了可能人傳人的危險性。利用醣晶片量化分析(Glycan array)發現，H5N1 禽流感病毒主要是結合α2-3 唾液酶受體，H7N9 安徽株(Anhui/1)、杭州株(Hangzhou/1)與 H1N1 流感病毒則較易結合α2-6 唾液酶受體，但是 H7N9 上海株(Shanghai/1)則顯現可以同時結合兩種唾液酶受體。H7N9 安徽株(Anhui/1)在雪貂實驗中發現其可以經由呼吸道飛沫傳播。而在抗病毒藥物感受性試驗中，H7N9 上海株(Shanghai/1)在第 294 個胺基酸位置有發生突變，當其由 R 變成 K 時，就會對 neuraminidase inhibitors 產生抗藥性，如果突變的病毒佔總病毒量的三成以上，現行的抗病毒藥物就會失效。結論是 H7N9 流感病毒可以在多種哺乳類動物宿主複製，而安徽株在雪貂實驗中發現其可以經由呼吸道飛沫傳播。



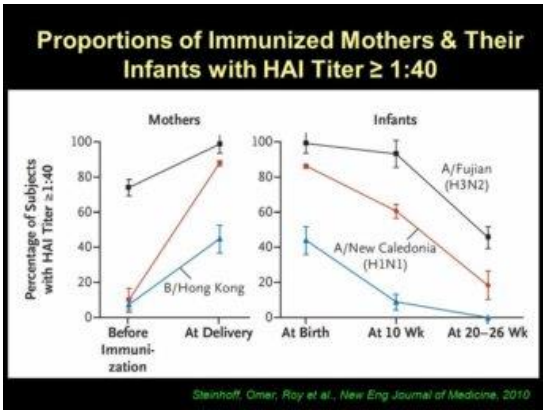
In vitro virus sensitivity to NA inhibitors

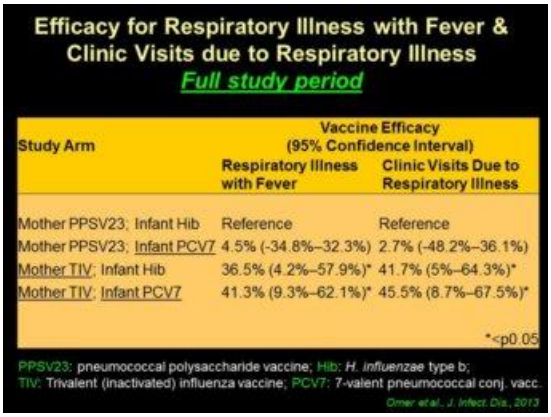
Drugs	IC_{50} value (nM)			
	Anhui/1 NA-294R	Shanghai/1 NA-294K	Shanghai/1-NA-294R	Shanghai/1-NA-294K
Oseltamivir carboxylate	0.49	0.47	0.16	5403.50
Zanamivir	0.65	1.32	0.32	15.50
Laninamivir	0.83	0.93	0.53	12.93
Peramivir	0.09	0.22	0.06	245.80

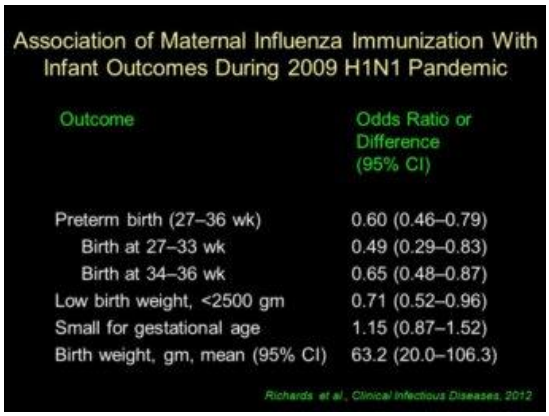


3. Morning Plenary Session 2—流行病學(9/6)

一共有三位講者，其中美國亞特蘭大 Emory 大學的 Saad Omer 博士發表孕婦施打流感疫苗的效益。其首先提到小於六個月大的兒童得到流感時有較高的死亡率(1.3 /10 萬人年)，此外，懷孕的婦女得到流感時，有較高機會發生併發症及住院，死亡率亦較高。因為目前沒有可以提供小於六個月大的兒童施打的流感疫苗，所以懷孕婦女施打流感疫苗，可以同時保護自己與孩子，證據顯示婦女於懷孕期間注射流感疫苗，其新生兒體內的流感病毒抗體可以持續到出生後 20-26 週。在 Omer 博士的研究中發現(*J Infect Dis. 2013;207(7): 1144-1147. doi: 10.1093/infdis/jit003*)，若以孕婦注射 23 價肺炎鏈球菌疫苗合併新生兒注射 B 型流感嗜血桿菌疫苗(Hib)為對照組，孕婦注射三價流感疫苗合併新生兒注射多醣體七價肺炎鏈球菌疫苗，可以有效降低兒童發生呼吸道疾病及發燒的風險達 41.3%(95% CI, 9.3-62.1%)，可以降低因呼吸道疾病合併發燒的就診比例達 45.5% (95% CI, 8.7%–67.5%)。若是在流感流行季節，更可以降低到 72.4%和 66.4%。所以孕婦接種流感疫苗不但可以保護自己，還可以加強七價肺炎鏈球菌疫苗對新生兒的保護力。有人會質疑接種流感疫苗是否會引發早產或新生兒體重過輕等問題，不過 Omer 博士利用 2009 年 H1N1 流感疫苗接種的資料顯示並無此現象(*Clin Infect Dis. (2013) doi: 10.1093/cid/cit045*)，接種流感疫苗的孕婦較不會早產(aOR: 0.63, 95% CI: 0.47-0.84)且其新生兒體重比未注射疫苗孕婦者平均重 45 克。因此他提到 2012 年起世界衛生組織的免疫戰略諮詢專家組(Strategic Advisory Group of Experts (SAGE) on Immunization)建議，應當將懷孕婦女列為季節流感疫苗接種的最優先對象。





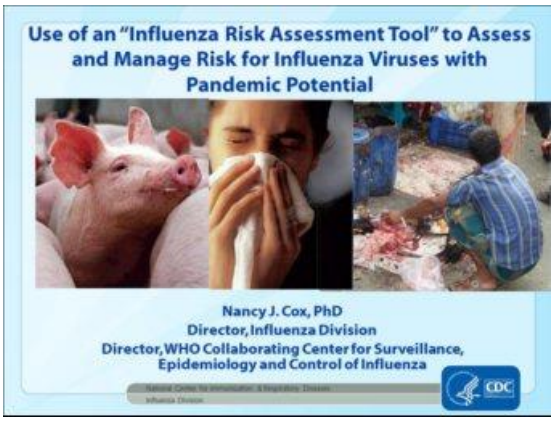


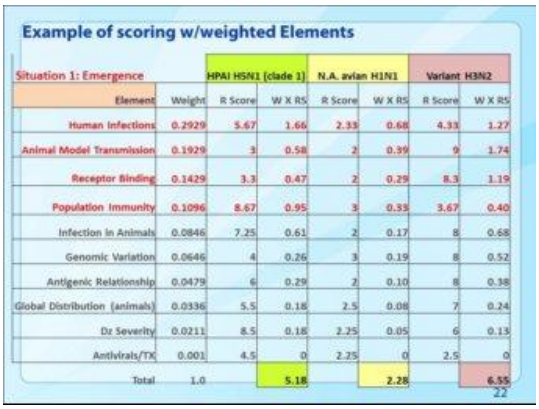
4. Future Cornerstone Session : Animal-Human Interface (9/7)

