國立臺灣大學 公共衛生學院 公共衛生碩士學位學程

碩士論文－實務實習成果報告

Master of Public Health Degree Program

College of Public Health

National Taiwan University

Master Thesis ─ Practicum Report

# 赴歐洲參加現場流行病學訓練計畫

# European Programme for Intervention Epidemiology Training (EPIET): A Two-Year Training Experience


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中華民國 104 年 01 月

January, 2015

# 國立臺灣大學碩士學位論文

# 口試委員會審定書

## 赴歐洲參加現場流行病學訓練計畫

## European Programme for Intervention Epidemiology Training (EPIET)：A Two-Year Training Experience

本論文係**簡淑婉**君（R99847023）在國立臺灣大學公共衛生碩士學位學程、所完成之碩士學位論文，於民國 104 年 01 月 14 日承下列考試委員審查通過及口試及格，特此證明

口試委員：方啓泰（簽名）

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# 中文摘要

歐洲現場流行病學訓練計畫(European Programme for Intervention Epidemiology Training, EPIET)，是歐洲疾病預防及控制中心（European Centre for Disease Prevention and Control, ECDC）重點長期訓練計畫之一。經 2007 年我國行政院衛生福利部疾病管制署（下稱疾管署）與奧地利健康暨食品安全署（Österreichische Agentur für Gesundheit und Ernährungssicherheit, 下稱 AGES )簽定合作備忘錄下，我國得派員以奧地利衛生調查訓練班訓練員身分，參加為期兩年之 EPIET 計畫。學生有幸通過疾管署遴選流程，自 2011 年 9 月至 2013 年 11 月在 AGES 進行 EPIET 訓練及實務實習。

EPIET 訓練內容包含 10 週流行病學相關課程及於代訓機構進行實務實習，以具備疫病調查、監測系統評估或建立、研究計畫撰寫及執行、教學經驗、學術發表等能力。受訓期間學生參與疫病調查及監測系統評估與學術成果發表等經驗摘要如下：1. 以回溯性世代研究法調查一起校園學生諾羅病毒感染事件，經分析結果顯示男住宿生（Risk Ratio: 3.4; 95%CI: 1.4-8.2）、食用酸奶醬（RR: 16.2; 95%CI: 3.9-67.5）及火雞肉片沙拉（RR: 5.2; 95%CI: 2.3-11.8）為經分層分析後感染諾羅病毒之危險因子，推測因該校學生餐廳廚房未依相關規定，執行危害分析重要管制點系統制度(Hazard Analysis Critical Control Point, HACCP)， 在餐點配製及料理過程中造成食物交叉污染。2. 奧地利流行性感冒季節性監測，以結合定點醫師監測、非定點病毒監測、類流感監測等，掌握流感季期間，類流感趨勢及病毒型別變化與疾病負擔。3. 闡述奧地利李斯特菌監測系統監測架構及評估其簡易性及時效性，於 2009 年該國法定傳染病線上通報系統啟用後顯著提升。4. 為評估省市間百日咳通報率差異，進行奧地利一般科醫師、小兒科醫生及肺專科醫生通報百日咳感染病例之知識、態度、行為（knowledge, attitude, practices, KAP）調查研究，發現於高通報率省份之教學醫院執業（Prevalence Ratio: 1.6; 95%CI: 1.1-2.2），及百日咳病原體實驗室診斷相關知識程度較高(PR: 1.4; 95%CI: 1.0-1.8)者，為具百日咳確定病例通報行為之獨立因子，推測醫師通報行為可能是造成省市間百日咳通報率差異原因之一。5. 於四場奧地利學術研討會或國際研討會進行口頭或壁報報告。6. 籌辦食媒性疾病疫情調查教育訓練，進行教材設計及教學 。

回國後，學生應用 EPIET 受訓期間所學，協助疾管署評估國際間 H7N9 及

H10N8 等新型流感疫情發生於我國之可能風險及衝擊，評估結果研判 H7N9 流感病毒於冬季流行期間境外移入風險提高，預期我國仍可能出現中國大陸移入病例，惟目前證據顯示病毒不具持續性人傳人之能力且造成社區感染風險低。另中國大陸 H10N8 流感疫情僅出現零星個案，推測我國出現境外移入個案之風險極低，惟仍建議加強我國禽畜相關從業人員及台商與入境陸客之健康監測，及持續掌握新型流感病毒特性及疫情變化，於必要時更新風險評估報告。

關鍵字：EPIET、奧地利、諾羅病毒、李斯特菌、百日咳。

# 英文摘要

The European Programme for Intervention Epidemiology Training (EPIET) hosted at the European Centre for Disease Prevention and Control (ECDC) in Sweden, provides training and practical experience in intervention epidemiology at the national centres for surveillance and control of communicable diseases in the European Union. In 2007, Taiwan Centers for Disease Control (TCDC) and Austrian Agency for Health and Food Safety (AGES) agreed the Memorandum of Understanding that set down the mechanisms and scope of cooperation, which enabled a Taiwanese trainee to join EPIET. It's a great honour for me to be elected as the representative of TCDC and AGES to participate in the programme during September 2011and November 2013.

The ten-week EPIET modules and practising in the training site provide knowledge and skills that lead the trainees to acquire the ECDC core competencies for field epidemiologist. During the training, I have accomplished the following learning objectives: 1. Investigation of a foodborne outbreak due to norovirus in a school in 2011, which indicated sour cream sauce (Relative risk: 16.1; 95% CI: 3.9–67.5) and turkey-strip salad (RR: 5.2; 95% CI: 2.3–11.8) prepared by the school kitchen as the most likely sources of the outbreak. The lack of a hazard analysis critical control point soncept (HACCP) in the school kitchen might have caused the failure of food safety procedures. 2. Analysis of influenza surveillance data during flu seasons (Week 40-Week 15), 2011-2013. 3. Evaluation of the surveillance system for listeriosis in Austria before and after implementation of the national electronic web-based reporting system (EMS) in terms of simplicity and timeliness. The implementation of the EMS eliminated two steps from the data reporting process and reduced the time needed between case identification and case reporting. 4. A knowledge, attitude and practice survey for pertussis among general practitioners, paediatricians and pulmonologists in Austria. We found that in the provinces of high notification rate of pertussis, paediatricians and pulmonologists who have high level of knowledge on laboratory diagnostics for pertussis and practice in a university hospital were independently associated with the behaviour of reporting a laboratory confirmed case of pertussis (adjusted PR: 1.4, 95%CI: 1.0-1.8 and adjusted PR: 1.6, 95%CI: 1.1-2.2 respectively). The observations may partly explain the differences of pertussis notification rates between Austrian provinces. 5. Oral and poster presentations in four Austrian or

international conferences. 6. Obtaining teaching experience through organizing a workshop about introduction of foodborne outbreak investigations.

After EPIET training, I assisted TCDC to assess the risk associated with emergence of avian influenza A (H7N9) and A (H10N8) virus and formulated appropriate prevention and control strategies. The result showed that risk of diseases widely spreading in Taiwan via humans in the near future is considered low, while a higher likelihood at the moment is imported case-patients who have acquired the infection in mainland China. Health monitoring and serological surveys of poultry workers were recommended to evaluate the risk of poultry-to-human transmission of the viruses. It is essential to continuously monitor the variations of H7N9, H10N8 and other influenza viruses and update the assessment of estimated risks.

Abstracts: EPIET, Austria, Norovirus, Listeriosis, Pertussis

# 第一章 緒論

## 1. 實習單位特色與簡介

### 1.1 參訓背景

歐洲現場流行病學訓練計畫 European Programme for Intervention Epidemiology Training, 下稱 EPIET)創立於 1995 年，為歐洲疾病預防及控制中心（European Centre for Disease Prevention and control, 下稱 ECDC）重點長期訓練計畫之一，該訓練計畫之目的為：1. 強化歐盟會員國間傳染病監測能力及重大公共衛生緊急事件之應變能力，2.提升歐盟會員國面對疫病威脅之因應及防治能力，3. 建立歐洲流行病學家間聯繫網絡及共同研究方法，並共享研究成果，4.建構歐盟地區傳染病監測及防治網絡。我國衛生福利部疾病管制署（下稱疾管署）於 2007 年與奧地利健康暨食品安全署（Österreichische Agentur für Gesundheit und Ernährungssicherheit, Austrian Agency for Health and Food Safety, 下稱 AGES )簽定合作備忘錄，其中一項為自 2007 年起，我國可派遣代表至 AGES 進行訓練，並以奧地利衛生調查訓練班訓練員身分，參加為期兩年之 EPIET 計畫。學生有幸通過疾管署遴選過程，於 2011 年 9 月至 2013 年 11 月期間，參加本計畫。此次訓練目的為加強個人流行病學監測及田野調查與論文發表能力，並為疾管署與歐盟國家建立聯繫及合作管道。

### 1.2 實習機構規模、特色及發展重點

AGES 係依據奧地利食品法規定於 2002 年成立，將 18 個不同領域的聯邦機構與部門，包括食品檢驗、微生物學、血清學、獸醫、農業及人類醫學等部門整合併入該機構內，負責食品來源、製程、運送、保存至消費等食品供給與生產鏈的安全，藥品查驗及藥物許可證審核，以及負責調查、預防及控制食媒及部分其他傳染病疫情等。AGES 約有 1350 名員工，分佈於維也納(Vienna)、下奧地利省(Lower Austria)、格拉茲(Graz)及因斯布魯克(Innsbruck)分署，其轄下由 7 大部門組成：人類醫學、農業、食品安全、獸醫學、藥品安全、能力中心、資料收集及分析與風險評估。

學生於人類醫學處下的傳染病及流行病學組進行實務實習，該組工作執掌主要包括疫病調查、傳染病監測與分析、傳染病監測系統評估、建立傳染病防治工作指引、教育訓練及擔任 EPIET 代訓機構等。

## 2. 實習機構與實習目標之相關性

受訓期間由 ECDC 安排學員參加專業課程訓練，包括基礎流行病學、疫病調查軟體應用、多變量統計分析、疫苗學、抽樣方法學、學年進度報告等必修課程，及時間序列分析與公共衛生事件緊急應變等選修課程，學員需完成必修課程及一項選修課程。另學員須於國內或國外期刊發表至少一篇論文，以及在國際學術研討會發表演說或壁報報告。學員須於訓練期間完成上開目標，以獲得田野流行病學調查及疫情監測等相關知能，並於執行實務實習單位所交辦任務時，實際運用及操作所學。

## 3. 實習內容相關文獻回顧

### 3.1 諾羅病毒感染群聚事件

奧地利在 2007 年 12 月發生疑似食媒性諾羅病毒感染事件，總計 60 名員工參加聖誕派對，由 6 名廚師供餐。調查結果顯示疫病侵襲率為 33%（21/63 人），其中包括兩名廚師，並於 3 人檢體中檢出第二型諾羅病毒（norovirus genogroup II)。分析性流行病學結果顯示，火腿捲（Risk Ratio: 4.5, 95% CI: 1.9-10）及糕點（RR: 2.4, 95% CI:0.9-6.4)與個案發生腸胃炎有關 。在控制性別、年齡及食物類別變項後，以 log-linear model 分析發現火腿捲與罹病風險達到統計上顯著相關(RR:3.9, 95% CI:1.6-9.8)。火腿捲係由一名廚工製作，其嬰兒於派對前二天診斷諾羅病毒感染並引發腸胃炎，推測該名廚工可能在更換嬰兒尿布時感染。奧地利諾羅病毒國家實驗室藉由分型方法，確定嬰兒感染諾羅病毒之型別與事件個案一致，而確定了感染源。因此，廚工加強手部衛生及廚房周遭清潔消毒，可有效預防諾羅病毒感染[1]。

### 3.2 李斯特菌症監測系統評估

奧地利法定傳染病通報系統於 2009 年起採線上通報，由於通報資料檢核機制尚不完善，該國聯邦衛生部及 AGES 正積極進行該系統功能擴充及提升

資料品質。就檢視美國李斯特菌監測系統架構進行比較，美國李斯特菌感染症係於 2001 年列為該國法定傳染病，每年平均通報約 1,650 例，其中 1,400 例住院及 250 例死亡。該國李斯特菌監測網（*Listeria* Initiative）為全國性李斯特菌症被動監測平台，使用標準化問卷收集李斯特菌確定病例之臨床及流行病學等資料後上傳，截至 2014 年累計 42 州參與，且法傳個案資訊上傳比例持續增加。系統監測目的為提高疫情調查時效性，縮短發現病例至衛生單位介入之間隔時間，在出現零星個案時，即逐一進行疫情調查，即時進行問卷調查可降低回憶偏差(recall bias)的出現。自疑似病例檢體、環境及食品樣本檢出之李斯特菌分離株，皆以脈衝式膠體電泳檢測法（Pulsed Field Gel Electrophoresis, PFGE)分型，再將李斯特菌 DNA 圖譜上傳至國家食媒性疾病病原體分子分型網（PulseNet）。若發現個案具有相同圖譜，則進行監測網資料庫分析，藉比較群聚個案及其他零星個案飲食暴露史，推測疑似感染源，此法解決病例對照研究中，對照組難於短時間內取得的問題。

以美國李斯特菌症年報資料，評估 *Listeria* Initiative 是否達到其監測目的，其評估指標包括涵蓋率、時效性及完整性。2014 年參與通報 *Listeria* Initiative 之州數達 42 州，較 2012 年減少 2 州，仍未及涵蓋率 100%的目標，另就通報李斯特菌症個案之疫調資料上傳至 *Listeria* Initiative 之比例，於 2012 年提高至 78%，高於 2009-2011 年平均值（68%），惟與 2014 年之目標（90%）仍有差距。PulseNet 資料庫中提供人類李斯特菌分離株之個案，通報 *Listeria* Initiative 之比例則持續上升，於 2012 年達 82%，較 2011 年上升 13%，縮小與 2014 年目標 90%之差距。另就資料時效性分析結果，2012 年疫情調查報告於疫調日起 7 日內上傳至 *Listeria* Initiative 之比例僅 21%，與 2014 年目標 70%差距較大。另菌株分離後 14 日內將分型資料上傳 PulseNet 之比例略降，2012 年（53%）較 2011 年(57%)減少 4%，與 2014 年目標 70%差距較小。另 2012 年 *Listeria* Initiative 資料庫中，使用標準化問卷及問卷內容具完整飲食暴露史資料之比例分別為 78%及 53%，而 2014 年目標值分別為 95%及 80%。故就涵蓋率、時效性、完整性等監測指標評估美國李斯特菌症監測網仍未達 2014 年目標，部分指標甚至呈現下降趨勢，另美國將評估結果以年報方式呈現，值得奧地利李斯特菌症監測體系學習[2]。

3.3　歐盟會員國百日咳疫情趨勢及疾病負擔

近 50 年來，歐盟及歐洲經濟區（EU/EEA）百日咳發生率在使用疫苗後持續下降且維持低發生率，惟近年歐洲多國及美國與加拿大等國之百日咳發生率出現上升跡象，且多發生於高百日咳疫苗接種率國家。百日咳病例數在各年齡層皆增加，其中以未滿一歲嬰幼兒發生率最高。ECDC 以挪威、荷蘭、英國及瑞典等資料完整國家之 2006-2010 年病例數資料進行時間序列分析，將 2011 年預測病例數區間與實際病例數比較，發現荷蘭及挪威與英國在 2011 年實際病例數皆高於預測區間，瑞典則無此現象。荷蘭及挪威百日咳感染族群主要為 5-9 歲孩童及 30 歲以上成人。在英國，則以 1 歲以下嬰兒及 30 歲以上成人為主。

荷蘭百日咳疫情趨勢呈週期性波動，在 1999, 2002, 2005, 2008 及 2012 年出現疫情高峰，該國百日咳基礎疫苗接種時程在 1999 年起由 3, 4, 5 月齡變更為 2, 3, 4 月齡嬰兒接種，2005 年起 4 歲孩童由接種全細胞性百日咳疫苗 (diphtheria-tetanus-whole-cell pertussis, DTwP)變更為非細胞性百日咳疫苗 (diphtheria-tetanus-acellular pertussis, DTaP)後，孩童發生率明顯下降，惟 2 個月以下嬰兒及 20 歲以上成人發生率仍持續攀升，且成人百日咳病例通報率仍不及實際病例數之 1%。在 2006-2007 年一項全國性調查發現，10 歲以上孩童每年約有 9%感染百日咳，此為 1995-1996 年時發生率的 2 倍，推斷 DTaP 的疫苗保護力逐年下降及病原變異為荷蘭百日咳發生率再度上升原因之一。

英格蘭及威爾斯在 2004 年起建議 2, 3, 4 月齡嬰兒百日咳基礎疫苗以 DTaP 取代 DTwP 後，發生率明顯下降，惟在 2011 年起接連發生學校及醫院百日咳群聚事件，病例集中於年輕族群及 35 歲以上成人，且疫情持續擴大至千人感染，並在 2012 年擴及各年齡層及死亡率最高的三月齡以下嬰兒。該國政府因此強烈建議婦產科及新生兒病房之醫事人員追加百日咳疫苗，另發現未達第 1 劑接種月齡之嬰兒感染病例占總嬰兒病例 50%，且第一劑疫苗保護效力僅 74% (95% CI, 58–84%)。為避免嬰兒感染百日咳致死，英國決定在 2012 年 10 月起提供懷孕 28-32 週齡婦女追加百日咳四合一疫苗（dTaP-IPV），後續追蹤研究顯示孕婦接種百日咳疫苗可有效降低新生兒百日咳感染率，且接種後對於孕婦及新生兒皆無明顯不良反應 [3,4]。

法國在 1998 年開始建議 2, 3, 4, 16-18 月齡嬰兒及 11-13 歲孩童接種

DTaP，基礎疫苗自 2007 年起接種率逾 95%。該國百日咳監測架構以定點兒童醫院監視為主，涵蓋率達 30%，自 1996 年起，該國疫情高峰發生於 1997, 2000, 2005, 2009 及 2012 年，累計近 4,000 例確定病例，其中 55%集中於 6 月齡以下嬰兒，並以未接種疫苗之 3 月齡以下嬰兒為主。確定病例中 96%為住院個案，18%曾於 ICU 治療及累計 36 例死亡。一項法國調查孩童百日咳感染源研究發現，孩童以 57%自父母親感染最高，另 22%源自兄弟姊妹及 20%源自其他成人，因此建議醫事人員及父母親接種疫苗，以保護新生兒，另提供 25 歲以上成人接種 TdaP。

挪威 1952-1997 年出生的世代接種 DTwP 疫苗，1998 年後出生的世代則變更為於 3, 5, 12 月齡接種 DTaP。近期則建議 7 歲及 15 歲孩童與成人每 10 年追加一劑。往年每 10 萬人口發生率約 100 人，疫情高峰週期約 2-3 年，10-19 歲青少年為發生率最高之年齡層。2011-2012 年小於 2 歲孩童百日咳發生率上升 2 倍，累計 92 例確定病例，其中 38%無接種疫苗，其餘個案皆發生於接種 DTaP 的世代，估計從完成基礎疫苗至發病間隔約 2.8 年，推斷 DTaP 疫苗保護力遞減快速，另流行血清型別亦轉換為 P2。

芬蘭自 2005 年起建議接種 DTaP,並提供 7 歲及 15 歲孩童追加疫苗，該國基礎疫苗接種率逾 99%，自 2000 年起 7 歲世代追加疫苗接種率約 7 成，主要以血清學檢測確定百日咳感染，PCR 檢測則主要使用於幼童及嬰兒之檢體，惟該國實驗室檢驗方法尚未標準化。該國於 2004 年出現疫情高峰後，近年疫情趨勢相對穩定，病例集中在 10-19 歲孩童。

奧地利自 1998 年起建議接種 DTaP, 並自 2003 年起，以六合一疫苗（DTaP-IPV-Hib-HepB）作為百日咳基礎疫苗。該國百日咳基礎疫苗免費接種時程於 2010 年由 3, 4, 5, 24 個月齡變更為 3, 5, 12 月齡嬰兒接種，另 7-9 歲孩童、18-20 歲成人及往後每隔十年建議接種追加疫苗。該國於 2009 年起百日咳通報率攀升達逾每十萬人口 5 人，以 1 歲以下嬰兒最高，15 歲以下孩童亦顯著上升，多數通報病例為非確定個案，且血清學檢測方法亦未標準化。