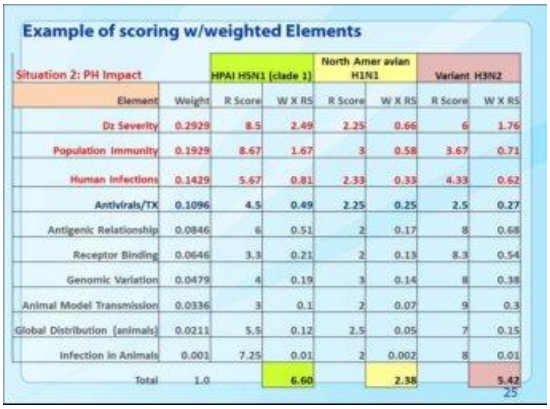
一共有四位講者，第一位討論了流感病毒基因對哺乳類動物感受性的研究，第二位講者是討論新型 H3N2 豬流感病毒(vH3N2)，並且發表其在美國養豬場進行的流感病毒監測情形。第三位講者是美國疾病控制和預防中心(CDC) 流感部主任考克斯 Nancy Cox，題目是動物流感病毒是否會引起流感大流行的風險評估。第四位講者 Peter Horby 博士則是分析 H5N1 禽流感病毒與 H7N9 禽流感病毒的人類感染病例臨床表現的比較。

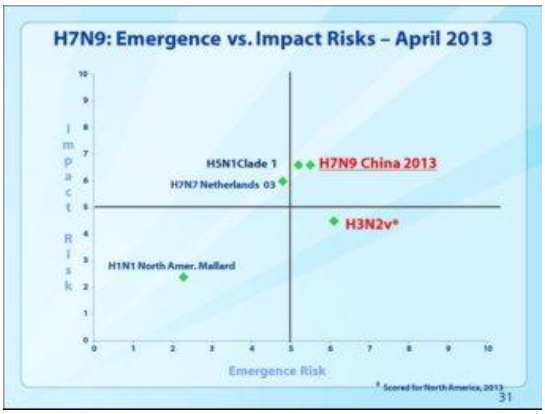
在此摘錄 Nancy Cox 博士的演講內容。她主要是介紹美國 CDC 發展的**流感風險評估工具(Influenza Risk Assessment Tool, IRAT)**。此工具的的重要性，主要是提供新型流感病毒的風險評估資訊，讓決策單位可以定是否進行進一步的監測或發展疫苗等計畫。此項評估工具不但可以使決策透明化，亦可以了解目前欠缺的知識與關鍵信息，促使學界進一步研究。此外，也可以做為與民眾溝通的工具，促使部門間的合作，更可以提供一個靈活的方式，隨著新的研究結果可以定期更新風險評估，做為流感整備計畫制定政策的參考。不過，此工具不是預測工具，

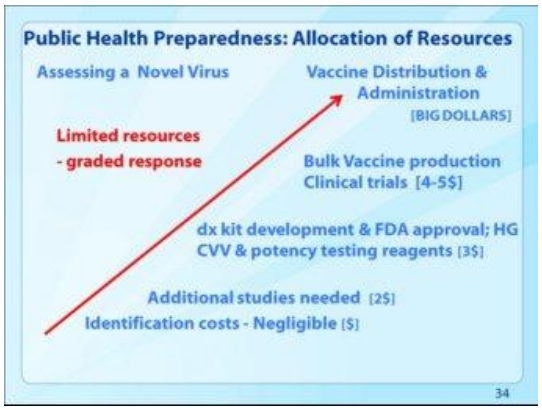
無法預測下一次大流行會是何種病毒，也無法精確的計算每個病毒的風險值，而且仍是需要各種專家的參與才能進行。進行 IRAT 的第一個步驟是集合獸醫、公共衛生專家、實驗室研究人員與流行病學專家等，組成一個工作組。先確認要評估流感病毒的風險以及對公共衛生的影響需要那些要件，訂定每個要件的定義，決定分數級距並確認每個要件的權重，最後再計算出總分。目前 IRAT 共訂定 10 項要件，有四項是屬於病毒的特性(病毒基因的變異性、與宿主受體的結合度、動物實驗的傳染力與抗病毒藥物的感受性)，有三項是對群眾的影響性(民眾的抗體盛行率、疾病嚴重度與抗原與疫苗株的差異)，最後三項是流行病學與生態學特性(病毒在全球的流行情況、動物的感染情形與人類感染情形)。每個要件在分成低(1-3 分)、中(4-7 分)、高風險(8-10 分)三個等級。計算權重時主要考量兩部分，情況一是發生的風險性(Risk of emergence)，即此病毒是否有持續人傳人(大流行)的可能性，情況二是此病毒對公共衛生的影響程度(Public Health impact)。以此二者為軸，評估每個病毒的風險。之後她舉了新型 H3N2 豬流感病毒(vH3N2)、高病原性 H5N1 禽流感病毒和北美 H1N1 禽流感病毒三者為例作說明，在發生的風險性上，vH3N2> H5N1> H1N1，而對公共衛生的影響程度則是 H5N1 > vH3N2 > H1N1。此外，當有新的知識時，應再次評估風險。在 vH3N2 人類感染個案僅 12 例時，美國 CDC 及做了第一次的評估，風險落在最高的象限，但隨著情況更清楚，人類感染個案數增加到 321 例時，重新評估的結果，其對公共衛生的影響程度就下降了。H7N9 流感病毒出現時，美國 CDC 也利用此工具進行評估。此評估工具可以可作為流感整備計畫中疫苗研發製造的參考。當病毒風險程度為低優先時，可能只需在實驗室製備疫苗株，風險提升時要考慮進入疫苗安全性試驗，風險再升高時就要考慮量產，風險為最高等級時就建議開始臨床試驗。不同的整備程度所需的資源差距很大，此評估工具可以提供決策單位資源分配的參考。