歐盟會員國對於百日咳病例定義、實驗室診斷方法及監測系統架構不盡相同，故比較會員國百日咳通報病例數有其限制，可比較一歲以下通報病例住院數以推測百日咳疾病負擔差異，另多年維持高百日咳疫苗接種率國家之群體免疫力下降情形應較近年才達高接種率國家明顯，可進一步研究確定此

是否為出現接種 DTaP 疫苗保護力差異之主因。

## 3.4 我國流行性感冒監測系統架構

我國流感監測系統網絡，包括法定傳染病通報流感併發重症及新型A型流感、門急診監測、病毒合約實驗室流感病毒型別監測、以及肺炎及流感死亡監測等四大監測架構。

### 3.4.1 法定傳染病流感併發重症及新型A型流感

我國自 2014 年 7 月 1 日起，將新型 A 型流感列為第五類法定傳染病，並自 2014 年 8 月 1 日起，原第四類傳染病「流感併發症」 修訂為「流感併發重症」，以掌握嚴重流感併發症及疑似感染新型流感病毒病患。新型 A 型流感以符合臨床及流行病學條件或僅符合檢驗條件者進行通報;流感併發重症通報定義之臨床條件以出現類流感症狀後兩週內因併發症(如肺部併發症、神經系統併發症、侵襲性細菌感染、心肌炎或心包膜炎等)而需加護病房治療或死亡者，進行通報，兩項通報疾病皆須自通報日起 24 小時內完成個案疫情調查。

### 3.4.2 急診即時疫情監視及健保門診及住院資訊

我國藉由疾管署建立之疫情監視及預警系統，透過全國逾 170 家責任醫院,將急診就診之健保診斷碼等類流感資料即時自動傳送至疾管署，主要欄位包含病患基本資料、通報醫院代碼、入院時間、主訴、ICD-9-CM 診斷碼等。藉此除可快速觀察急診類流感就診率波動及流行趨勢外,疾管署亦每週彙整分析系統資料並以圖表方式公布於該署網頁。

### 3.4.3 病毒合約實驗室流感監測

我國現今病毒性感染症合約實驗室共計 8 家,進行採檢定醫監測檢體檢驗，分布於全國北中南東各區，以實驗室主動監測方式針對全國各年度流感病毒流行型別、抗原性以及抗藥性進行監測，俾利了解病毒型別變化、疫苗株與流行株是否吻合、以及建立我國病毒基因及

生物材料資料庫。檢體來源主要來自合約實驗室所在醫學中心門診、住院及急診病患與診所病患且符合類流感定義（發燒 38 度以上，出現咳嗽、喉嚨痛或肌肉痛，並排除輕微鼻炎、扁桃腺炎及支氣管炎等）者，於發病 3 日內採集鼻咽拭子送檢。

3.4.4 肺炎及流感死亡監測

本監測係藉使用衛生福利部統計處死亡登記資料，利用由醫療院所登載之死亡通報之死因欄位搜尋相關關鍵字如肺炎、感冒、流感等查詢標的，合併死因研判規則，分析每週肺炎及流感死亡趨勢，並比較其他系統綜合掌握流感疾病負擔。

# 第二章 訓練內容

## 1. EPIET 課程

### 1.1 基礎流行病學

為期三週，地點為西班牙小島 Lazaretto，係第一次與同期學員共同研習的課程。課程內容主要包括田野流行病學家所需基本知能如疫病調查，實際案例研究，基礎分析流行病學，監測系統建立與評估，研究計畫撰寫及公眾溝通。以上午授課，下午分組討論疫病調查案例方式進行。另學習撰寫研究計畫，並於期末進行分組報告。最後學員共同評估授課品質及提供課程修正意見，以供課程設計教師參考。學生藉此課程認識多位頂尖歐洲公衛人才及專家，並向同期學員學習歐洲風土民情及文化。

### 1.2 疫病調查軟體應用

本課程主要介紹疫病調查時常見之分析工具包括 MS-Excel 及 EpiData/Entry 與 Stata。學員於課程中學習利用相關軟體進行疫調表單匯入及資料分析，並以流行病學方法進行假說驗證。學員同時學習判讀統計軟體結果，輔以微生物學及食品安全或環境衛生相關調查，綜合研判調查結果，以協助因應及控制疫情，避免類似疫病再度發生。最後學員學習疫調報告及論文摘要撰寫格式，以運用於未來疫情調查。

### 1.3 多變量回歸分析

本課程主要介紹運用廣義線性迴歸模型(Generalised linear model, GLM)如線性迴歸（Linear regression），羅吉斯迴歸（Logistic regression），布阿松迴歸（Poisson regression)，及生存分析(Survival analysis)等進行多變量分析，學習各迴歸方法之優缺點，及運用 Stata 軟體選擇模型以解釋資料，並正確判讀分析結果。

### 1.4 時間序列分析

本課程主要介紹如何建立模型以妥善分析具時序性之監測資料。本課程之基礎模型建立採用簡單線性迴歸公式，解釋監測資料的長期趨

勢，再以 sine, cosine 數學函數模擬時序資料的週期性變化，進而預測未來疫情趨勢以及界定疫情警戒閾值。時間序列分析適用於具季節性或週期性趨勢之傳染病如登革熱及腸病毒等，並說明兩種常用時序分析工具，即自相關函數(Autocorrelation)及頻譜分析(Spectral analysis)。

## 1.5 疫苗學

本課程主要介紹現今疫苗可預防傳染病(Vaccine-preventable diseases, VPD)，說明疫苗史、VPD 監測、VPD 疫情案例分析、疑似疫苗不良反應監測、疫苗臨床試驗發展、疫苗成本效益評估、疫苗學基本辭彙簡介及計算接種率等。課程中亦邀請疫苗可預防性傳染病專家如 Dr. David Heymann 及 Dr. Roger I. Glass 等授課及經驗分享。另以剛果共和國小兒麻痺疫情及英國麻疹疫情為例進行案例討論，藉此了解小兒麻痺撲滅計畫大要及如何運用疫苗來控制疫情，並運用監測資料評估疫苗接種計畫成效。再以芬蘭孩童嗜睡症與流感疫苗關係為例，說明如何監測及解讀疑似疫苗造成的不良反應，並討論相關因應措施，包括後續流行病學調查及民眾風險溝通等。

## 1.6 抽樣方法學

本課程簡介常見抽樣方法如機率抽樣及非機率抽樣，機率抽樣包含簡單隨機抽樣，分層隨機抽樣，系統抽樣，集體抽樣，多階段抽樣；非機率抽樣包含便利樣本及滾式樣本等。另以希臘西尼羅病毒疫情調查及希臘孩童疫苗接種率調查案例，說明研究設計及抽樣方法，包括如何收集樣本資料、分析及解讀，並評估目標族群特性及探討調查時可能的限制，經綜合討論後，再次選擇合適的抽樣方法。

## 2. 實習機構訓練內容

AGES 微生物及流行病學大樓內之傳染病及流行病學組，係 EPIET 代訓機構之一，亦為奧地利衛生調查訓練班所在，業務職掌事項包括協助跨省市疫情調查、季節性流行性感冒監測、結核病監測及傳染病研究等。代訓機構於 EPIET 訓練期間協助學員完成疫情調查、監測系統建立或評估、專題研究、教學經驗、學術發表等訓練項目，學員經由執行代訓機構指示之業務內容，從中學習並同時完成訓練項目。EPIET 計畫訓練指導員會於訓練期滿 1 年時參訪代訓機構，與代訓機構指導員及學員討論訓練進度，及學習過程的困難及問題等。訓練結束前學員會再度與 EPIET 指導員訪談，訪談內容主要為學員於訓練期間在代訓機構工作的心得與建議，納入未來 EPIET 訓練計畫內容及政策走向參考。

# 第三章 訓練成果

## 1. 疫情調查-職業學校諾羅病毒感染群聚事件

### 1.1 背景

諾羅病毒(Norovirus)為單股 RNA 病毒，是人類常見造成急性病毒性腸胃炎的病原體，可經由嘔吐時產生之氣霧、污染的食物及環境、糞口途徑等方式傳播[5,6]，僅需 10-100 個病毒顆粒即可造成人類感染，常見的潛伏期為 24-48 小時，是冬季病毒性腸胃炎主要病原體[7,8]。由於諾羅病毒傳染力極強，在歐洲備受公共衛生及食品安全權責機構重視，且常有廚工或食品相關從業人員有症狀或無症狀感染後，進而污染食物造成疫情之報告[5,6,9,10]。病毒分子診斷最常見方式為基因序列及親緣演化分析，藉判定病原之基因型別以追溯可能的感染來源[11]，近年來歐洲最常見流行型別為第四型諾羅病毒。奧地利於 2006 年起省市衛生單位需向聯邦衛生部(Bundesministerium für Gesundheit, BMG)通報當地發生的諾羅病毒疫情事件。奧地利諾羅病毒國家實驗室自 2008 年起加入歐洲諾羅病毒監測網(Noronet)，依據監測網公布該國諾羅病毒疫情事件於 2008-2012 年累計件數為 34、39、54、21 起，2008-2009 年常見型別為 GGII.4-2006b、2010-2011 年則為 GGII.4-2010[12–14] 。

2011 年 11 月 28 日，一所位於薩爾斯堡（Salzburg）的職業學校校醫通知 AGES，該校於 11 月 24-25 日發現約有 40 名學生出現急性腸胃炎症狀，其中 5 件自學生採集之糞便檢體檢出諾羅病毒，懷疑可能是學生衛生習慣不良導致疫情發生。薩爾斯堡省衛生局於 11 月 30 日提請 AGES 進行調查。由於奧地利行政體制為省市自治，故省內發生之疫情需由衛生局提出協助後，才得進行調查。

### 1.2 材料及方法

在食品調查員進行初步調查發現有多名罹病學生留宿學校，三餐大多於學校餐廳消費，因此要求學校餐廳提供 11 月 21-25 日（週一至週五）供餐名單。依據供餐名單內容以 EpiInfo7 軟體設計問卷，內容包括學生基本資料、臨床症狀描述、餐點名單、有臨床症狀之接觸者名單等，由校醫轉

交班導發放以供學生填寫及回收問卷，再以EpiInfo7匯入資料及使用Stata10軟體進行資料分析，在95%的信心水準下，以回溯性世代研究法，Chi-square test 及 Fisher's exact test 計算食物項目的風險比(Risk Ratio, RR)。

為釐清可能污染之食物，第一階段分析 11 月 21-25 日之每日飲食侵襲率，以學生當日飲食狀況及 24-48 小時後有無出現腸胃炎定義食因性病例。舉例來說，11 月 21 日在學生餐廳飲食且於 11 月 22-23 日間出現腸胃炎症狀的學生，定義為 11 月 21 日感染病例[15]。第二階段再以第一階段風險比顯著較高之日期，進一步分析學生在高風險日之飲食情形，計算各項食物的 RR，並以分層分析解釋可能的交互作用或干擾作用。

本疫情事件可能病例定義為:在 2011 年 11 月 21 至 12 月 5 日期間出現腹瀉或嘔吐症狀之該校學生。確定病例定義為：經實驗室診斷確定為諾羅病毒感染之可能病例。食因性可能病例定義為：在 2011 年 11 月 21 至 11 月 28 日期間出現腹瀉或嘔吐症狀之該校學生，主要考量為學生餐廳及廚房於 11 月 26-27 日關閉進行清消。另自二件糞便檢體檢出之諾羅病毒分離株，由奧地利國家實驗室送至德國諾羅病毒參考實驗室，以 real-time RT-PCR 及 nested multiplex RT-PCR 進行基因型別鑑定及定序[16]，再以 neighbour-joining tree analysis 分析 RNA-dependent RNA polymerase gene open reading frame 1 (ORF1, 275 個核苷酸)及 open reading frame 2(ORF2, 140 個核苷酸)[17]之基因序列。

## 1.3 結果

### 1.3.1 敘述性流行病學

有效問卷共計 351 份，包括 196 名住宿生(回收率 94.7%)及 155 名非住宿生(回收率 95%)，年齡中位數為 15 歲(13-20 歲)，男女人數比值為 1.2，共計 48 名學生符合事件可能病例定義，侵襲率為 14%，其中 39 名（81%）為食因性可能病例，3 名（6%）為確定病例，其他 6 名（13%）推測為二代感染之可能病例。個案之臨床症狀包括噁心(77%)、嘔吐(60%)、胃痛(60%)、腹瀉（50%）及發燒(33%)，年齡中位數為 17 歲(14-20 歲)，39 名男性(81%)及 38 名住校生(80%)。以個案發病日描述疫情趨勢顯示疫情區間為 11 月 23 日至 12 月 5 日，

11 月 24 日為疫情高峰（如圖一）。因 11 月 26 至 27 日學校餐廳關閉及廚房進行全面性清潔消毒，故推測 11 月 26 日以後之零星個案可能為人傳人之二代感染病例。

1.3.2 分析性流行病學

經分析個案之基本資料發現，男性(RR: 2.2; 95%CI: 1.1-4.4)及住宿生(RR: 3.0; 95%CI: 1.5-5.8)罹病之風險較高，惟經分層分析調整，只有男性住宿生之風險達統計上顯著差異(RR: 3.4; 95%CI: 1.4-8.2, p=0.003)。第一階段以 39 位疑似食媒性且得知發病日之個案進行分析， 顯示曾經在 11 月 22 日及 23 日食用學校餐廳提供之餐點的學生，其侵襲率最高(AR: 10 %及 12.4 %)，11 月 24 日次之（AR：4.7%）（如表一），因此以 11 月 22 日至 24 日的食物，進一步分析學生在此三日之飲食情況。單變量分析顯示 11 月 22 日提供之鹿肉燉肉、紅色高麗菜餃、小紅莓、烤馬鈴薯及酸奶醬皆達統計顯著差異（如表二），再進一步以最高風險比值及較可能大量增殖諾羅病毒之酸奶醬進行分層分析後，其他單變量分析達顯著之食物不再具統計顯著性。另外餐廳在 11 月 23 日提供之維也納炸肉排（Wiener Schnitzel）、火雞肉片沙拉及馬鈴薯達統計顯著性，再進一步以較可能大量增殖諾羅病毒之火雞片沙拉進行分層分析後，其他單變量分析達顯著之食物不再具統計顯著性（如表三）。共計 33 名（85%）於 11 月 23 日至 25 日期間發病之學生，曾經食用 11 月 22 日提供之酸奶醬或 11 月 23 日提供之火雞肉片沙拉，另 11 月 24 日提供之餐點則皆未達統計上顯著差異。

1.3.3 實驗室檢測與環境調查

德國諾羅病毒實驗室在 5 名發病學生糞便檢體中，共計 3 件檢出第二型（GGII）諾羅病毒，且該病毒為基因型 GGII.7 及 GGII.6 重組組成，其 ORF1 片段與基因型 GGII.7 基因序列相似度達 94.3，另 ORF2 片段與基因型 GGII.6 基因序列相似度達 94%。另外依據校醫提供之訊息，學校餐廳廚工在學生發病期間或發病前一週並無急

性腸胃炎或請病假的情形，惟食品衛生稽查員發現，該校學生餐廳廚房並無依相關規定執行危害分析重要管制點系統制度(Hazard analysis critical control point, HACCP)，以管理餐點配製及料理過程，與人員及食材的衛生清潔。

1.4 結論及討論

疫情調查結果顯示，位於薩爾斯堡的職業學校諾羅病毒感染之群聚事件，共計 48 名學生出現急性腸胃炎症狀，分析結果推測與該校學生餐廳提供之餐點有關，另外 8 名在 11 月 26 日後發生之個案可能與學生手部衛生習慣不足而造成人傳人感染有關。自個案分離之諾羅病毒，是奧地利第一次分離出 GGII.7 及 GGII.6 重組型病毒。在瑞典，在 2002 至 2006 年期間共計 101 起食物和水相關之諾羅病毒疫情，主要由 GGI.3, GGI.4, GGI.b, GGII.4 諾羅病毒引起[18,19]另有 4 件疫情為 GGII.7/II.6a 重組病毒感染[20]，且近期由重組諾羅病毒引起疫情事件有增加趨勢[20,21]，惟有關該病毒之毒性及傳播能力，仍有待未來分析探討。本次食媒性疫情事件與酸奶醬及火雞肉片沙拉有關，未煮熟的食物常與食媒性諾羅病毒疫情有關[9,15,22]，其他疑似餐點如維也納炸肉排或烤馬鈴薯等熟食，諾羅病毒污染可能性低，此與分層分析後不再具統計顯著性一致。 另外，急性腸胃炎個案在住校生之侵襲率較高，可能是因為酸奶醬及火雞肉片沙拉皆為晚餐餐點，非住校生通常不會在學校吃晚餐，因此侵襲率顯著較低。

人口密集機構如學校或養護中心皆有因有症狀或無症狀廚工污染食物造成疫情之報告[15,23,24]。諾羅病毒感染者有近 20%為無症狀感染，因此廚工可能在感染期間持續工作進而污染食物[23,24]。一項日本研究指出，無症狀感染廚工之糞便檢體的病毒量與有症狀之廚工無顯著差異[25]，在愛爾蘭亦有無症狀感染廚工污染三明治進而造成疫情之報告[26]，在奧地利亦有養護中心、派對期間發生類似疫情的紀錄[1]。由於病毒可在廚房表面約 20℃ 的環境存活達 28 天[27]，因此廚房如無依相關規定執行危害分析重要管制點系統制度(Hazard Analysis Critical Control Point, HACCP)，可能有食品衛生疑慮，增加諾羅病毒感染之廚工污染食物的可能。惟本事件學校未能提供廚工糞便檢體、廚房食餘及其他環境檢體，因此無法釐

清諾羅病毒污染廚房的途徑。在疫情發生第三天（11 月 25 日），學校教室、廁所及其他公共設施皆進行環境清消，學生餐廳及廚房亦於第四天起關閉二天，進行全面清潔消毒。另外，校醫加強教育學生及訓練廚工使用手部清潔劑(Bode Sterilium Virugard®, Hartmann, Heidenheim, Germany)，並在廁所及廚房提供使用。在疫情發生第六天後，僅出現二例急性腸胃炎病例。奧地利立法規定公用廚房應建置 HACCP 系統， 然而發生本疫情事件之職業學校或其他養護機構，礙於人力資源不足，確實履行 HACCP 系統不易。奧地利聯邦衛生部及 AGES 出版諾羅病毒防治工作手冊，建議未來若有類似事件發生，相關機構或單位應遵循工作手冊內容，辦理相關預防及控制措施。

## 2. 季節性流行性感冒病毒監測

依據奧地利傳染病法規，流感病毒或新型流感（如 H5N1 流感）陽性的檢體，均需通報聯邦衛生部第三司轄下之傳染病防治及院感與緊急應變部門。流感病毒及類流感監測則分屬維也納醫學大學(Medical University of Vienna)國家流感實驗室（National Reference Center for Influenza Virology）及 AGES 國家流感流行病學中心（National Reference Center for Influenza Epidemiology）負責，並由 AGES 進行流感實驗室資料及類流感監測等資料彙整及分析。學生於受訓期間負責 2011 年至 2013 年流感季（第 39-40 週至隔年 14-15 週）資料分析及撰寫流感季節監測週報。以下簡述奧地利流行性感冒病毒監測架構。

2.1 流感病毒監測（如圖二）

2.1.1 定點醫師監測（Diagnostisches Influenza Netzwerk Ö sterreich, DINÖ）：流感季監測期間約為每年的第 40 週至隔年的第 20 週，由分屬全國 9 省市之簽約定點醫師（約 50 名），採檢送驗符合類流感症狀病人之檢體，再由國家流感實驗室以即時定量聚合酶連鎖反應（Real time PCR）進行診斷及分型判定，流感檢體陽性率可從 0%到流感高峰期的 80%，相關經費由羅氏藥廠（Roche）提供。國家流感實驗室每週五發送當週定點採檢結果的報告，通知 AGES 等相關單位及人員，並在網站公布(http://www.influenza.at/)。

2.1.2 非定點病毒監測：除了定點監測外，非定點醫師可將疑似流感病例檢體送至維也納醫學大學檢驗，部分陽性檢體病毒分離株則進行核酸序列比對是否與疫苗株相符，及進行病毒抗藥性試驗。另有五家流感實驗室分別位於奧地利的首都維也納以外的四個大城(Graz, Innsbruck, Linz, Salzburg), 亦有非定點流感病毒監測，但這五家流感實驗僅能進行流感抗體、流感抗原及 H1N1 新型流感 PCR 及是否為流感病毒 PCR 的陽性判定，無法進一步進行流感病毒次分型（如 H3, B），而這五家實驗室及維也納醫學大學照傳染病法規定，每週亦會將檢驗結果送至 AGES。