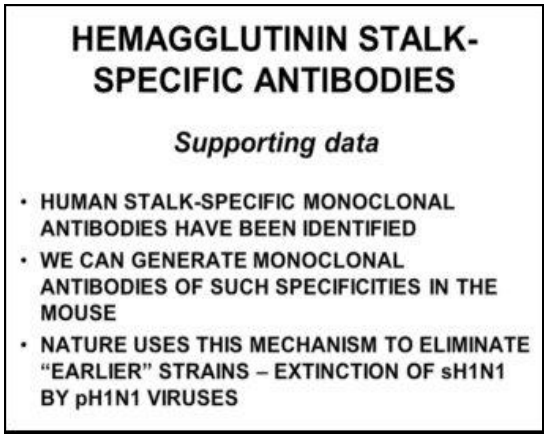


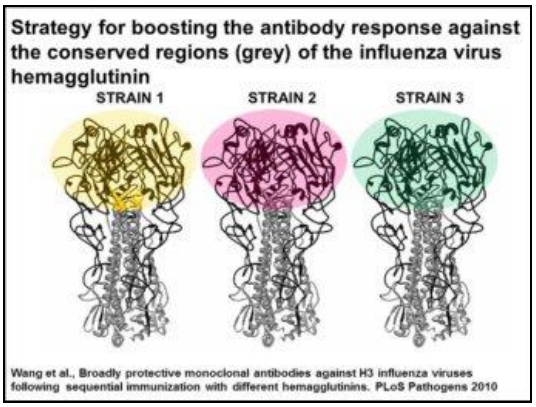
5. 流感病毒「功能獲得」研究的正反意見論壇 (The Pros and Cons of Influenza Gain of Function Studies) (9/7)

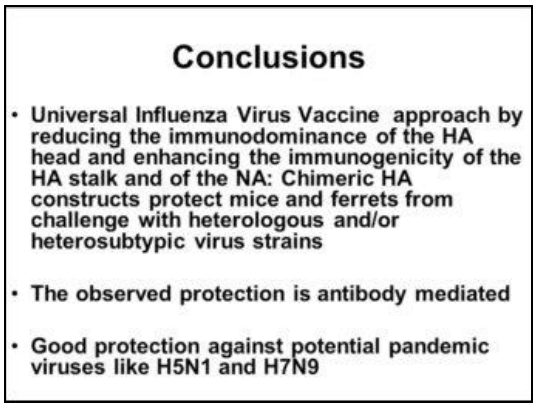
所謂功能獲得研究(Gain of Function Studies)是指在實驗室中對野生的病毒株進行各種改造，以確定哪些特性能夠增加其毒性。這種實驗具有爭議性，因為存在可能被利用為生物恐怖攻擊的風險，或者病毒從實驗室意外釋放的風險。因此，這種實驗一直被一些科學家和生恐安全部門的官員所反對。以流感病毒為例，這類研究一直存在爭論，因為變種流感病毒若意外釋出，可能導致大流行的等嚴重公共衛生災難。但是支持方的論點認為此類研究有助於確認病毒有哪些特徵可能引發全球性大流行，進而利用於流感防治整備工作，例如從 H5N1 型禽流感病毒的研究中發現，此病毒可能會造成大流行的風險，促使公衛發展並儲備疫苗因應。此次大會安排了正反方各三位學者來討論此議題。支持方提出用嚴格的實驗室生物安全規範，可以減低意外釋放的風險，反對方認為世界各國實驗室安全規範不一，無法保證沒有意外。而在大流行風險上，支持方認為可以由實驗得到確切證據，反對方則認為以低病原性流感病毒來試驗即可，不須以變種病毒來試驗，此可能違背人體試驗倫理規範。經過一個半小時的討論，這個問題仍未能達成共識。

6. Cross-Cutting Keynote Speech(9/8)

此場原排定講者紐約西奈山醫院伊坎醫學院的Peter Palese博士因故不能出席，故由著名的流感專家Adolfo García-Sastre博士代為報告，討論的題目是廣效型疫苗(universal influenza vaccine)的發展。廣效型流感疫苗的定義是可以提供對抗所有種類的流感病毒的疫苗。流感病毒是一種很容易產生突變的病毒，其基因會經由抗原改變(antigenic shift)與抗原更換(antigenic drift)等方式生變異，造成主要表面抗原的改變。現行的流感疫苗是依據每年監測計畫取得之該年流行病毒株的表面抗原來製造，此疫苗的保護力到了隔年便會因病毒抗原改變而降低，因此每年都需要再接種一次。廣效性流感疫苗的發展就是希望能突破此限制，甚至希望能涵蓋未來可能的造成大流行新興流感病毒。目前的研究方向是利用流感病毒不易變異的結構部位來製造疫苗，研究發展中的包括利用流感病毒的M2e抗原、NA(神經氨酸苷酶)、HA(血球凝集蛋白, Hemagglutinin)以及其他結構蛋白的保留性序列等。Adolfo García-Sastre博士此次主要討論的是利用HA的軸柄部(stalk domain)產生的單株抗體。流感病毒HA的軸柄部是比較穩定的構造，在不同的流感病毒型別中，其軸柄部變異很小，因此以此為基礎引發的中和抗體，可以對抗不同型別的流感病毒。此外，若可以降低HA頭部抗原的影響，加強HA軸柄部與NA的抗原特性，可以引發出具有對抗不同抗原流感病毒的中和抗體。Peter Palese博士在此次大會發表的海報論文(編號P2-548: A universal influenza virus vaccine based on the stalk domain of the hemagglutinin)，即是利用此疫苗進行的動物實驗。以不同型別的流感病毒進行動物感染試驗，結果顯示接受疫苗注射的老鼠，可以有效降低致病率與死亡率。更重要的發現是利用H7N1病毒試驗時，其引發的高濃度抗體可以有效對抗此次在中國流行的H7N9病毒，因此是流感疫苗發展的明日之星。





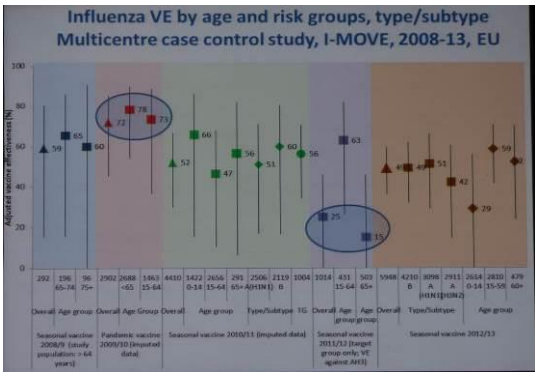


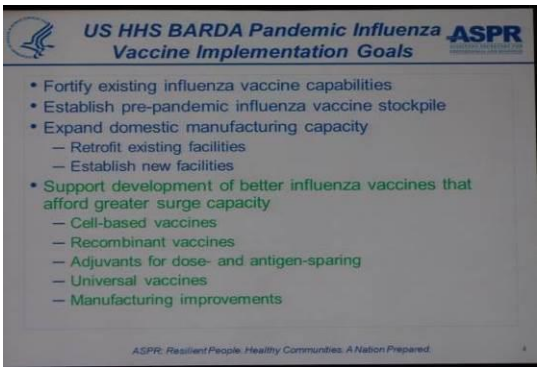
7. Mid-Day Plenary Session 4—疫苗(9/9)

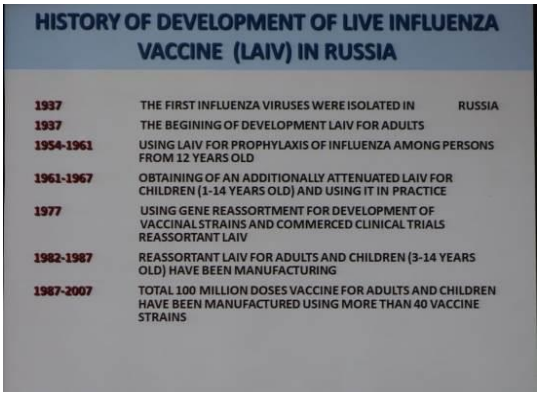
中午時段的演講討論主題是疫苗。第一位講者是 Alain Moren 博士，介紹由其主持的 I-MOVE network 所進行的流感疫苗的效能測量(Measuring Influenza Vaccine Effectiveness)。此計畫是聯合歐盟、美國、澳大利亞與加拿大一起合作進行的，一共有 17 個國家參與計畫。方法是選定類流感或急性呼吸道感染門診病人超過 1000 人的診所作為定點監測點，在流感疫苗接種計畫開始後 14 天起，抽樣對病人進行鼻咽拭子採檢，進一步做 PCR 與病毒培養。此監測已進行多年，其目的是希望能知道不同流感病毒型別的疫苗效能差異，亦希望能了解不同品牌疫苗的效能差異，這些資料可以提供 WHO 作為選定疫苗株時的參考。今天是初步報告結果，監測的資料很多，初步可以看到流感疫苗的效能在不同的病毒型別、宿主年齡層等均有差異，但是樣本數不夠大，所以在某些問題點上並不能得到統計上的差異。但是若要增加樣本數，則需要龐大的經費，所以 Alain Moren 博士邀請有興趣加入監測的國家可以與其聯絡。

第二位講者是由美國衛生部整備辦公室(Office of the Assistant Secretary for Preparedness and Response)之 BARDA(Biomedical Advanced Research and Development Authority)部門的 Sheng Li 博士來討論新一代流感疫苗的發展方向。三大目標是製造量能提升、保護效力提升與產程加速。李博士討論了目前正在進行臨床試驗與已經上市的各種疫苗。

第三位講者是來自蘇俄的 Larisa Rudenko 博士，介紹減毒流感疫苗的發展研究與目前的應用。







8. Closing Plenary Session—公共衛生

第一位講者是英國衛生部的 Guy Walker 博士，討論流感大流行的疫情模型推估。模型推估在流感大流行時可以用來推估疫情規模及評估介入模式的效果。英國的流感大流行模型推估，是以最壞的情況(Reasonable Worse Case, RWC)為基礎，RWC 定義包括：以全國總人口數比例來估算，罹病率超過 50%、10-25%會發生併發症、在尖峰期間每週新發病人數約是 10-12%、尖峰期間的缺席率 15-20%、需要住院率達 4%(平均住院 6 天)、流感致死率達 2.5%。在這個前提假設下，有效的介入措施包括：抗病毒藥物治療、家庭接觸者的抗病毒藥物預防性投藥、季節流感疫苗接種(兒童與鋼風險群)與抗生素。可能有效的介入措施包

括：居家隔離、學校與大型公共場所關閉、注射大流行流感疫苗以及減少感染源(早期診斷隔離，不過十分困難)。無效的方式包括：將疾病阻絕於境外、旅遊限制以及個人衛生習慣的宣導(民眾無法反映多種訊息與活動)。接著他以此模型推估應用於英國 2009 年 H1N1 大流行的應變作了一些討論。在大流行期間，模型推估主要是要回答三大問題：疫情嚴重度(個案數、住院人數、死亡人數)，疫情期間(尖峰期時間、可能時間)，政策方向(限制抗病毒藥劑使用、關閉學校等)。整體來說，此模型推估在該段大流行時期的準確度還不錯，但是，大眾對推估的數據有過高的期待，而決策者對於依據真實疫情推估得到的較溫和疫情結果態度保守，此外，模型推估需要及時的抗體盛行率與病毒學資料才能有較準確的結果。因此建議組成專家小組來進行流感模型推估，而且要設定不同的情境(不只是 RWC 一種)，以便能有效率的應變。不過，Guy Walker 博士語重心長的說模型推估畢竟只是一種用來協助風險分析的工具，不是占星術。而民眾與政客最想知道的一些微小的細節，並不是使用模型推估工具可以知道的。

第二位講者是 Benjamin Cowling 博士，主要是討論流感大流行時，非醫療處置(non-pharmaceutical intervention，NPI)的效能與結果，其主要是討論個人層次(口罩、手部衛生)、社區層次(關閉學校)與國際層次(出、入境管制與旅遊限制)。根據 Cowling 博士在香港與曼谷的實驗發現，對於有症狀(發燒與咳嗽)的感染源，戴口罩與洗手衛教是可以達到保護家戶接觸者的目的。而關閉學校對於 0-12 歲的兒童也有保護的效果。至於出入境管制在流感大流行的防治上則無效益。不過，NPI 的臨床研究與證據較少，仍有許多問題待解答。

最後一位講者是 WHO 的 Marie-Paule Kieny 博士討論最新的全球疫苗政策。WHO 最新的目標有三項：提高季節流感疫苗的使用率、增加疫苗製造生產能力與疫苗的未來研究發展方向。第一項目標中，根據 2012 的免疫戰略諮詢專家組(SAGE)的建議，季節流感疫苗注射的五大優先族群包括：孕婦、醫護人員、小於 5 歲的兒童、年長者以及有慢性疾病的族群。但是目前有國家型季節流感疫苗接種計畫的國家佔不到 50%，而且只有少數國家達到在老年族群季節流感疫苗接種率超過 75%的目標。流感疫苗的取得價格過高與注射涵蓋率監測資料不齊全，都是需要繼續努力的挑戰。至於增加流感疫苗產能與研發的部分，雖然有些進展，但仍有很長的一段路要走。

SPI-M Blackett Meeting

- Conclusion - If you are going to have a RWC then the current ones should be retained (CAR of 50%, CFR 2.5% etc.)
- But is there a better approach?
  - Not just 1 scenario- the RWC
  - Probability weighted scenarios (as used in DH for countermeasures)
  - Practical approximation to probability distribution for cost benefit analysis
  - Consider the "transition points" of the current systems

Introduction Individual Community International **Comments** Acknowledgments

Discussion

- Main observations in the WHO papers published in EID in 2006:
  - Very limited evidence base for the effectiveness of NPIs
  - Exit screening might have potential, other international measures including travel restrictions not likely to be feasible, focus should be on national and community-level measures.
  - National and community-level transmission-limiting measures may delay epidemic in time to allow arrival of vaccines.
- Updated knowledge base now

RJ Cowling Slide 26

Work Plans to Achieve GAP-II Goals

GLOBAL ACTION PLAN FOR INFLUENZA VACCINES (GAP)