2.2 類流感監測

2.2.1 定醫監測：定醫監測為奧地利類流感監測的重心，目前由維也納、Graz 及 Innsbruck 三個城市約 44 名內科家醫或一般科及 11 名小兒科醫師通報每週看診的類流感病人數，資料會統一由 AGES 收集，並依 ECDC 提供的公式，推算成全國每週每 10 萬人的類流感發生率，但監測只從第 40 週進行到隔年的第 14 週左右。

2.2.2 學校監測：目前僅維也納及 Graz 市衛生局，有針對部分的幼稚園、小學的學生及老師進行每週類流感病假人數或比率的統計。

2.2.3 軍營監測：Graz 衛生局有針對所在的駐軍進行每週類流感請假人數統計。

2.2.4 病假統計監測：奧地利有 20 多家健康保險公司，其中各省省營社會安全健康保險公司(Gebietskrankenkasse, GKK)較具規模，有加入社會保險的人，請病假皆需要通知其所屬的保險公司，而保險公司有專人將病假原因以國際疾病分類診斷碼第 10 版(ICD-10)將病假原因分類，目前有四省立保險公司(Vienna, Tyrol, Carinthia, Upper Austria) 每週會將新的符合類流感 ICD-10 的人數統計及該保險公司旗下最新總投保人數的資料送至 AGES 進行流感流病分析。

2.3 流感住院及死亡監測

2.3.1 住院監測：奧地利以往曾進行年度按週流感住院統計，但並非為常規監測系統，但自 2009 年 H1N1 新型流感疫情進入減災期（mitigation phase）後，確診 H1N1 新型流感而住院或死亡的病例需要逐例通報至聯邦衛生部的法定傳染病電子通報系統 (Epidemologische Meldesystem, 下稱 EMS)，直到 2011 年 11 月底才停止通報。

2.3.2 流感死亡監測：奧地利統計部(Statistik Austria)負責各項死因 ICD-10 統計，而 AGES 自 2009 年起，開始年度的每週全死因統計與流感趨

勢的相關性分析研究，但亦非常規監測。

2.4 監測資料分享

2.4.1 每週流感的監測資料，由 AGES 整理後公布於官網 (http://www.ages.at/ages/gesundheit/mensch/influenza/)，另流感年報則公布於奧地利聯邦衛生部官網（http://www.bmg.gv.at/）。

2.4.2 國際通報：目前由衛生部第三司將每週病毒及類流感監測資料，透過歐盟疾病管制局(ECDC) 的電子平台(TESSy)通報，每週四中午過後，ECDC 的每週流感概況(Weekly Influenza Surveillance Overview)會公佈上週歐盟各國的流感監測資料，此外，因 2010 年起，因 ECDC 與世界衛生組織歐洲區屬辦公室（WHO Euro）達成協議，同樣的通報資料也會呈現在 WHO Euro 項下的 Euroflu (http://www.euroflu.org) 網站，而 IHR 平台的相關通報也是由衛生部第三司負責，並於 2013 年底，轉由 AGES 進行 IHR 通報。有關流感週報（德文）請參考下列連結。

（http://www.ages.at/ages/gesundheit/mensch/influenza/aktuelle-influenzameldungen/）

## 3. 李斯特菌感染症監測系統評估

### 3.1 監測架構

奧地利李斯特菌監測係依據人畜共通傳染病防治法(Zoonosengesetz)及傳染病防治法(Epidemiegesetz)成立，目的為及時監測李斯特菌症發生情形及疫情變化，並及時提供疫情資訊以因應疫情控制及預防，及作為政策擬定依據，另可依監測資料結果提出假說進行研究。奧地利李斯特菌症監測於 1996-2006 年期間由位於 Innsbruck 李斯特菌國家參考實驗室負責個案資料彙整及呈報奧國聯邦衛生部（Bundesministerium fuer Gesundheit)。衛生部於 2007 年在奧地利健康暨食品安全署(AGES)成立李斯特菌國家流行病學中心及國家參考實驗室，遂轉由該中心提報流行病學及實驗室檢驗相關資料。

李斯特菌症為奧地利法定傳染病之一，其法定傳染病通報系統(Epidemologische Meldesystem, EMS) 無獨立設計， 與其他傳染病相同，由臨床醫師或實驗室主動通報疑似病例。通報系統架構為由臨床醫師向區級衛生單位通報疑似病例，再由區級公共衛生官上傳個案資料至 EMS。另外，例行性檢測之環境或食品樣本由環境或食品衛生稽查員送至 IMML (The Institute for Milk Hygiene, Milk Technology and Food Science)檢測，其中陽性樣本再由國家實驗室進行分型。臨床醫師採集疑似病患之血液或腦脊髓液檢體後，送至具李斯特菌檢測項目之臨床實驗室進行檢驗，陽性檢體再移由國家實驗室分型。由李斯特菌國家流行病學中心彙整臨床通報資料及實驗室檢驗結果並上傳至 EMS。省市衛生局僅具所轄地區病例資料查詢權限，衛生部則可查詢於國家李斯特菌流病中心彙整後之全國匿名資料，並將資料整併修正，提報歐洲疾病預防及控制中心法定傳染病通報系統 TESSy (The European Surveillance System)（如圖三）。

### 3.2 奧地利李斯特菌症疫情概要

奧地利李斯特菌症通報定義於 2008 年前使用 WHO 建議之通報定義，2008 年起則依歐盟規定 Decision No 2119/98/EC 執行。奧地利李斯

特菌症發生率自 2006 年起顯著上升。2008-2012 年累計四起李斯特菌群聚事件，其中以 2009-2010 年最為嚴重（如圖四），奧地利及德國與捷克三國累計 34 名病例，5 名死亡，在跨國性流行病學調查結果證實病例罹病與食用軟乳酪（Quargel）有關，該牌乳酪於奧地利生產後再外銷至其他國家。2011-2012 年李斯特菌症確定病例以散發個案為主，懷孕個案病例數亦無明顯上升（如圖五）。

3.3 歐盟食品及微生物檢測規定

針對李斯特菌控制與預防，奧地利依據歐盟食品檢測及實驗室檢測規定 Dir. 92/46/EEC, (EC) No. 2073/2005, ISO18593, EN/ISO 11290-1 及 11290-2 執行相關檢測。以現成熟食為例 (ready-to-eat food)，其中供嬰兒或特殊醫療目的之現成熟食需於 25 公克食品採樣中無檢出李斯特菌。其他類現成熟食產出時檢測可容許量規定亦為零檢測，若食品已於超市上架時檢測，可容許量則為每克食品 100cfu(colony-forming unit)。因一般非嬰幼兒食品類之上架現成熟食可容許檢出少量李斯特菌，因此食品儲存溫度不足提高李斯特菌大量增殖風險。

3.4 監測系統內容

3.4.1 監測目的

依據奧地利人畜共通傳染病防治法及傳染病防治法，李斯特菌症的監測目的包括：

1. 監測李斯特菌症發生率及流行趨勢，在出現異常或高於警戒值時及時因應，以做為政策擬定及公衛作為之實證參考依據。
2. 監視李斯特菌症群聚事件之人時地及來源等流行病學資訊，以進行公共衛生因應作為。
3. 選定高暴露風險族群以提供防治措施。
4. 提出污染來源、傳播模式及高風險族群等假說，了解是否具研究或調查需求。
5. 依據歐盟法律（Decision No 2119/98/EC）規定，向歐洲疾病預防及控制中心法定傳染病通報系統（TESSy），通報奧地利李斯特菌

症病例數。李斯特菌症通報系統架構於法定傳染病通報系統項下，涵蓋全國人口近 850 萬人、9 省份（Burgenland, Carinthia, Lower Austria, Upper Austria, Salzburg, Styria, Tyrol, Vorarlberg, and Vienna）、及 106 區。

3.4.2 病例定義

奧地利於 2008 年以前使用 WHO 病例定義通報李斯特菌症，自 2009 年起則依據歐盟國會 No 2119/98/EC 決議，使用歐盟建議之通報定義（詳如表四）。

3.4.3 監測指標及公布

由衛生部及 AGES 官方網站發布月報（Monatliche Statistik meldepflichtiger Infektionskrankheiten）及年報（Report on zoonoses and zoonotic agents 及 Statistik meldepflichtiger Infektionskrankheiten vorläufiger Jahresbericht）呈現李斯特菌症發生率、年齡、性別、及所在省市之累計數目，其中月報約延遲一個月。自 2009 年起，年報及月報的公布則改由李斯特菌國家實驗室執行。另外，李斯特菌國家實驗室年報則發布檢驗結果次級資料，包括血清型及脈衝式電泳（pulse filed gel-electrophoresis, PFGE）型別、每 10 萬人口發病後 28 天死亡率、致死率、及每年全國通報李斯特菌疫情事件數。

3.4.4 重要變革

2009 年 8 月奧地利與德國國家參考實驗室共同合作下，在人類病例分離株檢出具特異性之李斯特基因圖譜且血清型為 1/2a。經流行病學追蹤調查發現介於 2009 年 6 月至 2010 年 1 月期間，累計 14 例李斯特菌感染個案，並追查出感染來源為一種在奧地利生產的軟乳酪(Quargel)，該產品於 2010 年 1 月 23 日公布自奧地利、德國、斯洛伐克、及捷克市場回收，在當時因回收時程過晚而引發極大爭議。奧地利法律規定在具有微生物學證據下，受污染食品檢出李斯特菌後，才能進行相關產品回收，惟現有檢驗技術從食品檢出李斯特菌並不容

易。奧地利政府遂於 2010 年 4 月 21 日修正食品安全及消費者保護法之相關規定，在衛生單位經由流行病學調查確認污染食品與感染個案相關性後，即可提出產品回收要求，不需於食品中檢出病原體後才得回收問題產品[28]。另外，本事件調查發現回收日公布後仍出現 2 名年長個案，個案於回收日後仍食用 Quargel，證明民眾接收回收產品相關訊息之風險溝通仍不足，特別是高風險族群如孕婦或老年人，另務必至個案居住處進行剩餘食品疫情調查，並告知其他家屬以進行送驗、清理及丟棄等預防措施。相較於其他食媒性疾病，李斯特菌症具潛伏期長(3-70 天)、致死率高(約 20%)、發生次數相對較少，且可能併發中樞神經系統感染、敗血症及流產等特性，且在此次群聚事件具有兩種 PFGE 型別，疑似是因為軟乳酪使用的菌種改變，因此當發現不同型別的病例，並不表示出現另一波疫情或是前一疫情已經結束。

## 3.5 監測系統評估內容

本報告以評估該系統的簡易性及時效性為主，評估衛生部於 2009 年啟用 EMS 後，李斯特菌症系統之簡易性及時效性的變化。

### 3.5.1 簡易性

2009 年在啟用 EMS 以前，李斯特菌個案通報採傳真通報，並由區級衛生單位公共衛生官通報至省級衛生單位，再以月報形式通報至衛生部，層層通報下，從個案發病至衛生部收到通報單之時間冗長。在 EMS 啟用後，當醫師通報區級衛生單位公共衛生官疑似個案後，衛生官即逕至 EMS 進行通報，無須再上報省級衛生官。另省衛生單位亦不需彙整病例月報及年報陳報衛生部。衛生部可直接自 EMS 下載去名化的個案資料，以供後續整理及分析，及陳報 ECDC。若地方實驗室在定期來自生產線及市場等食品及環境樣本檢出陽性檢體結果，則陳報檢體資訊及提供細菌分離株，由李斯特菌國家參考實驗室進行細菌分型，並將結果上傳至 EMS，因此若出現疑似群聚事件,人類、食品、及環境檢體結果皆可於 EMS 查詢，俾利及時提供資訊以協助流行病學家進行疫情調查。因此，EMS 啟用簡化了李斯特菌監測系統架構（詳如圖三）。

### 3.5.2 時效性

李斯特菌國家實驗室自 1997 年起即負責彙整李斯特菌症通報個案名單，而奧地利傳染病統計年報則自 2005 年起公布李斯特菌症年通報病例總數。以資料庫日期相關欄位資訊，計算 EMS 啟用前後通報時程差異，評估 EMS 啟用後是否提升系統時效性。經查 1996-2008 年個案名單欄位中與日期相關之欄位名稱為採檢日及臨床實驗室檢體收到日， 檢體種類包括腦脊髓液及血液。1996-2008 年累計 172 例病例，其中 55 例具有採檢日及臨床實驗室檢體收到日資訊，資料完整度為 32%，從採檢日至臨床實驗室檢體收到日所耗費天數介於 0-688 日，中位數為 6 日，以地方臨床實驗室所在省市比較時程中位數介於 2-11 天，其中以 Tirol 省最短及 Salzburg 省最長（如圖六）。EMS 在 2009 年啟用後，系統李斯特菌症個案資料庫中，日期相關欄位為發病日、臨床實驗室診斷日及通報日，與啟用前之日期欄位不同。2009-2011 年累計 107 例病例，其中 96 例具有發病日及臨床實驗室診斷日資訊，資料完整度為 90%，從發病日至臨床實驗室診斷日間隔天數介於 0-17 日，中位數為 2 日。另累計 101 例具有臨床實驗室診斷日及通報日資訊，資料完整度為 94%，從臨床實驗室診斷日至通報日間隔天數介於 0-28 日，中位數為 1 日。因此從個案發病、實驗室確診至個案通報間隔天數明顯較 EMS 啟用前縮短。另在 50 例標記發病日、臨床實驗室診斷日及居住省市個案中，從發病日至臨床實驗室診斷日間隔天數以 Carinthia 省最短及 Vorarlberg 省最長，在 55 例標記臨床實驗室診斷日、通報日及居住省市個案中，從診斷日至通報日之間隔天數以 Styria 省最短及 Tyrol 省最長（如圖七）。

## 3.6 討論與建議

李斯特菌症監測系統在 EMS 啟用後，即時監測李斯特菌症發生率及流行趨勢，並在出現異常或高於警戒值時及時因應，以做為政策擬定及公衛作為之實證參考依據，另經線上整合人類病例、食品及環境樣本檢策資料，掌握李斯特菌症群聚事件之人時地及來源等流行病學資訊，俾利進行相關防疫作為。依據評估結果證實 EMS 於 2009 年啓用後，李斯

特菌症通報不需由省級公衛單位收集區級資料後，再陳報衛生部之流程，由區級衛生單位公共衛生官直接登入 EMS 系統通報，簡化通報流程，且各層級衛生單位皆具資料查詢權限，權限劃分則確保個案個人資料安全性。另 EMS 系統縮短個案確診及通報間隔天數，使疫情監測資料更能及時掌握。因李斯特菌症個案死亡率高，縮短疫情發生至監測系統發現異常之時間下，更能及時進行相關調查及因應。提高系統簡易性及時效性下，亦可提高個案資料陳報 ECDC 之時效。

因 1996-2008 年李斯特菌症個案資料庫內容完整度有限，且僅具採檢日及臨床實驗室檢體收到日之資訊，無法評估時序上個案診斷日及通報日之間隔天數，亦無從得知自個案發病至衛生部接到通報個案資訊所需時間，為本次系統評估主要限制。建議本系統未來可擴充使用者權限至醫療院所，由臨床醫師直接進行李斯特菌症個案通報，可再縮短個案通報時間及簡化系統流程。有關本監測系統評估報告，詳見附錄六。

## 4. 奧地利臨床醫師百日咳相關知識、態度、行為調查研究

### 4.1 研究背景

以描述性流行病學方法觀察奧地利傳染病通報系統資料發現，百日咳通報病例有上升趨勢，且有地域上的差異。2006-2012 年在 Styria, Salzburg, Upper Austria 及 Tyrol 四省皆有通報率顯著上升趨勢，其他五省份則無(如圖八)。另分析 2009-2011 年百日咳通報資料中，小於 15 歲之青少年及孩童之通報率顯著上升（圖九）。百日咳發生率在地域上出現顯著差異的原因可能為真或人為因素造成，若監測資料觀察的通報率為真，病例數增加可能與疫苗接種率不同、醫療資源可近性、少數族群分布及特殊宗教文化等相關。另一可能則是人為造成通報率的差異，可能與醫師通報行為、實驗室診斷方法、醫師對於百日咳的認知、衛生單位傳染病因應作為之資源分配比例不同等相關。在比較百日咳通報率不同之省份後，推測醫師對百日咳認知及通報行為在執業省份間具有差異之論點下提出研究假設。

其他可能原因如各省百日咳基礎疫苗或追加疫苗之涵蓋率差異或省市間實驗室檢驗量能及方法差異等因素，經其他橫斷式問卷調查研判無省市上顯著差異。

### 4.2 研究目的

為了解奧地利百日咳在不同省份出現通報個案出現顯著差異的可能解釋。因百日咳病例主要諮詢醫師對象為一般科醫師（general practitioners）、兒科醫師（pediatricians）及肺專科醫師 （Pulmonologists），下稱專業醫師，故調查此三類專業醫師在百日咳臨床表徵及實驗室診斷方法學等知識之認知、百日咳通報行為及依據實驗室檢驗確認疑似感染百日咳病例之頻率。另評估上開因素在所執業之省市上是否具差異。調查結果可提供衛生部對醫事人員進行百日咳相關教育宣導之參考依據，並針對特定地區之醫事人員加強百日咳通報宣導。

## 4.3 研究方法

### 4.3.1 研究設計

以橫斷式 KAP 調查(Cross-sectional knowledge, attitude, and practice survey)，藉由電話訪談及線上問卷填寫方式調查專業醫師對於百日咳臨床表徵及實驗室診斷方法學等知識之認知、百日咳通報行為及依據實驗室檢驗確認疑似感染百日咳病例之頻率，再分析醫師進行醫療行為之所在地與百日咳通報率之關係。調查對象來源為於奧地利醫師公會註冊執業之專業醫師，總計 5298 名（詳如表五）。由於以隨機抽樣方式進行問卷調查之回收率過低，遂改以便利取樣方式進行問卷調查，以便提高問卷回收率。

在樣本中 50%為非暴露組（知識低、通報行為差、送驗供實驗室確診頻率低），95%顯著水準、80%檢力及最低盛行率比（Prevalence ratio）為 1.3 下，預計需要 283 名兒科醫師、350 名一般科醫師以及 276 名肺部專科醫師完成問卷填寫，並依照省市人口比例分配樣本數（如表六）。另奧地利百日咳應變小組及醫師公會代表成員決議不進行問卷初探性研究。

### 4.3.2 問卷設計

經徵求奧地利肺專科醫學會、家庭醫學會及小兒科及青少年醫學會同意，取得專業醫師電子郵件信箱及聯絡電話、以電子郵件通知調查對象直接線上填寫或經 AGES 同仁電話訪問方式收集問卷，問卷共計 32 題，其中包括個人基本資料如職業別、執業地點及涵蓋範圍，專業醫師對於百日咳臨床表徵及實驗室診斷方法學等知識之認知、百日咳通報行為及依據實驗室檢驗確認疑似感染百日咳病例之頻率。大多數問題為選擇題，填充題主要為詢問送驗實驗室名稱及填寫採集鼻咽拭子的步驟。問卷題目屬性可分為四類，其中必選題為分析專業醫師能力之計分題：

1. 通報行為：題 1-3, 8-11 及題 31 共計八題，皆為是非題及必選題。
2. 百日咳臨床表徵相關知識：題 4-7 及題 14 共計九題，為單選或多選題。題 4 及題 5 為必選題，累計 7-9 分以上定義為具高臨床表

徵知識之專業醫師。

3. 百日咳實驗室診斷相關知識：題 15-17, 19, 21-26, 28 及題 30 共計 12 題，必選題為 15-17, 19, 23-24, 28 共計 7 題，總分 17 分，累計得分在前 25%之專業醫師定義為具高臨床表徵知識之專業醫師。
4. 依據實驗室檢驗確認疑似感染百日咳病例之頻率：題 12 及題 13 共計二題，若 75%以上之疑似病例皆進行採檢及實驗室診斷之專業醫師定義為高頻率確定百日咳疑似病例感染情形之專業醫師。