5 YEAR STRATEGIC PLAN FOR WHO INTERNAL COORDINATION IN SUPPORT OF GAP OBJECTIVES

OBJECTIVE 1 Evidence based vaccine use and uptake	OBJECTIVE 2 Increase vaccine production capacity	OBJECTIVE 3 R & D	GENERAL
Global vaccination recommendations and facilitation of country policy development - Review impact of seasonal influenza vaccination (IVR/WIP) - Update global seasonal vaccine policy recommendations (SAGE/IVR) - Develop regional workshops for vaccine policy development with all regional offices (IVR) - Continued monitoring of vaccine policy implementation and coverage (IVR/IVR) - Enhance vaccine deployment plans	*Road-mapping for vaccine technology transfer* - Analysis of developing regions and countries needs for vaccine production in technology transfer project (IER)* - Analysis on long term production capacity for pandemic vaccine in developing countries based on business plans of manufacturers for domestic and export markets (IER)* *Strategies on new approaches for technology transfer and sustainability:* - Consider longer term mechanisms and develop strategic approaches to ensure	*Landscaping on vaccine research and development* - Annual conference on non-clinical research and clinical evaluation of influenza vaccine technologies that induce cross-protective and long lasting immunity (IVR) - Building database on influenza vaccine clinical trial results for public access through internet (IVR) - Continued monitoring of global vaccine pipelines development (IVR/IER)	*Develop indicators of success for GAP-I/GAP-II* - Develop and monitor indicators identified for measuring success for GAP objectives and provide updates (IER/IVR)* *Decade of Vaccine (DoV)* - Align activities in GAP with the DoV initiative (IVR)* *PIP Framework* - Identify and align activities in GAP with the PIP Framework objectives for influenza vaccine

311 Update on global vaccine policy – 9 September 2013 World Health Organization

肆、心得與建議

本屆流感防治年會會議的內容相當的豐富，從病毒的基礎研究、臨床個案的處置以及疫苗研發進展議題都有涵蓋。近年來在流感病毒的基因分析與致病機轉等研究有許多豐碩的成果，可以做為流感防治的基礎。不過，流感病毒的獲得功能試驗一直以來存在著支持與反對的兩派意見。因為如果實驗室管理不慎，很可能引起流感大流行，造成人類的浩劫。但是，如果能知道病毒的致病性基因，則對疫苗的研發、流感大流行的預測均有助益。依據目前的規範，要進行此類型試驗，需要在P3 plus或P4等級以上的實驗室才能進行，且相關的實驗室安全管理亦十分嚴格，以美國的規定來說，此類研究必須得到國家衛生部門的核准才可以進行，台灣目前仍未有學者進行此類相關研究，若未來有學者有此意願，衛生部門應訂定相關規範來監督。

本屆年會因為年初時中國爆發的H7N9禽流感疫情，使得動物與人類間的界面成為流感大流行防治的重要議題。目前對於動物疫情的防治策略仍是以阻斷此介面為手段，不過在中國與東南亞地區人民的生活型態，完全阻絕是極為困難的。大會對此議題的專題討論中，聚焦在病毒基因的分析研究及風險評估，對於防治的策略則未有著墨。在口頭論文的報告中，有一些較有趣的報告：例如有學者是利用滑動式的鍋蓋取代可以分離掀開的鍋蓋，或是利用塑膠袋密封方式來宰殺，以減少家禽宰殺時引起的排泄物噴濺汙染。另外有學者是調查禽畜業者對禽流感的知識、或販售動物藥劑的藥局或調劑者的禽流感的知識等，希望能藉此了解如何宣導。但是這些研究多是在東南亞等相對落後的地區，其研究報告不易應用於台灣。不過，台灣自2013年5月17日起，頒布了在傳統市場禁宰與禁售活禽的法規，這應該是最有效的阻斷人類與動物界面的策略。未來除了繼續執行此策略外，應定期監測禽類與豬的流感病毒流行情形，及早確定病毒基因的改變，加上公共衛生與農業部門密切的合作，才能因應可能的流感大流行。

在流感疫苗的研發方面，本次會議焦點在於廣效型疫苗的研發，利用流感病毒的HA 軸柄部產生的抗體，可以對抗不同型別的流感病毒，此確實是一項重大的突破，不過要進入臨床試驗仍需要二至三年的時間。而在抗病毒藥物的研發方面，僅有新型的抗流感病毒藥物favipiravir(T-705)的第二期臨床試驗的初步結果發表，其他藥物或治療方面，沒有重大突破。

此次大會在流感病毒的人類個案的臨床表現、治療反應等有多項討論。也特別安排了與流感病毒感染相關的其他肺部感染致病菌的專題演講。此外，世界衛生組織亦派專家來說明「對抗呼吸道病毒的宣言」(Battle against Respiratory Viruses (BRaVe) initiative)，指出每年全世界有390萬人死於急性呼吸道感染，雖然肺炎鏈球菌疫苗與與B型流感嗜血桿菌（Hib）疫苗的發明，有效的減輕了細菌性呼吸道感染的疾病負擔。病毒性感染則仍未有較大的進展，更甚者，新興的呼吸道病毒如SARS、H5N1與H7N9禽流感病毒、中東呼吸道症候群冠狀病毒等，對全球公共衛生造成很大的威脅，因此呼籲各國應積極投入防治與研究。此部分呼應了我國自2012年底開始加強不明原因肺炎的監測，不過，如要有完整的監測，需要投入更多的檢驗等實驗室相關預算，以要持續與醫界溝通，才能及早發現新興傳染病，即時啟動防疫機制來降低疫情擴散。

至於在流感疫苗接種政策部分，雖然世界衛生組織已呼籲多年，有季節性流感疫苗接種計畫的國家仍未達50%，而免疫戰略諮詢專家組(SAGE)的建議，季節流感疫苗注射的五大優先族群孕婦、醫護人員、小於5歲的兒童、年長者以及有慢性疾病的族群之接種率亦未達目標。我國自1998年開始推行公費季節流感疫苗注射計畫，逐步擴大公費疫苗注射對象，到2013年時，上述建議之對象除了孕婦外，皆已納入我國公費接種對象。不過接種率在65歲以上之年長者與小於5歲的兒童仍不甚理想。為了提高流感疫苗的接種率，本署近年來加強與各醫學會合作辦理醫護人員的在職訓練，開發數位學習課程，以提升臨床醫師在疫苗可預防疾病、疫苗學及接種實務上的知能。，此外也透過多元宣導管道及增設接種地點

等方式，積極鼓勵民眾踴躍接種，希望能實現預防勝於治療的效果。

此次國際會議不僅在流感防治的議題上有充分的討論，我國有多篇海報論文的發表，亦增加我國國際間的能見度。建議未來在經費許可下，可以增派人員參與此盛會，除了可以參觀其他國家的經驗外，也可進行國際衛生外交，拓展視野。整體而言，由於我國自2003年SARS以來，對流感大流行已投注大量人力物力進行準備工作，各項新資訊都能及時擷取應用，相關的重點目標均已納入我國的「因應流感大流行整備計畫」中執行。不過因為自2009年H1N1流感大流行後，沒有新的流感大流行疫情，加上近年來國家財政較為困難，使得本署的整備相關預算逐年減少，這是一個重要的警訊，因為就如同大會主席Marc Mendelson博士所說的，關於流感，唯一可預見的就是它的不可預測性。因此，我們不能對此掉以輕心，仍須持續且積極的執行流感大流行整備計畫， 以期能保障人民的健康與生命。

Health literacy of influenza prevention in Taiwan – a scale development

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Background

In 1990 the concept of health literacy was created in the United States to examine people's ability to utilize medical recourses and comprehend doctor's advice regarding chronic diseases. The WHO, US HHS and IOM defined health literacy as 'The degree to which individuals have the capacity to obtain, process and understand basic health information and service needed to make appropriate health decisions'. In the field of infectious diseases, health literacy studies are rare, with the exception of studies on HIV carriers.