4.3.3 定義

2006-2012 年通報率顯著上升之 Styria, Salzburg, Upper Austria 及 Tyrol 四省定義為高通報率省份，其他五省則定義為非高通報率省份。另調查對象如一般科醫師、兒科醫師及肺專科醫師定義為在奧地利醫師職業公會註冊之執業醫師。

4.3.4 資料分析

使用 QuestionPro 線上軟體產生及彙整問卷，再以 Excel 格式呈現，並使用 Stata 軟體第 11 版進行資料分析。敘述性統計就職業別分別計算答對四項屬性問題之百分比，並依據各省市專業醫師分布比例進行加權，最後呈現加權後百分比。

4.4 結果

調查累計回收問卷共 270 份，其中包括一般一般科醫師 78 份、兒科醫師 150 份及肺部專科醫師 42 份，回收率分別為 22%、53%及 15%。由於一般科醫師問卷回收人數僅佔一般科醫師總人數的 2%，因此不進行分析性統計。依據敘述性統計結果，其中僅有 28-34%的專業醫師通報百日咳病例時先確認病人符合通報定義之臨床條件，且平均僅有 10%會通報疑似或可能病例，另平均 60%的專業醫師曾有通報百日咳確定病例之經驗。另外，具備較高百日咳臨床表徵相關知識之專業醫師以兒科醫師比例最高（67%），肺部專科醫師（40%）及一般科醫師（34%）次之，且高達 91%之兒科醫師認知百日咳症狀在 0-3 個月、4 個月-9 歲、及 10 歲

以上族群之差異，肺部專科醫師（69%）及一般科醫師（59%）則較低。會依據實驗室檢驗確認疑似感染百日咳病例之頻率仍以兒科醫師最高(86%)及一般一般科醫師最低(60%)（詳如表七）

分析結果顯示，小兒科及肺專科醫師在高通報率或非高通報率省份執業，在百日咳臨床表徵及實驗室診斷方法學等知識之認知、百日咳通報行為及依據實驗室檢驗確認疑似感染百日咳病例之頻率並無顯著差異（詳如表八）。惟當分析曾有通報百日咳確定病例經驗之專業醫師中，若醫師在高通報率省份之教學醫院執業（PR: 1.55; 95%CI: 1.12-2.17）及具備較佳的百日咳實驗室診斷知識(PR: 1.35; 95%CI: 1.02-1.80)為醫師通報百日咳確診病例行為之獨立因子。即在具有通報百日咳確定病例經驗之醫師中，在高通報率省份教學醫院執業的醫師，通報百日咳確定病例較非教學醫院醫師高 55%，另在高通報率省份執業且具備較高百日咳實驗室診斷知識之專業醫師，其通報百日咳確定病例較知識程度較低者高出35%，惟此差異在非高通報率省份則不顯著（詳如表九），推測醫師通報行為可能為部分省份百日咳通報率明顯高於其他省份的可能原因之一。

## 4.5 結論與建議

兒科醫師在認知百日咳臨床表徵及實驗室檢測知識與以檢測確定疑似病例比例較高，可能與百日咳被一般科醫師視為孩童特有的傳染病有關，一般醫師對於成人無發燒且咳嗽長達 2 週以上之鑑別診斷，較少考量到百日咳。本研究顯示具通報確定病例經驗醫師中，在高通報率省分教學醫院執業或具備較佳的百日咳實驗室診斷相關知識者，其通報盛行率顯著較在診所執業或較不具百日咳實驗室診斷相關知識者高，推測教學醫院通常附設實驗室，對於教學醫院醫師，進行百日咳檢測可近性較高，但此現象在非高通報率省份則無。另外，專業醫師通報疑似病例比例低，若有通報經驗者，多通報確定病例，其中小兒科醫師採檢送驗以確定疑似病例是否感染百日咳之比例較肺專科醫師及一般科醫師高。

本次研究主要限制包括 1. 奧地利百日咳通報資料不全，部分個案無法判定為疑似、可能或確定病例, 2. 無各省市歷年百日咳疫情紀錄，造成無法排除或校正群聚事件發對於各省份監測趨勢的影響。3. 一般科醫師之問

卷回收率過低，無法進行後續分析。4.兒科醫師及肺部專科醫師填寫問卷之回收數未達具代表性之樣本數。5. 調查後期因回收率過低，改以便利抽樣取代簡單隨機抽樣，提高了選樣誤差。本研究結果雖未能代表奧地利醫師對百日咳認知及通報行為，仍可顯示一般科醫師及診所開業醫師為加強百日咳相關知識及通報頻率等相關教育訓練之主要對象。有關本專題研究報告，詳見附錄八。

## 5. 食媒性疾病疫情調查教育訓練

### 5.1 目的

本次教學目的為讓地方衛生官了解 AGES 在食物中毒事件中所扮演的角色，及當省市衛生單位尋求 AGES 介入調查時，地方衛生及食品查驗相關人員如何協助及配合調查，並理解基本流行病學詞彙及疫病調查基本步驟及意義，藉以增進與地方衛生人員合作關係。

### 5.2 內容

授課主題為食因性傳染病疫情調查訓練，共計 8 小時，訓練對象主要為各省市的公共衛生部門人員，公衛醫師及食品查驗員等共 28 位。課程內容上午為傳染病流行病學概論、疫病調查、分析流行病學概論（世代研究及病例對照研究）。下午則運用學生撰寫的食因性傳染病案例進行討論，由學生撰寫英文版本後再請同事協助修改為德文版本。

本案例討論為一件 2011 年發生於維也納的食品中毒事件，並在部分個案檢體檢出 Salmonella Typhimurium DT3，依據世代研究分析結果顯示，派對餐點的馬鈴薯沙拉為可能的感染源，廚師同時製作其他食物如蛋餃及烤乳豬，另廚師經營一家幼豬飼養場，飼養場環境檢體包括豬隻糞便檢體、廚師穿著之雨靴底部檢體亦檢出同一 PFGE 型別之 Salmonella Typhimurium DT3。調查人員赴廚師購買雞蛋之蛋雞場進行環境及雞蛋檢體檢測後，亦有部分檢出同一 PFGE 及 VNTR 型別之 Salmonella Typhimurium DT3。疫情事件發生後一個月在下奧地利省的一間酒館發生另一起食物中毒事件，部分個案檢體再度檢出相同型別之沙門氏菌，該酒館使用之雞蛋來源與第一件疫情事件相同，在調查小組獸醫師通報陽性蛋雞場後所有蛋雞皆已撲殺，並進行環境清潔消毒。藉由此案例討論，期望學員了解疫情調查的步驟、繪製疫情趨勢圖、計算侵襲率、勝算比及風險比、環境調查及實驗室檢測之重要性，以及提供因應及防治措施建議（詳見附錄九）。

## 5.3 討論

美國 CDC 於 1951 年成立田野流行病學家訓練計畫(Epidemic Intelligence Service, EIS)，是全球最早成立田野流行病學家訓練的國家，並協助多國公衛機構成立衛生調查訓練班(Field Epidemiology Training Program, FETP)，其中包括歐洲 EPIET(1995 年成立)及我國 FETP(1984 年成立)，無論是台灣 FETP 或歐洲 EPIET，皆以美國 EIS 訓練精神及教學模式為基礎。學習內容及技能包括應用流行病學概念、主動參與討論、建立解決問題能力等。應用流行病學概念包括疫病調查、監測系統、研究設計、資料剖析、敘述及分析方法等。教案設計者則依教學目的，編列講師使用及學員使用版本。比較台灣及奧地利疫情調查教學案例，皆以該國國內疫情調查之結案報告或發表文章為基礎，協助學員熟悉該國國內傳染病疫情調查方式及限制，並依循 EPIET 或 EIS 教學模式進行教案設計，以問與答方式進行小組討論，學員藉此學習以不同身分觀點討論、計算或繪圖等技巧，第一題結束後，再翻頁閱讀第一題的參考答案及第二題情境背景與題目，題目的順序依循疫情調查進展鋪陳。

## 6. 學術發表

### 6.1 OEGHMP2012 (33rd Annual Meeting of the Austrian Society for Hygiene, Microbiology and Preventive Medicine)

該會議為奧地利衛生、微生物及預防醫學年會，本次會議在薩爾斯堡舉行，為期四天。多數會議內容以德文發表，但亦有以英文發表的報告。學生於該會議以壁報方式報告奧地利諾羅病毒疫情事件，相關壁報內容詳如附錄四。

### 6.2 ESCAIDE 2011-2013 (European Scientific Conference on Applied Infectious Disease Epidemiology)

ESCAIDE 是受訓期間每年皆需參加之國際研討會，該研討會主要匯集歐盟會員國公共衛生專家及決策者，由 ECDC 主辦，每年都有數百位與會者參加。預計從 2013 年起，每年皆於 ECDC 所在城市瑞典斯德哥爾摩舉行，會議主題包括藉食物和水之傳染病、監測系統評估、抗藥性議題、疫苗可預防性疾病、疫病調查、流感、病媒病毒傳染病、國際健康議題、結核病及其他呼吸道疾病、分子流行病學議題、人畜共通傳染病、性傳染病、新興方法學運用等，議題多元豐富。學生於 2012 年之會議進行口頭報告，報告主題為「A foodborne norovirus outbreak in a boarding school, Austria, November 2011」，詳細投影片內容如附錄五。

### 6.3 IMED2013 (International Meeting on Emerging Diseases and Surveillance)

IMED 會議對於新興傳染病相關議題如人畜共通傳染病以及 One health 相當重視，2013 年之舉辦地點為維也納，學生於該研討會進行壁報報告，主題為 2005-2011 年奧地利百日咳之流行趨勢，敘述病例數及通報率在不同年齡群、省分及發病月份的比較（附錄七）。

### 6.4 台奧第二次傳染病國際研討會

2010 年 11 月份第一次台奧傳染病國際研討會於疾病管制署舉行，本次研討會由奧方於 2013 年 5 月 13-16 日在維也納 AGES 微生物及傳染病醫學大樓舉行。我國選派共計 11 位專家學者及疾管署官員參與，學生負

責會前籌劃及接待，並於該研討會中進行口頭報告。本次研討會主題包括結核病、細菌抗藥性、醫源性疾病、高致病性細菌、腸病毒、蟲媒病毒、傳染病監測議題、食因性傳染病等。我國與會專家共計發表 11 篇口頭報告，奧地利 AGES 專家則發表 16 篇口頭報告。學生於該次研討會中報告近年歐洲及奧地利百日咳疫情趨勢(詳如附錄十)。本會議亦有雙邊專家學者經驗交流並商討未來可能合作方向之目的。我國與會專家對於奧地利 AGES 食因性傳染病監測印象深刻，從人、環境到食品檢驗監測皆由 AGES 負責，更能有效將訊息統合分析，我國則因分責於不同機構，於資訊統合上較為不易。另外，奧地利實驗室硬體架構相當完善且符合相關國際規定，而疾管署因昆陽實驗室歷史悠久，部分硬體設備難以符合國際規範。

# 7. 新興傳染病疫情風險評估

## 7.1 人類感染 H10N8 禽流感病毒風險評估報告(評估日期：2014 年 2 月 7 日)

### 7.1.1 前言

A 型流感病毒各種亞型普遍存在禽鳥間，有些亞型於禽類為無症狀或輕症感染，惟該等病毒對人類造成衝擊不一，因此早期發現新型禽流感人類病例並及時因應，為降低疫病傳播的不二法門。全球曾有包括如 H7N7、H9N2、H7N2、H7N3、H10N7 等亞型禽流感零星人類報告病例，症狀以結膜炎或一般類流感症狀為主，個案經治療後均已康復。我國亦曾於 2013 年發布全球首例人類感染 H6N1 禽流感病例，肺炎經治療已康復。造成重症肺炎、呼吸道感染且致死率高之亞型為 H5N1 禽流感，以及自 2013 年 3 月迄今已造成逾 470 人感染之 H7N9 禽流感疫情[29]。新型禽流感個案於發生初期，由於該亞型對於動物及人類流行病學等相關資訊較不完整，需持續追蹤及瞭解病毒人傳人之能力、疾病嚴重性及病毒抗藥性等相關資訊，以評估對全球疫情流行風險之可能性及衝擊及調整相關防治整備及因應措施。

根據中國大陸官方網站於 2013 年 12 月 17 日發布全球首例人類感染 H10N8 禽流感病毒死亡個案，個案為江西省南昌市一名 73 歲婦女，有高血壓、糖尿病和重症肌無力等慢性病史，且曾進行胸腺摘除術及具免疫功能低下情形，其於 11 月 27 日發病，11 月 30 日入院治療後於 12 月 6 日死亡，臨床診斷為嚴重肺炎。個案有活禽市場接觸史，其家人和密切接觸者並無病徵和其他異常情況。約一個月後，中國大陸再發布全球第 2 例 H10N8 病例，個案亦居住於江西省南昌市，55 歲婦女，於 2014 年 1 月 8 日發病，1 月 15 日入院治療，臨床診斷為重症肺炎，目前病情穩定，個案曾於 1 月 4 日至當地某活禽市場，其家庭成員等密切接觸者均未出現症狀。第 3 例 H10N8 病例則為居住於江西省南昌市一名 75 歲男性，其於 2014 年 2 月 4 日入院治療後於 2 月 8 日死亡，臨床診斷亦為重症肺炎。截自 2014 年 3 月 4 日，中國大陸共發布 3 例 H10N8 人類感染病例[30]。為因應中國大陸陸續傳出人類感染 H10N8 禽流感疫情，本文分析目前 H10N8 禽流感疫情

概況及相關資料，評估疫情對國人健康影響風險及造成可能衝擊，以提供國內防治政策及整備工作之參考依據。

7.1.2 材料與方法

本文傳染病風險評估方式係參考國際公共衛生機構如世界衛生組織、美國疾病預防及控制中心(CDC)及歐洲疾病預防及控制中心(ECDC)等傳染病風險評估或風險模擬架構，蒐集風險評估要項所需之 H10N8 禽流感疫情資訊與相關研究，包括病毒特性(病毒變異性與人類呼吸道細胞受體結合力及抗藥性)、實驗動物感染情形、國內外動物生態學及流行病學、國內外人類流行病學、國內易感族群及群體免疫力與疫苗等資訊，並依上述評估項目之科學證據，評估 H10N8 禽流感疫情造成我國發生境外移入病例之可能性以及對國內疫情造成之衝擊。

7.1.3 結果

7.1.3.1 病毒特性及實驗動物感染情形

中國大陸於 2007 年曾在湖南省洞庭湖濕地區域，於環境中檢體分離出 H10N8 禽流感病毒，經遺傳學親緣分析結果顯示，該病毒株具多源組合性，係由不同病毒亞型之多基因片段重組而成，其中內部基因可能來自 H5 及 H7 亞型病毒，H10N8 禽流感病毒於禽類屬低病原性病毒，但該病毒在小鼠肺臟細胞可複製良好，且經適應培養後複製效率更佳，經適應培養的病毒甚至可於小鼠肺臟外的其他器官分離到，並擴及腦部。其毒性於兩次繼代後增強，可造成小鼠死亡。將不同繼代之病毒株基因定序分析後發現，其分離的病毒株在肺臟細胞適應培養過程中有多胺基酸序列突變的情形，該病毒株命名 A/environment/Dongting Lake/Hunan/3-9/07 (H10N8)[31]。

非 H5 及 H7 之低病原性禽流感病毒在文獻中曾有數次重組而變異為高病毒株的紀錄[32]。另有研究指出，2012 年 1 月份曾於廣東省活禽市場的鴨隻分離到 H10N8 禽流感病毒，由基因親

源演化分析判定該病毒血清凝集素基因來自歐亞種系(Eurasian lineage)，神經胺酸酶基因來自北美種系（North American lineage）。其病毒株命名為 A/Duck/Guangdong/E1/2012 (H10N8)[33]。近期研究分析全球首例中國大陸 H10N8 禽流感個案上呼道分離病毒之基因序列資料顯示，該病毒之血清凝集素蛋白源自湖南鴨隻之 H10N3 禽流感病毒 (A/duck/Hunan/S11205/2012)，神經胺酸酶蛋白則源自南韓綠頭鴨之 H10N8 禽流感病毒 (A/mallard/Korea/1041/2010)，其他 6 段病毒內部基因則皆源自 H9N2 禽流感病毒重組而成，且基因親源演化分析顯示該病毒屬新型 H10N8 禽流感病毒，已與 2007 年及 2012 年分別於洞庭湖及廣東檢出之 H10N8 禽流感病毒屬不同的次分支(subclade)。就病毒特性分析病毒與宿主細胞受體結合能力、人體感受性及抗藥性，該新型 H10N8 禽流感病毒株在血清凝集素蛋白第 226 位點胺基酸未發生突變，顯示該病毒仍以結合禽類細胞受體為主，較 H7N9 禽流感病毒已於該位點由麩醯胺酸(Glutamine) 突變為白胺酸(Leucine)的情形不同，因此該病毒與哺乳動物上呼吸道細胞結合能力較差；另在神經胺酸酶未有變異，因此對於神經胺酸酶抑制劑類抗病毒藥劑如克流感及瑞樂沙等，仍具敏感性；在聚合酶蛋白(PB2) 第 627 位點胺基酸已有由麩胺酸(glutamic acid) 突變為離胺酸(lysine)的現象，此與增加哺乳動物毒性有關，尚需密切監測病毒流行與演化情形[30]。

7.1.3.2 國際生態學及流行病學資料

H10N8 禽流感病毒過去曾於中國大陸廣東省活禽市場與湖南省洞庭湖濕地，以及日本、南韓、美國、加拿大、義大利及瑞典的候鳥或家禽發現(表十及圖十)[34–39]。近期多種亞型禽流感病毒仍持續在中國大陸南方循環及演化，常見亞型包括 H3、H5、H6 及 H9[40]，中國大陸南方的活禽市場被認為是家禽將禽流感病毒傳播至人類的重要途徑之一[41,42]。中國大陸於 2011 年

冬季至 2012 年春季，曾主動監測湖南省洞庭湖區域周遭養鴨場之禽流感病毒盛行情形，經採集鴨隻及環境檢體，檢出禽流感病毒亞型包括 H3、H4、H5、H6、H9、H10、H11、H12，其中鴨隻檢體檢出陽性率為 3.5%[43]。經分析該地區除為飼養鴨隻的主要地區外，亦為野生水禽及來自西伯利亞及大陸北方遷徙度冬之候鳥棲息地，因此洞庭湖區域為禽流感病毒重組及循環的溫床，病毒株的基因重組情形頻繁。

另有關人類感染其他 H10 亞型禽流感疫情，首次發生於 2004 年埃及伊斯梅利亞省(Ismaillia)，當時出現 2 例均 1 歲孩童感染 H10N7 低病原性禽流感病毒，出現發燒及咳嗽症狀後復原，其中 1 名個案之父親為販禽商人，經常往返伊斯梅利亞省及杜姆亞特省(Damietta)間，其中杜姆亞特省在 2004 年 4 月期間，曾自市場販賣的 5 隻野鴨檢體檢出同亞型病毒，惟後續採集 75 件個案接觸者及 13 件市場其他候鳥檢體皆為陰性[44]。另一事件則發生於 2010 年澳大利亞新南威爾斯省，7 名屠宰場工人感染 H10N7 禽流感病毒，產生之結膜炎疫情，其中 2 名工人有鼻炎及 1 名喉嚨痛之症狀，其檢體檢出 H10 亞型禽流感病毒基因，惟無法培養分離病毒，經基因親源演化分析顯示，其血清凝集素蛋白基因來自北美種系。後於 2012 年研究證實，H10N7 禽流感病毒約自 2007-2008 年間傳入澳大利亞野生水禽族群，並已在澳國境內與其他病毒種系重組演化[43]。

7.1.3.3 國內生態學及流行病學資料

我國農業委員會家畜衛生試驗所曾於 2005 年監測 4,506 件野鳥樣本，共分離 49 株病毒株，其中該年 1-4 月於台北野鴨排遺 5 件檢體中檢出 H10N8 禽流感病毒，2011-2014 年，我國境內候鳥禽流感病毒帶病毒監測結果則未於候鳥檢體檢出(表十一)。

我國自 1999 年起，以流感併發症為法定傳染病監測項目，並針對社區類流感病患及不明原因肺炎住院病患採檢送驗，經

由系統性監測國內流感病毒活動情形及臨床實際狀況，每年檢驗之檢體件數約 1 至 2 萬件，至今累計超過 25 萬件，共計分離約 86,000 株流感病毒，未曾自人體檢體中檢出 H10N8 禽流感病毒。

7.1.3.4 風險評估結果

就現有資訊評估，由於中國大陸目前公布之 3 例病例均屬散發個案，且無人傳人之證據，推測國內出現境外移入新型 H10N8 禽流感個案可能性低；中國大陸曾有動物感染 H10N8 禽流感監測資料，我國野鳥監測亦曾發現 H10N8 禽流感病毒紀錄，推測 H10N8 禽流感仍可能經由大陸貿易及走私禽鳥傳入我國或於國內環境中具暴露病毒之風險；惟就基因親源演化分析，中國大陸病例所感染之新型 H10N8 禽流感，與野鳥分離之病毒不同，研判國內發生新型 H10N8 禽流感人類病例風險可能性極低。國內未曾出現人類感染 H10N8 禽流感或新型 H10N8 禽流感病例及動物等疫情，推測國人應不具該等病毒之免疫力，推斷國人應無保護力，所幸新型 H10N8 禽流感病毒之傳播力及對哺乳動物受體結合力尚差，甚較近期持續出現人類感染病例之 H7N9 禽流感病毒不佳情況下，若國內發生 H10N8 禽流感疫情，推測僅可能有散發個案，造成社區傳播之可能性極低。但目前 H10N8 禽流感病毒之保毒動物、動物傳播及人類感染途徑皆不明，僅有病毒對哺乳動物細胞適應性之動物實驗資料，因此仍須持續監測及更新資訊及相關研究。

目前人類 H10N8 禽流感病例雖為重症或死亡，且由實驗室資料顯示 H10N8 禽流感病毒對於小鼠有強毒性，惟新型 H10N8 禽流感病毒之傳播力及對哺乳動物受體結合力尚不及 H7N9 禽流感病毒，加上經病毒序列分析神經胺酸酶未變異，對神經胺酸酶類抗病毒藥劑如克流感及瑞樂沙仍未出現抗藥性，充足之抗病毒藥劑整備將可降低疫情之衝擊。另我國自 2013 年 5 月 17 日實施傳統市場禁宰活禽政策等各項防治因應作為，整體而

言，現階段中國大陸 H10N8 禽流感疫情對我國造成之衝擊極低[45]，惟對於該病毒毒性及對人類侵襲之嚴重度尚須持續收集資料觀察。綜合評估 H10N8 流感對我國感染機率及衝擊之風險皆低(表十二)。

7.1.4 結論

依據世界衛生組織 2013 年 12 月 20 日公布之評估報告顯示，H10N8 禽流感個案應屬散發病例，推測與中國大陸加強流感監測有關；雖然該病毒於當地禽鳥間盛行率不明，但若病毒持續於當地循環，預期仍將有零星人類病例出現[46]。目前新型 H10N8 禽流感病例之接觸者均無臨床症狀，且無證據顯示病毒具人傳人之跡象，病毒傳播效率亦不高，推測對公眾健康構成風險的機會低，惟仍需持續密切監視疫情再評估風險[47]。

本文囿於 H10N8 禽流感病毒及流行病學等相關資訊有限，風險評估結果有其限制性；依現有 H10N8 禽流感病毒之證據顯示，該病毒傳播風險低於 H7N9 禽流感病毒，推估中國大陸 H10N8 禽流感疫情，目前對我國未構成立即性的風險，國內疫情等級亦無提升之必要性，惟 H10N8 禽流感病毒對國人感染率及後續疫情發展，仍需持續觀察以評估對我國的衝擊。

以人類感染 H10N7 禽流感病毒病例經驗來看，H10 亞型禽流感病毒之毒性及致死率不高，且多屬輕症；惟感染 H10N8 禽流感病毒之三例個案均屬重症或死亡，在該病毒傳播途徑、病毒毒力與致病性等均未明之情形下，建議維持現有監視及通報定義以及對民眾衛教宣導內容，另加強相關研究及監測資訊蒐集，另建議國內農政單位應持續進行溼地監測及加強走私禽鳥查緝工作，以降低國人風險。

## 7.2 人類感染 H7N9 流感病毒風險評估報告 (評估日期：2014 年 1 月 15 日)

### 7.2.1 疾病背景資訊

#### 7.2.1.1 人類流行病學：入秋前 H7N9 流感疫情描述 (2013 年 3 月 31 日至 9 月 30 日)

WHO 於 2013 年 4 月 1 日公布全球首例人類感染 H7N9 禽流感病例，截至 9 月 30 日入秋前病例已分布於中國大陸 12 省市（安徽省、廣東省、河北省、河南省、湖南省、浙江省、福建省、江蘇省、江西省、山東省、北京市、上海市），累計 134 例 H7N9 流感確定病例（圖十一），其中 45 例死亡，病例自 2013 年第 8 週起通報，至第 15 週達通報病例數高峰後下降至第 18 週達最低點，後續週別則為零星通報。另香港及台灣各別通報 1 例自中國大陸移入病例 。根據自人類分離之病毒與自動物及活禽市場環境分離之病毒相似、約 75%的人類病例有接觸活禽的接觸史、可於活禽市場販賣禽類中檢出病毒、活禽市場關閉後人類發布病例數下降等因素，WHO 綜合研判個案多與接觸感染活禽及活禽市場環境有關。入秋前我國自 2013 年 4 月 3 日起將「H7N9 流感」列為第五類法定傳染病，累計共 446 例通報病例，其中 39 例為中國大陸來台人士，1 例境外移入確定病例，445 例排除 H7N9 感染(其中 56 例檢出 H1N1 流感，40 例檢出 H3N2 流感，6 例檢出 B 型流感。

另自 2013 年 1 月 1 日起累計通報 447 例「不明原因肺炎」個案，其中 240 例曾有中國大陸旅遊史，6 例曾有香港旅遊史，5 例曾有澳門旅遊史，餘均排除 H7N9 感染。自 2013 年 1 月 1 日起通報「流感併發症」且曾經有中國大陸、香港或澳門旅遊史的個案共 69 例，其中 21 例為流感併發症確定病例(10 例 H3N2；11 例 H1N1)，餘均排除 H7N9 感染。

國內 H7N9 通報病例中，19-64 歲佔 77%，依身分別分別為國人(89%)、中國大陸籍人士(9%)、其他國籍旅客(2%) ，醫療院所通報佔 89%、機場港埠後送佔 11%，通報病例中檢出流感

陽性率佔 23%，其中以檢出 H1N1 為主(54%) ，其次為 H3N2 (39%)。

7.2.1.2 人類血清流行病學調查

中國大陸於 2012 年 1-11 月以血清凝集抑制試驗(HI)檢測上海市、浙江省、江蘇省及安徽省禽業相關從業人員回溯性血清檢體共計 1544 件，陽性率為 0.5% (HI≥1:20)，但微量中和試驗則皆未呈現陽性，推測中國大陸上開省分於 2012 年 11 月以前尚未檢出 H7N9 病毒[48]。另一項 2013 年 4-5 月在浙江省及其他已發佈人類病例省市進行血清學調查發現，累計 1129 位一般民眾檢體皆未檢出 H7N9 流感病毒，另 396 位禽場工作者中檢出率占 6.3% （HI:>1:80），推測接觸感染家禽為人類感染 H7N9 流感之重要來源，並可出現輕症或無症狀感染[49]。

7.2.1.3 動物感染及全球分布

H7N9 屬低病源性禽流感病毒，感染禽類多不具臨床症狀。H7N9 禽流感病毒曾於美國、加拿大、瓜地馬拉、西班牙、瑞典、埃及、蒙古及台灣出現分離記錄，其中自亞洲分離到 H7N9 之分離率小於 0.01%，推斷自野鳥排遺檢出中國大陸 H7N9 禽流感病毒流行株之機率相當低，建議野鳥監測應以曾檢出病毒之環境及曾通報人類個案等高風險區域為主[50]。

7.2.1.4 動物血清流行病學調查

入秋前中國大陸通報省分除湖南省與北京市之外，其他發布 H7N9 病例省份皆在活禽市場家禽或環境檢體檢出 H7N9 流感病毒。

7.2.2 病毒特性

7.2.2.1 基因變異性

一項中國大陸研究發現 H7N9 流感病毒由 4 段不同來源之

禽流感病毒重組而成，且至少包含兩段支系，其中病毒血清凝集素(HA)基因可能源自中國大陸長江三角洲地區感染 H7 亞型禽流感病毒之鴨群，推測經由東亞遷徙線路上的候鳥傳入該區鴨群中。另神經胺酸酶(NA)基因可能源自遷徙候鳥，判定 HA 基因較早進入鴨群，且可能藉鴨群將病毒由野鳥傳至家禽。H7N9 流感病毒 6 段內部基因源自廣於中國大陸家禽間流行之 H9N2 禽流感病毒且具多源性，其中非結構蛋白基因（NS）可能源自江蘇省周邊的雞群，而其他 5 段基因則源自上海市及浙江省附近的雞群中，並推測基因片段多樣性可能與運輸家禽有關 [51]。

7.2.2.2 宿主受體結合能力

一項研究利用 Fetuin-binding、醣晶片量化分析（glycan array）及人類組織結合力分析(human tissue-binding assays)方法，評估 H7N9 流感病毒結合人類氣管上皮細胞受體能力發現，人類 H7N9 流感病毒分離株之受體結合能力已提高，且對 α-2,6 及 α-2,8 唾液酸受體結合能力增加，對於 α-2,3 唾液酶受體結合能力則下降，惟其 α-2,6 唾液酶受體結合力仍不及季節性流感病毒 [52]。

7.2.2.3 病毒在實驗動物的傳播能力

一項研究發現 H7N9 流感病毒可在多種實驗動物體內複製，且安徽株(A/Anhui/1/2013)可造成雪貂間飛沫傳播 [53]，相較於其他禽流感病毒(如 H5N1)，H7N9 流感病毒黏附於人類支氣管及肺泡上皮細胞數量明顯較多，且更能集中黏附於鼻甲、氣管與支氣管的纖毛細胞上，顯示其具有有效人傳人之潛力。另外，H7N9 病毒之聚合酶蛋白(PB2)出現 E627K 胺基酸位點變異，在小鼠實驗發現病毒株增加肺部細胞激素濃度及病毒複製能力，推測胺基酸突變與增加小鼠致病性及哺乳動物細胞培養適應性有關 [54]。

7.2.2.4 病毒對抗病毒藥劑之抗藥性

一項研究分析比對 H7N9 流感病毒安徽株及上海株（A/Shanghai/1/2013)NA 基因發現，上海株出現 R294K 胺基酸位點突變，可能造成神經胺酸酶抑制劑如 oseltamivir、zanamivir、peramivir 和 laninamivir 生現不同程度之抗藥性， 惟突變亦造成病毒複製能力下降致不足成為流行株，因此現有抗病毒藥劑仍可用於 H7N9 流感病毒的臨床治療[55]。

7.2.3 H7N9 流感入秋後疫情描述(自 2013 年 10 月 1 日起)

中國大陸入秋後病例首度出現於浙江省，12 月病例集中於浙江省及廣東省，另上海市、江蘇省、福建省則屬散發病例。香港與我國分別通報 3 例及 1 例境外移入病例，香港個案為廣東省深圳市移入病例，我國個案為江蘇省移入病例；入秋後累計 39 例(含香港 3 例及我國 1 例)(圖十二)，5 例死亡，男女比例為 1：0.6，50 歲以上占 56%，約 60%有禽鳥接觸史。目前正值候鳥南遷及禽流感好發季節，廣東省深圳市、廣州市、珠海市、汕頭市活禽市場已陸續檢出 H7N9 流感病毒，疫情有南下擴散趨勢，並以珠三角地區尤需關注。廣東疾控中心表示廣東個案具中老年人、曾圈養或多次接觸活禽、多出現於邊緣或近郊地區等三特點，並推測人類感染重要來源為鄉鎮及城郊活禽市場。

自 2013 年 4 月 3 日起截至 2014 年 1 月 6 日累計 477 例通報病例，其中 2 例為境外移入確定病例，473 例排除 H7N9 感染(其中 58 例檢出 H1N1 流感，41 例檢出 H3N2 流感，7 例檢出 B 型流感)，2 例檢驗中。另自 2013 年 1 月 1 日起，截至 2014 年 1 月 13 日共通報 588 例「不明原因肺炎」個案(其中 291 例曾有中國大陸旅遊史，8 例曾有香港旅遊史，7 例曾有澳門旅遊史)，其中 1 例檢出 H7N9 陽性(為第 2 例 H7N9 流感境外移入確定病例)，另有 6 例檢驗中，餘均排除 H7N9 感染。

自 2013 年 1 月 1 日通報「流感併發症」且曾經有中國大陸、香港或澳門旅遊史的個案共 81 例，其中 26 例為流感併發症確定病例(12

例 H3N2；14 例 H1N1) ，3 例檢驗中，餘均排除 H7N9 感染。國內 H7N9 通報病例中，19-64 歲約佔 77%；另國人佔 89%、中國大陸籍人士佔 9%、其他國籍旅客佔 2% ；醫療院所通報約佔 90%、機場港埠後送佔 10%;通報病例中檢出流感陽性約佔 23%,其中以檢出 H1N1 為主(約 54%) ，其次為 H3N2 (約 38%)。

7.2.4 風險評估內容

7.2.4.1 感染機率(probability)

目前我國出現兩例境外移入確定個案,分別於 2013 年 4 月 24 及 12 月 31 日皆自江蘇省入境，推測春節期間往返中國大陸旅客將增加，並可能有台商回國治療或回台發病，預計移入個案數將會增加。

我國曾於 1998-2011 年間自 44,786 野鳥排遺樣本中檢出 8 件 H7N9 陽性檢體，其陽性率為 0.02%，其中包括涉禽 3 件、鷗科 2 件、鷺科 2 件及其他鳥類 1 件 [50]，另國內家禽未曾檢出 H7N9 禽流感病毒。

7.2.4.2 易感族群與群體免疫力

我國第 2 例境外移入病例係經不明原因肺炎通報檢出，其餘個案 H7N9 流感檢驗均陰性，推測國人目前對 H7N9 流感病毒尚無群體免疫力。

7.2.4.3 疾病傳染力

WHO 風險評估仍推斷 H7N9 以零星感染個案或有限人傳人為主，近期文獻仍無造成社區感染之證據。

7.2.4.4 衝擊(impact)

截自 2014 年 1 月 13 日,全球共計 174 人感染,52 人死亡，致死率 30%，30 歲以上成人佔 91%。中國大陸於 10 省市發燒篩檢門診之回溯性檢體檢出 6 例確定病例，陽性率為 0.03%，

推測類流感門診病患檢出 H7N9 流感病毒之機率極低，該 6 名病患皆居住於 H7N9 流感已發布之省份，其中 2 名孩童不需住院治療，另其他 4 位成人則症狀較為嚴重，推測 H7N9 流感病毒感染在孩童症狀較為輕微[56]。

7.2.4.5 治療與控制

根據病毒抗原性分析，WHO 建議以 A/Anhui/1/2013-like virus(例如：A/Shanghai/2/2013)病毒株為疫苗株。目前登記 8 件人用 H7N9 疫苗第 1-2 期臨床試驗，大多位於北美，WHO 於 2013 年 12 月 20 日公布建議 H7N9 流感病毒疫苗株如圖十三。

目前仍以神經胺酶抑制劑為主要治療用藥，近期研究發現 H7N9 變異病毒對抗病毒藥劑 Oseltamivir、Eramivir 及對 Zanamivir 已產生部分抗藥性[57]，病毒變異造成抗藥性等相關資訊仍須持續追蹤。

一項研究分析中國大陸於 2013 年關閉部分活禽市場後，發現可有效降低上海市、杭州市、湖州市及南京市每日感染個案數達 81-100%，推測關閉活禽市場可有效控制疫情[45]，惟疫情趨勢具季節性，疫情趨緩是否歸因於活禽市場關閉則具爭議性。廣東省於 2013 年 12 月 23 日及 2014 年元旦與春節前夕實施活禽市場關閉措施，並執行一天一清洗、一週一大掃除和一個月休市一天等制度。上海市則公布自 2014 年起，每年農曆大年初一至國曆 4 月 30 日全市暫停活禽交易。

我國因應 H7N9 流感疫情，於 2013 年 4 月 3 日成立 H7N9 流感中央流行疫情指揮中心，訂定 H7N9 流感防治工作指引，並於 2013 年 5 月 17 日起實施傳統市場禁宰活禽政策，禁止活禽屠宰及販售並查核及調查攤商，地方縣市政府配合辦理各項衛教宣導、防疫物資查核以及禁止活禽屠宰及販售聯合查核（緝）等工作。

7.2.5 風險評估結果

依據美國 CDC 風險評估工具提供之 10 項風險評估項目，H7N9 疫情發生風險詳如表十三。另評估對我國公共衛生衝擊，評估項目重要性依序為：疾病嚴重度、國人抗體盛行率、人類感染情形、抗病毒藥物的感受性、病毒抗原性與疫苗株的差異、病毒與宿主受體的結合度、病毒基因變異、實驗動物傳染力、感染動物全球分布、動物的感染情形。另若考量環境(context)因子，我國整備及因應措施持續進行，惟整備及因應單位之直接成本較難即時取得，及加強進行公眾風險溝通，以降低國人恐慌。

依據風險評估項目推測我國疫情出現可能性及衝擊風險皆為中級，整體研判 H7N9 疫情對我國構成立即性的風險，建議持續對一般民眾及禽畜相關從業人員進行相關風險管理與溝通。

WHO 於 2013 年 10 月 29 日發布人類 H7N9 流感風險評估推斷多數個案具活禽市場及禽鳥接觸史，惟禽類感染症狀輕微，且在傳播途徑及保毒動物未明下，病毒仍可持續在中國大陸及鄰近國家傳播擴散，預期冬季及春節期間活禽需求增加及運輸頻繁下，預期仍會出現動物及人類感染病例。個案多屬散發病例及出現 5 件家庭群聚，推測病毒出現持續性人傳人及造成社區傳播可能性低。另一般民眾不建議進行 H7N9 流感病毒暴露後投藥，惟高風險及具慢性病史者建議接觸確定病例後口服 Oseltamivir 或吸入 Zanamivir 預防性投藥。

7.2.6 結論與建議

就現有資訊評估我國 H7N9 流感疫情發生風險為中級，目前已有兩例境外移入個案，且入秋後中國大陸南方 H7N9 流感病例持續增加，預期我國未來仍可能出現境外移入個案，建議持續進行流感疫情監測，並適時提供警訊。另 H7N9 疫情對我國造成衝擊之風險等級為中級，疾病致死率高且國人多無免疫力，惟目前相關研究指出，經境外移入個案造成社區傳播的風險極低，建議加強一般民眾、社區及高風險族群(如禽畜相關從業人員及往返大陸旅客)之風險管理與溝通。另建議持續追蹤 H7N9 流感相關資訊，如傳播途徑、病毒變異及

抗藥性情形、儲備實驗室檢測量能以及提高臨床醫師如以 H7N9 通報流感併發症或不明原因肺炎疾病通報率。

# 第四章 評析與政策建議

## 1. 奧地利傳染病調查及監測機制與我國之比較

### 1.1 傳染病調查

奧地利由各省市自行調查轄下傳染病群聚事件，若疫情擴及其他省市，聯邦衛生部即指派 AGES 傳染病及流行病學組，協助省市衛生單位進行疫情調查，並指示 AGES 每週陳報書面資料及進行電話會議，以掌握疫情調查進度。另若省市研判轄下疫情特殊，需 AGES 協助調查時，AGES 得介入調查。因此，若單一省市轄下發生傳染病疫情，AGES 不會主動介入亦不被告知。囿於 AGES 在奧地利聯邦衛生部或省市衛生單位要求時，才進行流行病學調查，因此 AGES 僅掌握其 FETP 協助調查之疫情事件資料。另 AGES 傳染病及流行病學組依據病原體特性，建立食媒性傳染病制式問卷模組，以初步了解個案及接觸者之飲食暴露情況，若具特定暴露來源如某餐廳餐點等依據之事件，則另行設計問卷，該國尚未建立線上問卷系統或是事件報告彙集平台等監測系統。