Taiwan has an influenza vaccination program that began in 1998, and began to stockpile influenza antivirals since the emergence of avian influenza virus A (H5N1) in 2003. During the H1N1 novel influenza pandemic in 2009, Taiwan launched the H1N1 influenza vaccination program on November 1st hoping to create herd immunity. However, inoculation decreased following the death of a 7- year-old boy one month after being inoculated with the H1N1 influenza vaccine. This study tries to implement the concepts and elements of health literacy into influenza prevention which led to the development of this scale.

We used a qualitative method to develop our scale which would serve our specific purpose since there is no existing scale that would cater to our study. We took a bottom-up approach in the development of the scale for 'health literacy in influenza prevention'. Thus, with the qualitative method and bottom-up approach, the scale we developed can become a tool to assess the public's ability to understand and interpret influenza prevention messages.

Materials and Methods

We reviewed literatures and held study groups in order to establish the knowhow and the definition of 'health literacy's role in influenza prevention'. In addition to making decisions on the context, pattern, and question types, we conducted four focus groups consisting of experts, mass media and two opinion leader groups. The purpose of the focus groups was to check the applicability of the scale used to develop the questions. Researchers first developed the draft scale, allowed the four focus group symposiums to discuss the preliminary scale, then researchers classified and analyzed the scale through transcribed texts of the focus group sessions. Lastly, the scale was reviewed by six experts, and revised to be the final scale(Table 1). (Figure 1)

Results

In our study, we set up a structure for 'health literacy in influenza prevention', which included the operative definition 'The degree to which people have the capacity to obtain, understand and apply basic health information and utilize services, with subjects both over the age of 18 and have completed at least junior high school education'. The scale framework is set up based on the 'three levels of prevention' and with the five preventative points of health protection, symptom conscientious, diagnosis, treatment and self-care in mind. We want to test one's ability to obtain, understand, apply and use basic health information and services. Because this scale was developed to test ability, every question has a correct answer, thus can be scored easily. Additionally, due to time constraints, the question difficulty was low and there were no open ended questions. The final scale developed, through the analysis of the data collected from focus groups, scale analysis, and behavior survey, was finalized to be formed from 7 categories and 22 questions. (Table2, 3)

Conclusion

Through our focus group symposiums we found that gaps exist between influenza prevention information provided by the government and the amount received and understood by the public. This study identified a potential area to apply the concept of health literacy, with special focus on infectious disease prevention. Although this study was developed initially to test 'health literacy in regards to influenza prevention', it needs to be further assessed and tested for the usability in other applications.

Figure 1.

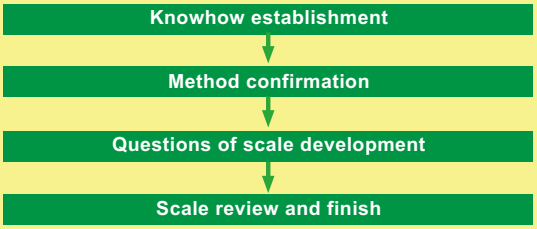

Table 1. The matrix of scale structure

	Obtain	Understand	Apply
Health protection			
Symptom conscientious			
Diagnosis			
Treatment			
Self-care in mind			

Table 2. Analysis of scale structure

(according to the prevention levels)

Categories of scale questions	Three levels of prevention				
	Primary prevention - preventing the occurrence of disease -		Secondary prevention - disease control -		Tertiary prevention - rehabil itation -
	Health protection	Symptom conscientious	Diagnosis	Treatment	Self-care in mind
1. Difference between influenza and common cold(2)		2			
2. Transmission and control of influenza(3)	1				2
3. Vaccination(3)	3				
4. Inoculate printed notice(4)	4				
5. Vaccine effect and safety(3)	3				
6. Antivirals usage(3)			1	2	
7. Antivirals Instructions(4)				4	
TOTAL	11	2	1	6	2

Table 3. Analysis of scale structure

(according to the comprehension levels)

Categories of scale questions	Obtain	Understand	Apply
1. Difference between influenza and common cold(2)		2	
2. Transmission and control of influenza(3)		1	2
3. Vaccination(3)		1	2
4. Inoculate printed notice(4)		2	2
5. Vaccine effect and safety(3)	1	2	
6. Antivirals usage(3)		2	1
7. Antivirals Instructions(4)			4
TOTAL	1	10	11

Taiwan CDC

Abstrct Number: 5048
Session: Policy and Risk Communication
Poster Group/ Board Number: I, P1-157

A preliminary report of the preparedness and response to avian influenza A(H7N9) infections, Taiwan, 2013

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Background

Outbreak of human infections with avian influenza A(H7N9) was reported by China in March 2013. This is the first time that humans infected by avian influenza A (H7N9) virus and cause fatalities. Human infections by this virus continue to be reported in China. Because of frequent cross-strait exchanges, human H7N9 infections in China are a menace to Taiwan society. This article described Taiwan's initial responses to influenza A(H7N9) infections from 31 March to mid-April.

Materials and methods

The responses are collected and sorted from everyday work logs of the Central Epidemic Command Center (CECC) for H7N9 influenza.

Results

The Infectious Diseases Advisory Committee meeting convened by Department of Health on April 3 recommended to enact the "Influenza Pandemic Preparedness Plan", use four major strategies and five defense lines in response.

Pandemic Preparedness in Taiwan

In addition, the experts participating in the meeting agreed to list "H7N9 influenza" as Category V Notifiable Infectious Disease and activate CECC for H7N9 influenza to closely monitor the situation, and collaborating and managing the resources to ensure effective response with relevant departments. Twenty-two cities and counties also established Local Epidemic Command Centers. As of April 16, CECC has hosted four meetings.

Governance Hierarchy

NSC (National Security Committee) chaired by the President

↓

CECC (Central Epidemic Command Center)
- **The Executive Yuan level**
- **The Vice Premier/ Minister of Health/ Director of CDC as the Commander**
- **31 ministries involved**

↓

22 Local Epidemic Command Centers

The preliminary responses included intensive surveillance, border quarantine, medical system assembly, risk communication and response, antiviral medicine stockpile, and vaccine preparation. To response timely, continue updating the newest outbreak information in domestic and international societies.

Physicians should report H7N9 suspected cases within 24 hours, and CECC continues to closely monitor the influenza A (H7N9) virus activity through various surveillance components, including the National Health Insurance Database, the Community-based Virus Surveillance, the Pneumonia and Influenza (P&I) Mortality Surveillance, and the Real-time Outbreak and Disease Surveillance (RODS). Moreover, CECC dispatched two epidemiologists to Shanghai on April 6 to better understand the ongoing H7N9 outbreaks in China.