我國 FETP 啟動原則包括食品中毒人數達 50 人或以上者、食品中毒事件有持續擴散之虞、社會大眾關注事件、病原體特殊者（如肉毒桿菌、麻痺性貝類毒素等）或其他特殊因素，由衛生局填列「疾管署流病調查支援申請單」，逕向 FETP 申請審核，符合啟動條件原則之事件，由疾管署區管制中心成立專案團隊，以掌握參與調查人員名冊，包括縣市衛生局疾管科(處)及食藥科(處)、疾管署區管制中心、食藥署區管制中心及 FETP 人員等。另我國疾管署問卷調查管理系統提供各縣市衛生局所疫調人員，就轄下需進行疫調之通報個案進行調查，並自行線上填答問卷，問卷依疾病類別設計，該系統與法定傳染病個案通報系統(下稱法傳系統)資料介接，因此疾管署得以掌握各縣市通報個案的疫調狀態及內容，另針對群聚事件提供事件報告上傳平台，俾利供其他相關單位查詢及分享。

### 1.2 監測機制

奧地利食媒性疾病監測系統架構，以李斯特菌症為例，地方臨床實驗室向區級衛生單位通知臨床檢驗結果，陽性檢體則提供病原體分離株逕送國家參考實驗室進行後續分型，臨床檢驗結果及分型結果由國家參考實驗室上傳至 EMS

系統。另食品及環境稽查員將待檢食品及環境樣本送至奧地利乳製品衛生及食品科技所檢測，若檢出李斯特菌，則將分離菌株送至參考實驗室進行後續分型，並由參考實驗室上傳食品及環境樣本檢測結果，因此 EMS 系統可綜合彙整環境、食品及通報個案之資料及檢驗結果，方便資料比較及分析。我國因農畜業安全、食品安全、人類傳染病等資訊由不同機關管轄，因此若成立疑似李斯特菌症群聚事件調查小組，需聯繫其他機關以獲取所需資訊，時效性因而延宕。

奧地利自 2009 年啟用 EMS，經與我國法傳系統初步比較，其特點為該系統與奧地利戶政系統介接，因此部分個人基本資料欄位可由戶政系統自動匯入，提高時效性及資料品質。另一特點為衛生單位權限設定保障個人資料內容，各省市衛生單位僅得查看轄下各區通報個案之詳細資料，聯邦衛生部可查閱該國所有通報個案資料，惟與個人資料相關的欄位僅包括姓名縮寫，居住省市及地區、出生年月日、年齡、性別及國籍，因此無法就通報資料判定個人。AGES 往年僅具其參考實驗室及聯邦衛生部授予管理之傳染病權限。EMS 系統於 2013 年 11 月份自聯邦衛生部移交由 AGES 接管，使 AGES 具所有通報傳染病資料分析權限，並同時進行功能擴充，目前除了衛生單位外，臨床實驗室已具備登入及上傳臨床檢驗結果之權限。相較於奧地利，我國法傳系統詳細記載個人資訊，如身分證字號及詳細居住地址等，並介接疾管署實驗室資訊管理系統（Laboratory Information Management System, LIMS）中，通報個案送驗資料及結果至法傳系統，因此權責機關須注相當重視資訊安全維護，避免資料外洩。

另 EMS 系統主要限制，係僅衛生單位人員具系統使用權限，醫師需向區級公共衛生單位通報後，由該區的系統負責人員上傳通報資料，包括個案個人資料、臨床診斷相關資訊及後續流行病學調查結果等。學生由受訓期間使用 EMS 系統中百日咳資料庫發現，資料庫欄位內容完整度不高，且資料品質於該系統啟用初期較差。相較於奧地利，我國法傳系統主要限制為尚未與醫療院所實驗室檢驗資料與電子病歷介接，因此目前我國正進行防疫雲發展計畫，其中包括「實驗室傳染病自動通報系統暨跨院所實驗室資料雲端交換平台」及「運用醫院電子病歷進行傳染病通報」兩項子計畫，藉建立自動資料交換機制，以減少重複登打之情況，並加速資料收集作業。

## 2. 德國腸道出血性大腸桿菌 (Shiga toxin producing E. coli , STEC ) O104 感染疫情流病調查及可供我國借鏡之經驗

### 2.1 敘述性流行病學調查 [58–62]

德國在 2011 年 5-7 月發生了大規模腸道出血性大腸桿菌（enterohaemorrhagic E. coli，簡稱 EHEC）O104:H4 感染事件，累計 855 名個案出現溶血性尿毒症候群（haemorrhagic uremic syndrome，簡稱 HUS），及 2,987 例急性腸胃炎病例，其中 68%HUS 及 58%EHEC 個案為女性，並以成人為主。病例主要集中於德國北部省市，並於 6 月初因問題苜蓿回收下架後下降，後續儘出現散發病例，主要為二代感染及實驗室感染個案，德國聯邦衛生機構 Robert Koch Institute（RKI）於該年 7 月 26 日宣布疫情終止。以下就本疫情事件流行病學調查部分進行探討，以供我國參考借鏡。

依據德國傳染病保護法第 6-7 項（§ 6-7 IfSG, Infection Protection Act），HUS 及 EHEC 疑似病例自 2001 年起即開始由臨床醫師進行線上通報及臨床實驗室檢驗，並由當地衛生單位蒐集個案相關資訊，自事件發生後，於 2011 年 5 月 23 日起，地方及省市衛生單位在接獲疑似病例通報後，即儘速通知 RKI 並進行後續流病調查及檢測，確定是否符合疫情病例定義。本事件疫情個案發病日自 5 月 8 日起迅速攀升，在 5 月 22 日達高峰後下降，最後個案發病日期為 6 月 23 日（如圖十四），另分析推測 HUS 個案暴露日期多在 5 月 23 日以前，且集中於 5 月 12-14 日間。相較往年 EHEC 疫情，本案 HUS 病例年齡趨勢明顯集中於成人，且 5 歲以下病例數僅占 HUS 病例 1%，另女性個案比例較 2001-2010 年增加（68%比 56%），且較往年 EHEC 事件潛伏期長（中位數 8 天，往年約 3-4 天）。6 月 1 日以後發病個案之年齡中位數及女性比例下降，且分散至德國北部以外其他省市，表示疫情後期之人口學特性已與往年 HUS 散發病例近似。RKI 及健康暨食品安全機構等聯邦及省市相關單位自 5 月 20 日起進行暴露來源調查。

## 2.2 參與醫院急診血便病例監測

德國自 2011 年 5 月 27 日起開始，進行該國各省市參與醫院急診血便症狀監測，以掌握更多疑似 EHEC 個案，資料內容包括每日急診人次及血便個案之性別及年齡（大於或小於 20 歲）分布數，並每日以電子郵件或傳真方式逕送 RKI。自 5 月 28 日至 6 月 30 日，累計 193 家醫院急診病房參與監測，疫情主要發生省份之血便就診病例百分比較其他省份高（3.3%比 0.7%），疫情後期則逐漸降低至監測背景百分比（如圖十五）。

## 2.3 感染源調查

### 2.3.1 疫情初期流行病學調查

初期疫情調查以人時地等敘述性流行病學調查為主，發現本次疫情與往年 EHEC/HUS 疫情相關之食品如生乳及生肉關連性低，第一次進行病例對照研究囿於病例數限制，僅發現個案食用蕃茄、小黃瓜及萵苣之頻率顯著較對照組高，惟後續食品安全機構調查結果並無相關證據證實上述食物與罹病之關係。

### 2.3.2 法蘭克福市之公司附設餐廳疫情調查

2011 年 5 月 9-17 日，兩家位於法蘭克福市之公司總計 60 名員工出現血便症狀，其中 18 例出現 HUS，9 例為實驗室確定病例。經調查 23 名病例及 35 名健康員工公司餐廳之消費收據紀錄發現，病例組員工購買生菜沙拉的比例高於對照組員工 6 倍（OR:5.8, 95%CI:1.4-23.9），並且 87%的個案皆有購買生菜沙拉的紀錄，其他食物則未達統計顯著性，因此推測生菜沙拉為可能感染源。經調查兩家公司員工餐廳生菜沙拉內容物中，僅混合苜蓿皆來自一家位於下薩克森省之苜蓿製造商。

### 2.3.3 以餐廳收據進行回溯性世代追蹤研究（recipe-based restaurant cohort study）

以向餐廳預定餐點之顧客進行調查，可減少顧客於流病問卷

訪問時出現回憶誤差之特性，RKI 調查小組從病例名單中，蒐集 5 月 12-16 日預約同一家餐廳用餐之 10 組(168 名)顧客，進行問卷調查，發現顧客 EHEC 侵襲率為 18%，除了已知預定餐點輔助調查外，亦以問卷結果及顧客提供之照片以提高資料正確性。另調查小組與廚師進行詳盡訪談，釐清每項餐點的製作方式及內容物比例等。調查結果發現食用苜蓿顧客之罹病風險為未食用者的 14 倍（RR: 14.2, 95% CI 2.4 -∞, p<0.01），且所有病例皆有食用苜蓿，其他食物如蕃茄、小黃瓜等調整後風險比皆未達統計顯著性。該餐廳使用之混合苜蓿亦源自下薩克森省之苜蓿製造商。

2.3.4 以一般飲食史進行病例對照研究調查

漢堡市政府在 5 月 20-21 日以一般食媒類傳染病包含多種食物類別之問卷型態進行個案飲食史調查，12 名病例中僅有 25%表示曾於潛伏期間食用苜蓿，因此飲食史之問卷設計僅包含 EHEC 群聚個案常見暴露食物及其他調查已懷疑之食物類別即可，以避免過多問題造成回憶誤差及偽陽性，導致疫情初期地方衛生單位之病例對照研究調查結果多與苜蓿無關。

2.3.5 食用生菜之病例對照研究調查

德國 3 個主要疫情發生城市在 5 月 29 日至 6 月 4 日間進行病例對照研究，目的為釐清不同種類蔬菜與罹病之關係，病例定義為當地於研究期間因 HUS 住院之成年病患，並以年齡及性別與居住地配對挑選對照組，病例組與對照組比例為 1:3，問卷內容主要以發病或訪問前兩週內食用之蔬菜及水果進行調查，累計病例組 26 名及對照組 81 名，年齡中位數為 47.5 歲（介於 29-75 歲），其中病例組及對照組曾食用苜蓿之比例分別為 25% 及 9%。單變量分析結果顯示，苜蓿（OR:4.4, 95%CI:1.1-18.0）及小黃瓜（OR:3.5, 95%CI:1.0-12.9）達統計顯著性，另在調整其他食物類別變項後，苜蓿（OR:5.8, 95%CI:1.2-28.6）及小黃

瓜（OR:6.0, 95%CI:1.1-31.3）仍達統計顯著性。本次研究亦調查飲食地點，發現 HUS 個案外食比例較對照組高達 9 倍( OR:9.4, 95%CI:2.7-32.8)，推測多數個案經外食生菜感染，另生菜沙拉常同時包括苜蓿和小黃瓜，疑似苜蓿較不容易被記得出現在生菜沙拉中，因此造成回憶偏差影響問卷填寫內容。

2.3.6 選擇特定群聚進行世代追蹤研究

國外旅遊團因有既定行程，因此可以確定團中發病成員之飲食地點，例如某一出現病例之丹麥旅行團僅於德國北部某一餐廳消費。群聚事件通常由臨床醫師、地方衛生單位、國外衛生單位（瑞典、丹麥及美國），甚至個案自行通報並提供相關資訊予 RKI，最終累計有 41 起群聚事件與本次疫情相關，累計逾 300 例病例。並在懷疑苜蓿為感染源之前，即於疫情初期發現之 3 起群聚事件進行世代研究，利用旅行團於餐廳消費之菜單內容進行旅行團員之飲食史調查，此次調查並無發現特定食物呈現統計顯著性，後續由其他調查發現苜蓿為可能感染源後，再進行餐廳食材備製調查發現，數項餐點皆以苜蓿裝飾搭配，對照飲食史發現所有病例其實皆有食用苜蓿。另經調查苜蓿來源亦皆為下薩克森省之苜蓿製造商，且 41 起群聚事件之感染源皆可追溯至該苜蓿製造商。另發現有兩名居住於下薩克森省之散發個案僅食用自行耕種的苜蓿，而個案使用於耕種之種子與苜蓿製造商使用之種子來源相同。

2.3.7 問題苜蓿下架停售後仍出現之病例調查

針對問題苜蓿下架回收後發生之病例，需調查是否與本事件同一感染源之方法，除了需要藉由實驗室檢測病原體是否為 EHEC O104:H4 外，再以 Shigatoxin 1, 2 (stx1, stx2) 分型確認。若確定該病例感染之病原體與本次疫情同型，再配合流行病學調查個案是因食用苜蓿感染或是經二次感染造成，或屬無流行病學關聯性之病例，惟仍要留意可能的回憶偏差。若有出現另

一群聚事件與苜蓿及二代感染皆無關連性，則需要進一步調查其他可能的感染源。

2.3.8 個案居家環境及帶菌者盛行率調查

RKI 及地方衛生單位進行 50 戶個案家及 50 戶個案家鄰近家戶之 EHEC O104 盛行率調查，並且同時進行前瞻性世代追蹤研究，探討發生個案家戶中發生二代感染的可能性及相關危險因子與帶菌者排菌時間等研究。

2.3.9 法國 EHEC O104:H4 疫情事件

在德國疫情已發生一段時間後，法國亦出現相同分型之 EHEC O104:H4 疫情，累計 15 例病例且發病日在 2011 年 6 月 15-20 日間，經調查個案飲食史，發現感染源來自一家法國苜蓿製造商，另發現法國與德國苜蓿製造商之葫蘆巴種子（fenugreek seeds）皆源自同一家位於埃及的種子供應商，惟種子未檢出 STEC。另外出現 1 例瑞典及奧地利本土個案，說明感染源非僅在德國。

2.4 結論與討論

現今監測並無證據顯示 EHEC O104:H4 疫情相關型別在德國本土持續流行，目前若出現血便或 HUS 症狀且符合疫情病例定義之個案，皆須儘速通報並以 RKI 特製問卷進行調查，以確定感染來源。疫情相關防治作為包括宣導加強個人及廚工手部衛生，以避免人傳人或經接觸污染器具表面感染。另調查發現該製造商以園藝公司註冊，食品稽查員定期調查相關硬體設施結果未曾出現異常紀錄，表示當時歐洲相關法規規範無法有效避免 STEC 汙染食物，且對於進出口種子或食物，應亦須檢測 STEC，

歐盟委員會於 2011 年 5 月 22 日經早期預警及因應系統(Early Warning and Response System , EWRS)接獲德國通知後，後續疫期資訊持續在 EWRS 及歐盟食品及飼料快速預警系統 (The Rapid Alert System for Food and Feed, RASFF)公布，歐洲國家藉此獲得疫情發展資訊。歐盟委員會正視此疫情對歐洲造成的衝擊，在 2013 年歐盟委員會以實施

條例 (EU) No 209-211/2013 修正(EC) No 852/2004 條文規定，除了地方食品衛生單位須至少至苜蓿生產廠抽驗及稽查一次，以確保符合相關衛生規定及民眾健康外，其他關於苜蓿生產廠的審查要求包括：

1. 生產廠的設計和硬體設施應建立良好的食品衛生生產鏈，包括防止生產步驟之間和過程中的污染，特別是食物處理區域表面（如設備表面）應保持在良好狀態且易於清洗及消毒。
2. 應提供足夠的設施以清洗及消毒與存放工作器具和設備。設施應易於清洗，且冷熱水供應充足。
3. 必要時有足夠設施以清洗食物，每個水槽或其他食物清洗設施之飲用水應充足供應並保持清潔，必要時進行消毒。
4. 種子和苜蓿接觸的所有設備，皆須保持良好程序、狀態及維修條件，以避免污染風險並保持清潔，必要時進行消毒。
5. 適當的程序皆須到位以確保苜蓿清潔，經常清潔和消毒相關設備以避免任何污染風險。

## 3. 歐洲食品安全管理機制與我國之比較：可供我國借鏡之處

### 3.1 ECDC 水媒及食媒傳染病疫情資訊系統 (EPIS-FWD platform)

歐洲會員國利用 EPIS-FWD 平台進行水媒及食媒傳染病之疫情資訊分享、討論及風險評估，以 Microsoft SharePoint technology 方式，彙集逾 350 名流行病學家、微生物學家、決策者及風險管理者，多數專家來自歐盟會員國及歐洲經濟區，其他國家如澳洲、加拿大、美國、日本等專家亦加入使用此訊息平台。第一版 EPIS-FWD 自 2010 年啟用，讓疫情發生早期，跨部會及國別之專家與調查人員即透過此平台，討論調查內容及分享資料，以達到早期偵測及協調因應作為之目的。系統權限設定分為一般論壇、特殊疫情論壇及疫情風險評估論壇等，疫情風險評估論壇之權限僅開放給風險評估小組成員，對於跨國疫情協調及溝通幫助良多。

ECDC 自 2013 年公布啟用第二版 EPIS-FWD，擴充二項系統功能，第一項為群聚事件病原體型別調查（Molecular Typing Cluster Investigation），以評析通報 Salmonella、Shiga toxin-producing Escherichia coli (STEC) 及 Listeria monocytogenes 感染症之病原體分子型別， 主要提供會員國的微生物學家及疫情發生國的流行病學家運用。第二項功能為緊急諮詢（Urgent Inquiries）及緊急諮詢相關論壇（Urgent Inquiries associated forums），作為疫情警訊及調查工具。所有登入者皆可使用緊急諮詢功能，緊急諮詢相關論壇主要包括疫情發生國相關調查人員及受邀加入討論的專家，包括獸醫師、食品安全及環境衛生專家等皆為論壇成員。論壇內容可能包括疫情討論、問卷填寫、及共同報告撰寫等，跨部會會員國專家及調查人員藉此平台交換重要資訊。另整合地理資訊系統，使歐洲跨國疫情即時以地圖呈現，俾利進行環域分析。

歐洲地區其他食媒傳染病相關監測系統包括歐盟食品及飼料快速預警系統（The Rapid Alert System for Food and Feed, RASFF）、早期預警及因應系統（Early Warning and Response System, EWRS），皆促進跨國及部會合作與溝通。2014 年，歐盟推出全新線上應用程式 iRASFF，設有 RASFF 系統的成員國均可藉此上傳公布食品警示。 同

時，歐盟設立 RASFF 消費者入門網站（RASFF portal），向消費者提供實用資訊，例如食品安全部門和企業發出的回收通知及警告。

3.2 食品安全及食媒傳染病權責機構充分交流與合作

歐洲環境局（European Environmental Agency, EEA）、歐洲食品安全局(European Food Safety Authority, EFSA)及 ECDC 是歐洲食品安全及食媒傳染病相關權責機構，EEA 執掌環境、氣候、水質、農業、漁業及食品安全相關業務；EFSA 則為歐洲食品及飼料安全性進行風險評估及風險溝通，另亦為動物健康與福利及植物健康把關；ECDC 執掌人類感染食媒傳染病相關監測、評估與建議。當跨國性食媒傳染病發生時，流行病學調查需從食品生產、製造、加工、販售、消費者食用而產生症狀等皆須調查，因此權責機構共同合作，才能有效控制疫情，並保障消費者健康。

EFSA 及 ECDC 分別在 2008 年及 2010 年簽訂及更新雙方合作備忘錄，對於機關共同執掌議題包括病原體抗藥性、食媒疾病疫情、科學交流與諮詢、病原體風險評估、疫病監測、流行病學調查、快速警示、早期預警及因應等，進行科學交流及資訊交換，並依需要進行聯合記者會、疫情調查報告、文章發表、線上討論及機構人員交換進駐等，以專責窗口及協調員確定合作備忘錄確實執行。另 ECDC 正進行其病原體分子監測系統(TESSy Molecular surveillance services)與 EFSA 國家參考實驗室病原體分型資料庫介接，資料內容主要為沙門氏菌、李斯特菌及大腸桿菌分型(PFGE 及 MLVA)結果，以實際進行資料庫共享方式，促進雙邊資訊交換時效(圖十六)。

相較於歐盟，我國食媒疾病跨部會合作及資訊交流尚無一整合性資訊平台，食媒性疾病疫情事件之產品生產鏈調查因涉及農政單位、食藥署及疾管署，有效跨部會溝通及合作相當重要，目前我國正在執行「整合與提升我國食媒性疾病及其病原監測防護網計畫」，為農委會、食藥署、疾管署共同合作計畫，其中包括重要食媒性疾病病原體調查研究及檢驗技術之開發與應用，與食媒性疾病資訊交流平台建置，惟如何實際整合監測體系及有效應變及合作，是當前努力的目標。

## 4. 歐洲聯盟跨國傳染病疫情資訊整合機制：在法規面及資訊技術面可供我國借鏡之處

ECDC 為歐盟傳染病預防及控制權責機構，成立於 2005 年，其主要目標之一為藉由建立歐盟會員國及歐洲經濟區傳染病疫情資訊整合機制，以有效辨認、評估及溝通傳染病相關風險，並達到傳染病預防及控制之目的。依據歐盟法規 Decision No 2119/98/EC、2000/96/EC 、2002/253/EC，歐盟委員會訂定歐盟傳染病通報定義，所有會員國及歐洲經濟區皆需要依據通報定義，通報該國傳染病個案不具名資料至 TESSy，另需建立歐洲傳染病監測網絡以達到及時預警及有效因應傳染病威脅。此外在 Decision No 1082/2013/EU 明定生物性、化學性及物理性等人為跨國性威脅亦須透過 EWRS 進行通報。

ECDC 傳染病監測架構可區分為指標性監測(indicator-based surveillance)及事件性監測(event-based surveillance)(如圖十七)，指標性監測架構以 TESSy 為主軸，歐洲 28 個會員國及 3 個歐洲經濟區明文規定須將 52 項法定傳染病資料上傳至該系統，其中包含 17 類傳染病指定監控網絡(Dedicated Surveillance Networks，DSNs )；事件性監測工具主要包括疫情監測資訊系統(Epidemic Intelligence Information System , EPIS)及傳染病威脅追蹤工具(Threat Tracking Tool ,TTT)。我國疾管署指標性監測架構以法傳系統為主軸，並依疾病類別及監測目的建立其他如傳染病問卷調查管理系統、學校傳染病監視系統、即時疫情監視及預警系統等特定監視系統。事件性監測系統主要由疾管署媒體室負責彙整國內外傳染病相關新聞事件或國際衛生機構新聞稿等，摘要產生每日媒體摘要、每日國際疫情、每日輿情摘要供機關內部使用，惟尚無風險評估分析及風險追蹤等系統提供協助，目前以人工方式進行。

# 第五章 結語

EPIET 受訓期間與歐盟會員國衛生機構的公衛人才一同受訓，其中在 AGES 實務實習期間，因為德文語言能力有限，疫病調查時無法直接與地方公共衛生官聯繫，因此學生大部份受訓期間，偏重於資料分析。雖稱為現場流行病學訓練學員，學生與一同受訓的奧地利籍同事皆未曾到現場進行疫情調查，甚為可惜。在 EPIET 共計十週的流行病學訓練課程中，印象最深刻的課程為疫苗學，地點位於倫敦的 Public Health England (PHE)。上課第一天第一堂課即由當時 PHE 的首長 Dr. David L. Heymann 為學員回顧疫苗的發展史。其他授課老師無論是 PHE 部門長官或受邀講者皆經驗豐富、課程內容相當精彩，PHE 人才濟濟，人力資源豐富，亦為我國疾管署國際合作的主要機構之一。另一門課則為學習疫情調查所需電腦軟體，授課地點為德國伯林 Robert Koch Institute (RKI)，RKI 的統計部門人員授課清晰詳盡，學員在實作課程若有疑問時，皆可及時解答。電腦實作課程中，其中一位指導員因可口說多國語言讓我印象深刻，使用學員的母語回答問題，讓學生更有自信可以提問。歐洲公衛人才通常具有第二國或多國外語能力，此為勝任公共衛生工作的必要條件之一。

在歐洲已開發國家之衛生機構如 RKI 或 PHE，皆具有生物資訊及生物統計分析部門，部門的同仁提供資料分析及研究方法學的諮詢及協助，因此一篇刊登論文中，常有統計部門人員在作者群中。設置資料分析顧問或部門，可協助業務或研究計畫之統計分析及解讀，對機構研究發展及模組分析與資料加值等運用，想必有相當大的助益，AGES 因囿於人數及經費限制，傳染病及流行病學組並無配置統計人才。

為協助 ECDC 分析歐盟會員國百日咳近年疫情趨勢，學生赴 ECDC 學習以 STATA 軟體進行時間序列分析，該機構建立時間序列分析專用視窗版模組(TSA tool)，在資料匯入後啟動模組對話視窗，可檢查及描述資料內容，並依據頁簽順序選擇時間、週期、趨勢、季節性、殘差、簡易模型及趨勢預測等分析條件後，以圖表及視窗呈現時間序列分析結果，可有效縮短軟體指令編輯時間，協助建立研究假說[63](如圖十八)。實務實習期間，學生利用此工具協助進行挪威、荷蘭、英國及瑞典於 2006-2010 年百日咳病例資料之時間序列分析，再預測 2011 年病例數區間，並與 2011 年實際病例趨勢比較，以推測 2011 年病例數是否超過流行閾值。

另外，百日咳監測資料需要由歐盟會員國的聯繫窗口確認資料完整性及正確性，因此在協調聯繫上佔用相當多時間，可想見 ECDC 需要維繫廣大的人脈網絡，才能有效完成工作，ECDC 員工精通多國語言，多是歐洲各國優秀的公共衛生人才，在互相激勵合作下共同成長精進，是相當正向的工作團隊。在 ECDC 工作的酬勞相當優渥，惟當地物價亦相當高，且需要適應北歐的氣候及有限的日照時間。學生於受訓時結識 ECDC 流感與呼吸道病毒組代理組長 Dr. Pasi Penttinen，並向其簡報我國登革熱防治經驗。Dr. Penttinen 亦受 AGES 邀請於第二次台奧研討會介紹 ECDC 疫情監測及風險評估工作內容。

歐洲學習期間，發現大多數學員具備良好語言能力，部分學員甚至精通多國語言，這也是學生感受的文化衝擊之一。因從小就在台灣長大，發現國際觀及語言能力皆不及同期學員，部份原因是因為不在歐洲成長，所以對於歐洲及非洲的歷史地理及文化了解不多，在二年多來與同學及同事互動後，對於歐洲人的生活及文化已逐漸熟悉。

奧地利首都維也納相當適合居住，空氣品質及居住生活品質佳，人口密度較台灣低，氣候較台灣乾燥許多，學生在台灣常年發生的過敏性鼻炎，到維也納後不藥而癒。維也納氣候宜人乾爽，惟冬季氣溫驟降，且十度以下低溫可持續至隔年五月，是較需適應的主要差異。維也納物價及薪資所得皆約為台灣的兩倍，在歐洲生活期間，發現自己也因環境的變化而改變，較懂得品味生活、健康飲食及培養運動習慣。剛到維也納時，德語環境讓初期生活常碰壁，不過兩年下來，耳濡目染下，聽力也多少進步，亦較能輕鬆在德語環境下生活。

此次實務實習訓練能順利完成，十分感謝疾管署長官給予機會，以及 AGES 與 ECDC 指導員的教導，最要感謝方啟泰老師在學生實務實習期間不斷的鼓勵與教誨，讓學生得以在他鄉學習成長。

# 參考文獻


1. Kuo, H.-W. *et al.* A foodborne outbreak due to norovirus in Austria, 2007. *J. Food Prot.* **72,** 193–196 (2009).
2. CDC - Surveillance - Listeriosis. at <http://www.cdc.gov/listeria/surveillance.html>
3. Dabrera, G. *et al.* A case-control study to estimate the effectiveness of maternal pertussis vaccination in protecting newborn infants in England and Wales, 2012-2013. *Clin. Infect. Dis.* ciu821 (2014). doi:10.1093/cid/ciu821
4. Kharbanda EO, *et al*. EValuation of the association of maternal pertussis vaccination with obstetric events and birth outcomes. *JAMA* **312,** 1897–1904 (2014).
5. Koopmans, M. Progress in understanding norovirus epidemiology. *Curr. Opin. Infect. Dis.* **21,** 544–552 (2008).
6. Dreyfuss, M. S. Is norovirus a foodborne or pandemic pathogen? An analysis of the transmission of norovirus-associated gastroenteritis and the roles of food and food handlers. *Foodborne Pathog. Dis.* **6,** 1219–1228 (2009).
7. Kroneman, A. *et al.* Data quality of 5 years of central norovirus outbreak reporting in the European Network for food-borne viruses. *J. Public Health* **30,** 82–90 (2008).
8. Teunis, P. F. M. *et al.* Norwalk virus: how infectious is it? *J Med Virol* **80,** 1468–1476 (2008).
9. Lopman, B. *et al.* Increase in viral gastroenteritis outbreaks in Europe and epidemic spread of new norovirus variant. *Lancet* **363,** 682–688 (2004).
10. Kroneman, A. *et al.* Increase in norovirus activity reported in Europe. *Euro Surveill. Bull. Eur. Sur Mal. Transm. Eur. Commun. Dis. Bull.* **11,** E061214.1 (2006).
11. Dingle, K. E. Mutation in a Lordsdale Norovirus Epidemic Strain as a Potential Indicator of Transmission Routes. *J. Clin. Microbiol.* **42,** 3950–3957 (2004).
12. Schmid, D. *et al.* An outbreak of Norovirus infection affecting an Austrian nursing home and a hospital. *Wien Klin Wochenschr* **117,** 802–808 (2005).
13. Fretz, R. *et al.* An outbreak of norovirus gastroenteritis in an Austrian hospital, winter 2006-2007. *Wien Klin Wochenschr* **121,** 137–143 (2009).
14. Krause, G. Ausbruchsabklärung: medizinische Notwendigkeit oder akademische Spielerei? *Wien. Klin Wochenschr* **121,** 69–72 (2009).
15. Schmid, D. *et al.* A foodborne norovirus outbreak due to manually prepared salad, Austria 2006. *Infection* **35,** 232–239 (2007).
16. Miller, I., *et al.* Norwalk like virus by light cycler PCR. *J. Clin. Virol. Off. Publ. Pan Am. Soc. Clin. Virol.* **25,** 231–232 (2002).
17. Oh, D.-Y., *et al.* Viral agents of acute gastroenteritis in German children: prevalence and molecular diversity. *J. Med. Virol.* **71,** 82–93 (2003).
18. Siebenga, J., *et al.* Food-borne viruses in Europe network report: the norovirus

GII.4 2006b (for US named Minerva-like, for Japan Kobe034-like, for UK V6) variant now dominant in early seasonal surveillance. *Euro Surveill* **13,** (2008).
19. RIVM - Noronet. at <http://www.noronet.nl/noronet/>
20. Lysén, M. *et al.* Genetic diversity among food-borne and waterborne norovirus strains causing outbreaks in Sweden. *J. Clin. Microbiol.* **47,** 2411–2418 (2009).
21. Reuter, G., *et al.* Epidemic spread of recombinant noroviruses with four capsid types in Hungary. *J. Clin. Virol. Off. Publ. Pan Am. Soc. Clin. Virol.* **35,** 84–88 (2006).
22. Showell, D., *et al.* Norovirus outbreak associated with canteen salad in Suffolk, United Kingdom. *Euro Surveill. Bull. Eur. Sur Mal. Transm. Eur. Commun. Dis. Bull.* **12,** E071129.6 (2007).
23. Moe, C. L. Preventing norovirus transmission: How should we handle food handlers? *Clin Infect Dis* **48,** 38–40 (2009).
24. Marshall, J. A. & Bruggink, L. D. The Dynamics of Norovirus Outbreak Epidemics: Recent Insights. *Int. J. Environ. Res. Public. Health* **8,** 1141–1149 (2011).
25. Ozawa, K., *et al.* Norovirus infections in symptomatic and asymptomatic food handlers in Japan. *J Clin Microbiol* **45,** 3996–4005 (2007).
26. Nicolay, N. *et al.* Potential role of asymptomatic kitchen food handlers during a food-borne outbreak of norovirus infection, Dublin, Ireland, March 2009. *Euro Surveill. Bull. Eur. Sur Mal. Transm. Eur. Commun. Dis. Bull.* **16,** pii: 19931 (2011).
27. Lamhoujeb, S., *et al.* Molecular study of the persistence of infectious human norovirus on food-contact surfaces. *Food Env. Virol* **1,** 51–56 (2009).
28. Pichler, J., *et al.* Lessons to be Learned from an Outbreak of Foodborne Listeriosis, Austria 2009–2010. *Int. Assoc. Food Prot.* **31,** 16–21 (2011).
29. To, K. K. W. *et al.* Emergence in China of human disease due to avian influenza A(H10N8) - Cause for concern? *J. Infect.* (2014). doi:10.1016/j.jinf.2013.12.014
30. Chen, H. *et al.* Clinical and epidemiological characteristics of a fatal case of avian influenza A H10N8 virus infection: a descriptive study. *The Lancet* **383,** 714–721 (2014).
31. Zhang, H., *et al.* Characterization of an H10N8 influenza virus isolated from Dongting lake wetland. *Virol. J.* **8,** 42 (2011).
32. Alexander, D. J. An overview of the epidemiology of avian influenza. *Vaccine* **25,** 5637–5644 (2007).
33. Jiao, P. *et al.* Complete Genome Sequence of an H10N8 Avian Influenza Virus Isolated from a Live Bird Market in Southern China. *J. Virol.* **86,** 7716–7716 (2012).
34. Manzoor, R. *et al.* Phylogenic analysis of the M genes of influenza viruses isolated from free-flying water birds from their Northern Territory to Hokkaido, Japan. *Virus Genes* **37,** 144–152 (2008).
35. Kim, H.-R. *et al.* Characterization of H10 subtype avian influenza viruses isolated

from wild birds in South Korea. *Vet. Microbiol.* **161,** 222–228 (2012).
36. De Marco, M. A. *et al.* Influenza surveillance in birds in Italian wetlands (1992-1998): is there a host restricted circulation of influenza viruses in sympatric ducks and coots? *Vet. Microbiol.* **98,** 197–208 (2004).
37. Pasick, J.*et al*. Avian influenza in North America, 2009-2011. *Avian Dis.* **56,** 845–848 (2012).
38. Senne, D. A. Avian influenza in the Western Hemisphere including the Pacific Islands and Australia. *Avian Dis.* **47,** 798–805 (2003).
39. Schlingemann, J. *et al.* Novel means of viral antigen identification: Improved detection of avian influenza viruses by proximity ligation. *J. Virol. Methods* **163,** 116–122 (2010).
40. Pepin, K. M. *et al.* Multiannual patterns of influenza A transmission in Chinese live bird market systems. *Influenza Other Respir. Viruses* **7,** 97–107 (2013).
41. Arzey, G. G. *et al.* Influenza virus A (H10N7) in chickens and poultry abattoir workers, Australia. *Emerg. Infect. Dis.* **18,** 814–816 (2012).
42. Vijaykrishna, D. *et al.* The recent establishment of North American H10 lineage influenza viruses in Australian wild waterfowl and the evolution of Australian avian influenza viruses. *J. Virol.* **87,** 10182–10189 (2013).
43. Deng, G. *et al.* Complex Reassortment of Multiple Subtypes of Avian Influenza Viruses in Domestic Ducks at the Dongting Lake Region of China. *J. Virol.* **87,** 9452–9462 (2013).
44. Pan American Health Organization. Avian influenza virus A (H10N7) circulating among humans in Egypt. 2004. at <http://new.paho.org/hq/dmdocuments/2010/Avian_Influenza_Egypt_070503.pdf>
45. Yu, H. *et al.* Effect of closure of live poultry markets on poultry-to-person transmission of avian influenza A H7N9 virus: an ecological study. *The Lancet* (2013). doi:10.1016/S0140-6736(13)61904-2
46. WHO | Monthly Risk Assessment Summary. *WHO* at <http://www.who.int/influenza/human_animal_interface/HAI_Risk_Assessment/en/index.html>
47. WPRO | Avian influenza A (H10N8). *WPRO* at <http://www.wpro.who.int/china/mediacentre/factsheets/h10n8/en/>
48. Bai, T., *et al.* Serologic study for influenza A (H7N9) among high-risk groups in China. *N. Engl. J. Med.* **368,** 2339–2340 (2013).
49. Yang, S. *et al.* Avian-Origin Influenza A(H7N9) Infection in Influenza A(H7N9)-Affected Areas of China: A Serological Study. *J. Infect. Dis.* **209,** 265–269 (2014).
50. Olson, S. *et al.* Historical Prevalence and Distribution of Avian Influenza Virus

A(H7N9) among Wild Birds. *Emerg. Infect. Dis.* **19,** 2031–2033 (2013).
51. Liu, D. *et al.* Origin and diversity of novel avian influenza A H7N9 viruses causing human infection: phylogenetic, structural, and coalescent analyses. *The Lancet* **381,** 1926–1932 (2013).
52. Dortmans, J. C. F. M. *et al.* Adaptation of novel H7N9 influenza A virus to human receptors. *Sci. Rep.* **3,** (2013).
53. Zhang, Q. *et al.* H7N9 influenza viruses are transmissible in ferrets by respiratory droplet. *Science* **341,** 410–414 (2013).
54. Mok, C. K. P. *et al.* Amino-acid substitutions in polymerase basic protein 2 gene contributes to the pathogenicity of the novel A/H7N9 influenza virus in mammalian hosts. *J. Virol.* (2014). doi:10.1128/JVI.02740-13
55. Wu, Y. *et al.* Characterization of two distinct neuraminidases from avian-origin human-infecting H7N9 influenza viruses. *Cell Res.* **23,** 1347–1355 (2013).
56. Xu, C. *et al.* Monitoring Avian Influenza A(H7N9) Virus through National Influenza-like Illness Surveillance, China. *Emerg. Infect. Dis.* **19,** (2013).
57. Hai, R. *et al.* Influenza A(H7N9) virus gains neuraminidase inhibitor resistance without loss of in vivo virulence or transmissibility. *Nat. Commun.* **4,** (2013).
58. Buchholz, U. *et al.* German Outbreak of *Escherichia coli* O104:H4 Associated with Sprouts. *N. Engl. J. Med.* **365,** 1763–1770 (2011).
59. Beutin, L. & Martin, A. Outbreak of Shiga toxin-producing Escherichia coli (STEC) O104:H4 infection in Germany causes a paradigm shift with regard to human pathogenicity of STEC strains. *J. Food Prot.* **75,** 408–418 (2012).
60. Bielaszewska, M. *et al.* Characterisation of the Escherichia coli strain associated with an outbreak of haemolytic uraemic syndrome in Germany, 2011: a microbiological study. *Lancet Infect. Dis.* **11,** 671–676 (2011).
61. Frank, C., *et al.* Results of surveillance for infections with Shiga toxin-producing Escherichia coli (STEC) of serotype O104:H4 after the large outbreak in Germany, July to December 2011. *Euro Surveill. Bull. Eur. Sur Mal. Transm. Eur. Commun. Dis. Bull.* **19,** (2014).
62. Werber, D. *et al.* Outbreaks of virulent diarrheagenic Escherichia coli--are we in control? *BMC Med.* **10,** 11 (2012).
63. Devaux, I. *et al.* Challenges and Opportunities in Routine Time Series Analysis of Surveillance Data. *Online J. Public Health Inform.* **5,** (2013).