Epidemic Surveillance Assessment

Taiwan National Influenza Center

Influenza vaccine consultative committee

Data sharing and International collaboration	Surveillance, analysis, and notification	Diagnosis and verification
• Collecting and analyzing nationwide influenza virus surveillance data. Creating, publicizing, and sharing analysis results		• Diagnosis and verification of influenza virus • Developing and standardizing new technology • Education and training

Contract Lab

Fever screening continued to be conducted at airports and seaports. Patients who developed respiratory symptoms after returning from areas affected by the H7N9 virus will be rushed to the hospital for further examination till the possibility of H7N9 infection is ruled out.

To ensure prompt treatment for patients diagnosed H7N9 infections, starting from April 6, reported H7N9 cases and close contacts of laboratory confirmed cases are included in the list of target individuals for the use of government-funded antivirals.

The regional commanders and vice commanders of the Communicable Disease Control Medical Network have completed site inspections of all the responding hospitals to reinforce health care capacity. Furthermore, CECC has also provided the "Hospital Preparedness Capability to H7N9 Checklist" to help hospitals evaluate and improve their preparedness.

CECC has utilized a variety of communication channels to communicate risks to prevent unnecessary panic and promote the importance of personal hygiene. CECC conducts press conference regularly every day to provide the latest H7N9 update in Taiwan and promote relevant response and prevention measures. In addition, health education materials have been published on websites and distributed to relevant units. Furthermore, Taiwan CDC also operates a toll-free 24/7 Communicable Disease Reporting and Care Hotline, 1922, for public inquiries.

Main Strategies of H7N9 Influenza Control

Four Major Strategies			
Surveillance & Assessment	**Interruption of transmission**	**Antivirals**	**Influenza Vaccine**
˙Containment outside borders	˙Border control ˙Community control ˙Health care preparedness ˙Individual and family protection	˙Assessment and maintenance of a stockpile ˙Multiple stockpiles ˙Increase availability of antivirus ˙Usage extension	˙No Vaccine ˙Contact WHO and vaccine company ˙Establish inoculation priority

Five Line of Defense				
Containment outside borders	**Border control**	**Community epidemic control**	**Maintenance of Medical System Functions**	**Individual and family protection**
˙Obtain international health data ˙Health detection of incoming passengers ˙Domestic surveillance ˙Gather virus data	˙Health information & travel alert ˙Immigration control	˙Social distancing	˙P't isolation ˙PPE preparedness	˙Fostering hygiene habits

Conclusions

Although the possibility of human to human transmission is still low, we should remain vigilant in face of the influenza A(H7N9) threats.

Taiwan CDC

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The overview of government-funded influenza vaccination program during influenza season 2011-2012

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Background

Influenza vaccination is publicly known as the most effective method for preventing influenza infection. To protect the public's health, the Taiwan Ministry of Health and Welfare started to launch influenza vaccination programs since 1998, focusing on high-risk groups. In the government-funded influenza vaccination program for influenza season 2011-2012, trivalent inactivated influenza vaccines (TIV) were used in six high-risk groups, including the elders aged more than 65 years, children aged six months through six years and elementary school students from grade one through four, residents and staff in nursing homes and other long-term care facilities, healthcare and public health personnel, poultry or livestock farmers and animal health inspectors, and people with catastrophic illness.

Materials and methods

The influenza vaccine uptake rates for each high-risk group were obtained via the Influenza Vaccine Information System (IVIS). The healthcare facilities responsible for inoculations reported the inoculation numbers to the system every day from October 1st 2011 to February 13th 2012, reported every week from February 14th 2012 to April 9th 2012, and reported every 30 days from April 10th 2012 to June 30th 2012.

Results

During the influenza season 2011-2012, 2,582,859 doses of influenza vaccines were inoculated. The coverage rates for each group were as follows: the elders aged more than 65 years: 40.2% (Table 1); pre-school children aged above six months with at least one dose: 31.9%, with complete vaccination: 28.7%, with partial vaccination: 7.2% (Table 2, 3); elementary school students from grade one through four: 72.2% (Table 4); high-risk groups above fifth grades in elementary schools and aged less than 65 years: 41.2% (Table 5). Overall, the coverage rates for each high-risk group increased significantly comparing with the 2010-2011 influenza season. The coverage rate increased by 4% for adult groups, by 2.7% for elementary school children, and by 6.2% for infants and toddlers aged less than six years.

Discussion

Overall, the coverage rates for all high-risk-groups in the program during the influenza season 2011-2012 increased significantly compared with the rates of previous influenza season. The rates increased by 4% for adult groups, by 2.7% for elementary school children, and by 6.2%, the greatest range of increase, for children aged less than six years. The increases in the coverage rates could be attributed to several strategies: conducted education program to strengthen the "healthcare workers' knowledge about influenza vaccines before the implementation of the program, invited medical professionals to advocate the vaccination program and limited the candidates of government-funded vaccines to high-risk groups only. Besides, no vaccine-associated adverse events reported in the media may be another important factor. However, the coverage rate for those aged more than 65 years was 40.2%, which was ranked 17th out of 21 members in Organization for Economic Co-operation and Development (OECD) , and was much lower than the expected target, 75% by 2010, recommended by WHO in 2005. The coverage rate for children aged less than six years old followed an upward trend during the influenza season 2011-2012, but was at the relatively low point over the years. For pre-school children aged between three and six years, the coverage rate was increasing every year.

Conclusion

In the future, we should keep on promoting vaccination advocacies, improving the accessibility to vaccination, and enhancing the awareness of prevention from influenza in kindergartens. We may expect that these actions should be helpful in increasing the coverage rates for high risk group.

Table 1. The coverage rates for the elders aged more than 65 years during recent three influenza seasons from 2009 to 2011

Influenza season	No. of inoculations	Coverage rate
2011-2012	1,011,008	40.2%
2010-2011	902,253	36.4%
2009-2010	932,885	37.6%

Table 2. The coverage rates for the children aged between six months and six years old (pre-elementary school) in recent three influenza seasons from 2009 to 2011

Influenza season	No. of inoculations	Coverage rates of at least one dose	Coverage rates of complete vaccination	Coverage rates of partial vaccination
2011-2012	331,846	31.9%	28.7%	7.2%
2010-2011	289,419	25.9%	23.8%	4.6%
2009-2010	381,870	28.5%	24.8%	8.5%

Table 3. The coverage rates for children aged 6-35months in recent three influenza seasons from 2009 to 2011

Influenza season	No. of inoculations	Coverage rates of at least one dose	Coverage rates of complete vaccination	Coverage rates of partial vaccination
2011-2012	168,232	40.2%	33.9%	9.2%
2010-2011	162,972	32.9%	29.3%	5.7%
2009-2010	253,993	60.8%	43.2%	11.9%

Table 4. The coverage rates for the first to fourth graders in elementary schools in recent three influenza seasons from 2009 to 2011

Influenza season	No. of inoculations	Coverage rates
2011-2012	646,496	72.2%
2010-2011	659,020	68.6%
2009-2010	818,235	79.6%

Table 5. The coverage rates for high-risk groups above fifth grades in elementary schools and aged less than 65 years

High-risk groups	No. of inoculations	Coverage rates
Persons who have catastrophic illness	38,691	-
Staff in nursing homes and other long-term care facilities	27,246	85.1%
Healthcare workers	243,005	88.4%
Public health workers		
Infection control workers	11,581	91.1%
Emergency medical technicians	5,714	56.5%
Airborne service corps	118	44.2%
Coast guards	6,990	69.4%
Border control workers	1,538	15.8%
Animal farm-related workers		
Poultry or livestock farmers	14,273	59.2%
Animal health inspectors	1,138	45.6%

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Seroprevalence survey of avian influenza viruses among poultry workers in Taiwan

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Background

Avian influenza viruses (AIVs) are zoonotic agents recognized as a continuing pandemic threat to human society based on their easily changing genetic nature. Since most human confirmed cases had exposure history to ill or dead poultry or contaminated environment, poultry workers with intense occupational exposure are thought to be a high risk group and serve as a bridge population between animals and human population. There were 6 outbreaks of highly pathogenic avian influenza (HPAI) H5N2 viruses occurred in 2012 in central and southern regions of Taiwan. This study was to evaluate possible infection rate of AIVs among Taiwan's poultry workers through serological survey.

Materials and methods

The study design was a case control study. The case group was live poultry vendors and poultry farmers. We randomly selected 335 live poultry stalls and 400 poultry farms depending on their distribution in 22 different cities/counties as study population. For each stall or farm, we would choose at most 2 personnel as the case group. As to the control group, we choose one non-poultry worker (NPW), most of them were government employees, who matched the poultry worker by sex, age, and administrative district of daily working (Figure 1). The study period started from May 2012 to July 2012. After consent was obtained, all participants should complete the standardized questionnaire. Then a 7~10 ml whole blood sample was collected for hemagglutinin inhibition assay to titrate the serological titers against H5N2 and H7N3. All the statistical analysis was performed with SPSS version 14.

Results

Demographics

There were a total of 335 live poultry vendors (LPV), 335 poultry farmers (PF), and 577 NPWs were enrolled for analysis. The majority of case subjects had worked more than 10 years (LPVs:86.57%, PFs:79.4%), and contacted poultry every day (LPVs: 90.45%, PFs: 94.03%). As to vaccination history, most LPVs and PFs (73.13~80.9%) had never received H5N1 vaccine. The vaccination rates of seasonal influenza vaccine were also low, only 19.1%~38.21% among LPVs and PFs in the past 2 years. Nevertheless, the seasonal influenza vaccination rate reached over 50% among NPWs during 2011 and 2010.

Seroprevalence

The titers (Table 1) against H5N2 among LPVs and PFs were significantly higher in comparison with NPWs (p=0.000 and 0.001 respectively). But the titers against H7N3 among LPVs and PFs, in comparison with NPWs, didn't show statistical significant difference. There are total 18 subjects with HI titers against H5N2 higher than 1:80. If we use this value as cut-off point, the seropositive rate was 2.99% among the LPVs and 1.79% among the PFs, significantly higher than NPWs; the odds ratios was 8.85 and 5.24 respectively (Table 2). There are total 7 subjects have HI titers of 1:40 against H7N3. If we use this value as the cut-off point, the seropositive rate was 0.6% among the LPVs and 1.19% among the PFs; though not statistically higher than NPWs (Table 3). In addition, we didn't find any correlations between influenza vaccination histories (seasonal or H5N1) and HI titers against H5N2 and H7N3. Furthermore, we found those PWs who worked in sub-level administrative districts where ever been demonstrated HPAI H5N2 poultry outbreaks in 2012 had significant higher antibody titers (p=0.028, odds ratio=5.574) (Figure 2).

Conclusion

Our cross-sectional study showed that frequent AIVs exposure was related to sero-positivity of poultry workers, especially live poultry vendors. The seropositive rate against H5N2 is higher than H7N3 among poultry workers, which was consistent with the epidemic situation in poultry in Taiwan where H5N2 occurred much more frequently than H7N3. For reducing opportunities of human exposure to AIVs, we should keep reinforcing our surveillance systems for both animal outbreaks and human cases, increasing influenza vaccination rate in high risk groups, and strengthening risk communication with poultry workers to improve their knowledge.

Figure 1. Summary of enrollment

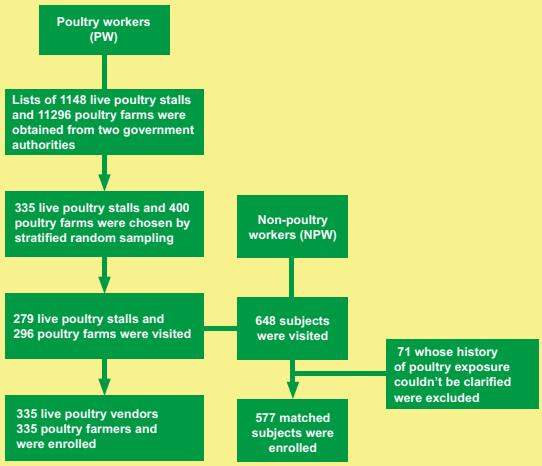


Table 1. Distribution of HI titers against H5N2 and H7N3 avian influenza

Virus strain / Group	n	<10	10	20	40	80
H5N2						
Live poultry vendors	335	5 (1.49)	23 (6.87)	170 (50.75)	127 (37.91)	10 (2.99)
Poultry farmers	335	10 (2.99)	36 (10.75)	169 (50.45)	114 (34.03)	6 (1.79)
Non-poultry workers	577	30 (5.20)	100 (17.33)	296 (51.30)	149 (25.82)	2 (0.35)
H7N3						
Live poultry vendors	335	307 (91.64)	16 (4.78)	10 (2.99)	2 (0.60)	- -
Poultry farmers	335	318 (94.93)	9 (2.69)	4 (1.19)	4 (1.19)	- -
Non-poultry workers	577	551 (95.49)	19 (3.29)	6 (1.04)	1 (0.17)	- -

Table 2. Seroprevalence of HI titers against H5N2 avian influenza

Group	negative		positive		P value	Odds ratio
	n	%	n	%		
Live poultry vendors	325	97.01	10	2.99	0.005	8.85
Poultry farmers	329	98.21	6	1.79	0.043	5.24
Non-poultry workers	575	99.65	2	0.35	-	-

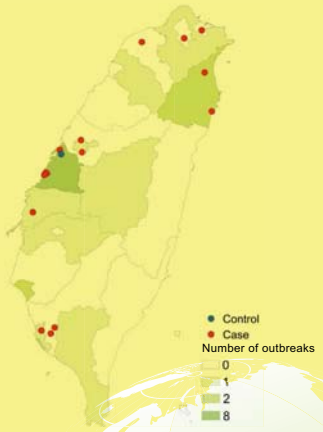
*cut point at 80 of HI titers

Table 3. Seroprevalence of HI titers against H7N3 avian influenza

Group	negative		positive		P value	Odds ratio
	n	%	n	%		
Live poultry vendors	333	99.40	2	0.60	0.312	3.46
Poultry farmers	331	98.81	4	1.19	0.083	6.96
Non-poultry workers	576	99.83	1	0.17	-	-

*cut point at 80 of HI titers

Figure 2. Geographic distribution of case and control subjects with HI titers of 1:80 against H5N2



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