# 圖表區

表一、奧地利諾羅病毒疫情事件單日侵襲率

| Days of exposure | Day-specific exposed participant[1] ($N_{exp}$) | Day-specific case[2] n | AR (%) $n/N_{(exp)}$ |
|---|---|---|---|
| Nov 21 | 245 | 1 | 0.4 |
| Nov 22 | 240 | 24 | 10.0 |
| Nov 23 | 242 | 30 | 12.4 |
| Nov 24 | 215 | 10 | 4.7 |
| Nov 25 | 60 | 1 | 1.7 |

[1]Day-specific exposed participants defined as participants with food exposure on that day; changing numbers of the participants due to exclusion of participants fallen sick before or on the day under study; [2]Day-specific case defined as a case, who fell sick within the 2 days following the day of food exposure

表二、個案所暴露食物之侵襲率及風險比

| Food items | Exposed | | | Unexposed | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Total | Cases | AR% | Total | Cases | AR% | RR | 95%CI | P |
| 22 November; N=344 | | | | | | | | | |
| Sour cream sauce | 143 | 23 | 16.1 | 201 | 2 | 1.0 | 16.2 | 3.9-67.5 | <0.01 |
| Baked potato | 161 | 23 | 14.3 | 183 | 2 | 1.1 | 13.1 | 3.1-54.6 | <0.01 |
| Ragout of venison | 199 | 22 | 11.1 | 145 | 3 | 2.1 | 5.3 | 1.6-17.5 | <0.01 |
| Red cabbage/ dumpling | 184 | 19 | 10.3 | 160 | 6 | 3.8 | 2.8 | 1.1-6.7 | 0.02 |
| Cranberry | 137 | 15 | 11.0 | 207 | 10 | 4.8 | 2.3 | 1.1-4.9 | 0.03 |
| 23 November; N=343 | | | | | | | | | |
| Wiener Schnitzel | 230 | 30 | 13.0 | 113 | 2 | 1.8 | 7.37 | 1.8-30.3 | <0.01 |
| Turkey strip-salad | 139 | 25 | 18.0 | 204 | 7 | 3.4 | 5.24 | 2.3-11.8 | <0.01 |
| Potatoes | 220 | 27 | 12.3 | 123 | 5 | 4.1 | 3.02 | 1.2-7.6 | 0.01 |

表三、高風險日暴露食物之分層分析風險比

| **Exposures** | **Crude analyses** | **Stratified analyses** | |
|---|---|---|---|
| | **RR (95% CI)** | **RR (95% CI)** | **RR (95% CI)** |
| **22 November** | | sour cream sauce exposed | sour cream sauce unexposed |
| **Baked potato** | 13.1 (3.1-54.6) | ∞ | 0.0 |
| **Ragout of venison** | 5.3 (1.6-17.5) | 1.9 (0.5-7.6) | 1.6 (0.1-24.9) |
| **Red cabbage/ dumpling** | 2.8 (1.1-6.7) | 1.0 (0.4-2.4) | 1.8 (0.1-28.8) |
| **Cranberry** | 2.3 (1.1-4.9) | 1.2 (0.5-2.6) | 0.0 |
| **23 November** | | Turkey strip-salad exposed | Turkey strip-salad unexposed |
| **Wiener Schnitzel** | 7.4 (1.8-30.3) | ∞ | 2.8 (0.6-13.9) |
| **Potatoes** | 3.0 (1.2-7.6) | 0.9 (0.3-2.6) | 2.8 (0.6-14.2) |

表四、奧地利李斯特菌症通報定義

| **Case Definition** | | |
|---|---|---|
| **Clinical Criteria** | Stillbirth | |
| | the first month of life:<br>at least 1 of the 5 following symptoms | • Granulomatosis infantiseptica<br>• Meningitis or meningoencephalitis<br>• Septicaemia<br>• Dyspnoea<br>• Lesions on skin, mucosal membranes or conjunctivae |
| | Pregnancy:<br>at least 1 of the 3 following symptoms | • Abortion, miscarriage, stillbirth or premature birth<br>• Fever<br>• Influenza-like symptoms |
| | Other:<br>at least 1 of the 4 following symptoms | • Fever<br>• Meningitis or meningoencephalitis<br>• Septicaemia<br>• Localised infections such as arthritis, endocarditis, and abscesses |
| **Laboratory Criteria**<br>At least 1 of the following 2 | • Isolation of Listeria monocytogenes from a normally sterile site<br>• Isolation of Listeria monocytogenes from a normally non-sterile site in a foetus, stillborn, newborn or the mother at or within 24 hours of birth | |
| **Epidemiological Criteria**<br>At least 1 of the following 3 epidemiological links | • Exposure to a common source<br>• Human to human transmission (vertical transmission)<br>• Exposure to contaminated food/drinking water | |
| **Additional information** | • Incubation period 3-70 days, most often 21 days | |
| **Case Classification** | Possible case | Not applicable |
| | Probable case | Any person meeting the clinical criteria and with an epidemiological link |
| | Confirmed case | Any person meeting the laboratory criteria<br>OR<br>Any mother with a laboratory confirmed listeriosis infection in her foetus, stillborn or newborn |

表五、奧地利各省市一般科醫師、兒科醫師及肺專科醫師分布

| **Source population** | **Province*** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Occupation | **B** | **CA** | **LA** | **UA** | **Sa** | **St** | **T** | **V** | **Vie** | **Total** |
| General practitioners (10,000 pop.) | 145 (50.5) | 230 (41.3) | 741 (45.6) | **718 (50.5)** | **231 (43.0)** | **576 (47.4)** | **309 (43.0)** | 150 (40.0) | 772 (44.1) | 3872 (45.6) |
| Paediatricians | 22 (7.7) | 44 (7.9) | 153 (9.4) | **150 (10.5)** | **65 (12.1)** | **132 (10.9)** | **100 (13.9)** | 42 (11.2) | 361 (20.6) | 1069 (12.6) |
| Pulmonologists | 5 (1.7) | 18 (3.2) | 45 (2.8) | **58 (4.1)** | **16 (3.0)** | **61 (5.0)** | **23 (3.2)** | 9 (2.4) | 122 (7.0) | 357 (4.2) |
| **Total(%)** | **172 (3)** | **292 (6)** | **939 (18)** | **926 (17)** | **312 (6)** | **769 (15)** | **432 (8)** | **201 (4)** | **1255 (24)** | **5298** |
| **Percentage of population** | **3%** | **7%** | **19%** | **17%** | **6%** | **14%** | **8%** | **4%** | **21%** | **-** |

*B: Burgenland, CA: Carinthia, LA: Lower Austria, UA: Upper Austria, Sa: Salzburg, St: Styria, T: Tyrol, V: Vorarlberg, Vie: Vienna

表六、奧地利各省市專業醫師預期樣本數

| | **Province n/N(%)** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **Occupation** | **Total** | **B** | **CA** | **LA** | **UA** | **Sa** | **St** | **T** | **V** | **Vie** |
| **General practitioners** | 350 | 13 | 21 | 67 | 65 | 21 | 52 | 28 | 14 | 69 |
| **Paediatricians** | 283 | 6 | 12 | 41 | 40 | 17 | 35 | 26 | 11 | 95 |
| **Pulmonologists** | 276 | 4 | 14 | 35 | 45 | 12 | 47 | 18 | 7 | 94 |

表七、百日咳問卷調查結果加權百分比分布

| Question no. and contents | n/N ( weighted %) | | |
|---|---|---|---|
| | GPs ($N_{total}$= 78 ) | Pediatricians ($N_{total}$= 150) | Pulmonologists ($N_{total}$= 42) |
| **Question** **Notification practice (8 required questions)** | | | |
| 1. Awareness of pertussis as a notifiable disease | 69/77 (90) | 142/147 (96) | 40/42 (93) |
| 2. Awareness of notifying a pertussis case to PH authorities. | 72/72 (100) | 138/138(100) | 39/39 (100) |
| 2a. Awareness of notifying a pertussis case to district PH authorities | 57/72 (74) | 86/138 (63) | 19/39 (49) |
| 3. Use the standardized notification form provided by MoH | 49/76 (68) | 110/142 (77) | 30/40 (78) |
| 8. Use an official case definition | 22/73 (30) | 39/144 (28) | 13/40 (34) |
| 9. Awareness of the ECDC case definition of pertussis | 3/73 (4) | 5/125 (4) | 0/34 (0) |
| 10. Notify a pertussis case based on the ECDC case definition | 2/36 (5) | 5/70 (8) | 0/17 (0) |
| 11. Notify a clinically suspected case | 10/73 (16) | 13/140 (8) | 2/37 (5) |
| 31. Notify a clinical suspected case again after having received a laboratory confirmation (report a lab. confirmed case) | 41/64 (65) | 100/135 (74) | 20/32 (63) |
| **Level of knowledge on clinical manifestation of pertussis (2 required questions )** | | | |
| 4. High level of knowledge on clinical signs and symptoms of pertussis infection ( gained 7-9 points from total 9 points) | 26/77 (34) | 102/149 (67) | 18/41 (40) |
| 5. Differentiate the clinical signs and symptoms by age (1 point) | 46/77 (59) | 137/149 (91) | 27/39 (69) |
| 6.1. Duration of cough in children aged ≤ 3 months | 51/73 (73) | 129/142 (91) | 23/30 (74) |
| 6.2. Cough-related symptoms of pertussis in children between 4 months - 9 years | 53/72 (74) | 99/137 (72) | 19/31 (69) |
| 6.3. Duration of cough in children aged ≥ 10 years | 64/73 (90) | 125/142 (87) | 26/34 (83) |
| 7.1. High level of knowledge on the clinical case definition in young children ≤ 3 months (gained 7-10 points from total 10 points) | 34/72 (44) | 58/135 (41) | 5/30 (12) |
| 7.2. High level of knowledge on the clinical case definition in children between 4 months - 9 years (gained 7-10 points | 15/70 (20) | 40/131 (32) | 9/30 (31) |

| | | | |
|---|---|---|---|
| from total 10 points) | | | |
| 7.3. High level of knowledge on the clinical case definition in children aged ≥ 10 years and adults (gained 7-10 points from total 10 points) | 31/71 (42) | 64/130 (49) | 17/34 (44) |
| 14. Three weeks threshold between early stage and late stage of pertussis infection | 41/73 (57) | 60/127 (46) | 17/31 (59) |
| **Level of knowledge on laboratory diagnosis (8 required questions )** | | | |
| 15. Chose correct tests for laboratory confirmation in the aged ≤ 3 months with clinically suspected B. pertussis infection (three points) | 15/67 (20) | 36/139 (25) | 11/34 (27) |
| 16. Chose correct diagnostic tests to confirm a clinical cases in children aged > 3 months, adolescents and adults (three points) | 10/68 (14) | 35/143 (26) | 7/36 (25) |
| 17. Chose correct diagnostic tests to confirm a clinical case in a cough duration of ≥ 3 weeks (three points) | 21/68 (29) | 26/140 (17) | 6/37 (20) |
| 19. Chose correct immunoglobulin(s) for serological testing (IgM alone is an incorrect answer) (three points) | 47/67 (67) | 104/135 (78) | 23/34 (61) |
| 23. Chose correct answer on the duration of not using IgG for diagnosis of pertussis in patients following pertussis vaccination (one point) | 43/60 (76) | 70/117 (59) | 18/30 (63) |
| 24. Chose we cannot use IgG-titer to discriminate recent vaccination and current infection (one point) | 41/65 (63) | 120/134 (90) | 27/33 (80) |
| 28. Chose correct types of specimens obtained for PCR or culture (gained 2.4-3 points from total 3 points) | 14/66 (20) | 36/139 (26) | 2/36 (5) |
| 21. Ask vaccination history from patients | 69/70 (99) | 131/132 (99) | 28/32 (87) |
| 22. Inform the information of vaccine history to the laboratory | 54/68 (81) | 96/128 (74) | 17/31 (56) |
| **Laboratory confirmation seeking behavior** | | | |
| 12. High frequency of seeking laboratory diagnostics (Frequency ≥75%) | 44/73 (60) | 122/142 (86) | 25/39 (63) |
| 13. The reasons for NOT seeking laboratory diagnostics | | | |

| | | | |
|---|---|---|---|
| a. The treatment started immediately as a case of pertussis is clinically suspected; there is no added value for awaiting the laboratory results, which will be too late. | 36/78 (46) | 47/150 (31) | 11/42 (26) |
| b. The sensitivity and specificity of the laboratory diagnostic tests for pertussis are poor | 6/78 (8) | 18/150 (12) | 8/42 (19) |
| c. Laboratory diagnostic test for pertussis is too expensive and funding is not covered by the social insurance companies | 9/78 (12) | 7/150 (5) | 6/42 (14) |
| **Place of practice** | | | |
| a. General Practice ("Ordination") | 73/77 (95) | 66/150 (42) | 19/42 (41) |
| b. General Hospital | 3/77 (4) | 65/150 (45) | 22/42 (57) |
| c. University Hospital | 1/77 (1) | 19/150 (13) | 1/42 (2) |

表八、小兒科及肺專科醫師屬性題目得分百分比

| Attributes | High-rate provinces (N=92) | | Stable-rate provinces (N=100) | | |
|---|---|---|---|---|---|
| | n/N (column%*) | 95%CI | n/N (column%*) | 95%CI | P value |
| **Satisfactory notification practice** | | | | | |
| 1. Aware pertussis is a notifiable disease | 86/89 (96.0) | 88.3-98.8 | 96/100 (95.7) | 89.0-98.4 | 0.82 |
| 2. Aware report to district PH authority | 53/92 (56.6) | 46.0-66.6 | 52/85 (62.1) | 51.1-71.9 | 0.79 |
| 3. Use MoH notification form | 66/87 (76.2) | 65.9-84.1 | 74/95 (76.9) | 67.0-84.5 | 0.75 |
| 4. Use official case definition | 23/88 (26.9) | 18.3-37.6 | 29/96 (29.7) | 21.2-39.8 | 0.54 |
| 5. Notify a clinical suspected case | 7/84 (7.6) | 3.6-15.3 | 8/93 (7.8) | 3.8-15.3 | 0.95 |
| 6. Notify again after receive a lab. confirmation report | 25/91 (27.7) | 19.3-38.1 | 22/76 (29.4) | 19.9-41.1 | 0.75 |
| **Level of knowledge on clinical manifestations** | | | | | |
| 1. High level of knowledge on clinical manifestation | 32/92 (34.0) | 24.8-44.5 | 40/100 (42.4) | 32.8-52.6 | 0.46 |
| (high: 7-9 point, total: 9 points) | | | | | |
| 2. Differentiate clinical manifestation by age | 15/89 (17.5) | 10.6-27.4 | 9/99 (9.4) | 4.9-17.3 | 0.11 |
| (Yes/No) | | | | | |
| **High level of knowledge on laboratory diagnostic procedures** | 47/92 (50.3) | 39.9-60.7 | 51/100 (51.5) | 41.5-61.4 | 0.99 |
| (high ≥11.8 point, total: 17 points) | | | | | |
| **Satisfactory laboratory confirmation seeking behaviour** (seek lab confirmation in ≥75% of all patients) | 70/86 (83.3) | 74.2-89.6 | 77/95 (80.1) | 70.4-87.1 | 1.00 |

表九、多變量分析達統計顯著性之屬性題目

| Variable | High-rate provinces<br>Adjusted PR (95%CI) for confirmed case reporter | Stable-rate provinces<br>Adjusted PR (95%CI) for confirmed case reporter |
|---|---|---|
| **Place of practice** | | |
| General Practice | Ref. | Ref. |
| General Hospital | 1.32 (0.94-1.87) | 1.18 (0.88-1.57) |
| University Hospital | **1.55 (1.12-2.17)*** | 1.16 (0.63-2.13) |
| **Level of knowledge on laboratory diagnostics** | | |
| Median or low level of knowledge (0 - <11.8 point) | Ref. | Ref. |
| High level of knowledge ( 11.8 -17 points) | **1.35 (1.02-1.80)*** | 0.90 (0.67-1.19) |

表十、全球 H10N8 禽流感病毒分離紀錄

| 國家/地區 | 分離時間 (西元年) | 檢體來源 |
|---|---|---|
| **義大利** | 1965、1992-1998 | 鵪鶉，白冠雞 |
| **美國** | 1979、2004-2006、2008 | 野生水鳥 |
| **加拿大** | 1998 | 綠頭鴨 |
| **瑞典** | 2003 | 綠頭鴨 |
| **台灣** | 2005 | 鴨 |
| **日本北海道** | 2006 | 野生水鳥 |
| **中國大陸湖南省洞庭湖區** | 2007 | 環境及水 |
| **中國大陸廣東省** | 2012 | 鴨 |
| **南韓** | 2012 | 綠頭鴨 |

表十一、我國 2011-2014 年禽流感病毒候鳥帶毒監測結果

| 年份 | 檢測件數 | 陽性件數 | 陽性率 | 檢出亞型（件數） |
|---|---|---|---|---|
| **2011** | 3935 | 27 | 0.7% | H3N6(3)、H3N8(1)、H4N6(7)、H5N2(4)、H7N3(1)、H7N6(2)、H7N9(6)、H10N7(3) |
| **2012** | 4428 | 18 | 0.4% | H1N1(1)、H1N3(1)、H4N6(1)、H7N1(13)、H10N7(2) |
| **2013** | 7858 | 21 | 0.3% | H5N3(4)、H6N1(2)、H7N3(1)、H7N7(2)、H10N7(10)、H12N5(2) |
| **2014~** | 1183 | 3 | 0.3% | H1N3(1)、H4N6(2) |

表十二、H10N8 流感疫情國內風險評估

| 感染機率<br>評估項目 | 證據 | 結果 | 風險等級 |
|---|---|---|---|
| **境外移入的可能性** | -中國大陸至今公布 3 例散發個案<br>-個案感染為 2013 年新病毒株，與先前大陸檢出 H10N8 禽類禽流感，屬不同病毒株<br>-近期未有 H10N8 禽類禽流感相關監測資料 | -個案數少，且未人傳人，境外移入風險極低<br>-H10N8 禽類禽流感經由大陸貿易及走私禽鳥頻繁下仍具境外移入風險 | 低 |
| **國內流行的可能性** | | | 低 |
| **1.由動物傳人感染機率** | - H10N8 禽類禽流感屬低病原性禽流感病毒<br>-2005 年台北 5 件鴨科排遺檢體檢出 H10N8 禽類禽流感病毒，2011-2014 年候鳥監測未發現相關病毒 | -國內雖曾檢出 H10N8 禽類禽流感病毒但與新型 H10N8 禽流感病毒不同，保毒動物、動物傳播及人類感染途徑目前皆不明 | |
| **2.易感族群與群體免疫力** | -公布個案數少，中國大陸境內是否有輕症或無症狀感染情形不明<br>-國內法傳、類流感及住院不明原因肺炎監測未曾檢出 H10N8 流感 | -推測國人無群體免疫力 | |
| **3.疾病傳播力** | -家人及密切接觸者均未出現症狀<br>- 新 H10N8 禽流感病毒株與哺乳動物細胞受體結合力差，惟具哺乳動物細胞適應性 | -病毒於人體細胞結合力差，推斷人傳人之風險低於 H7N9 禽流感病毒 | |

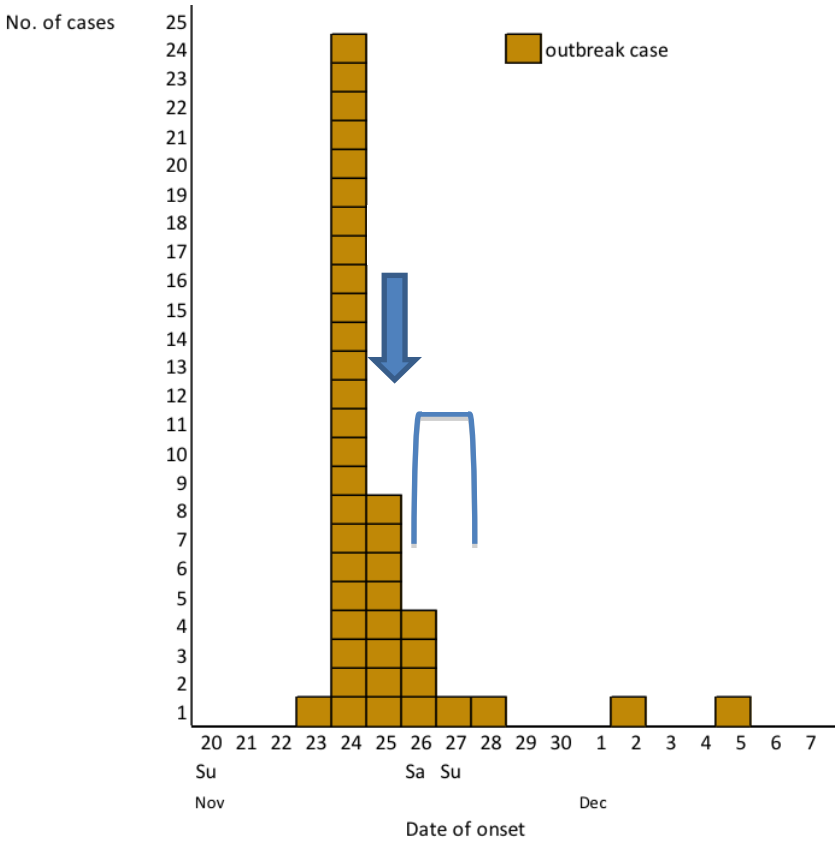
| 衝擊<br>評估項目 | 證據 | 結果 | 風險等級 |
|---|---|---|---|
| **疾病嚴重性** | -目前兩例個案症狀皆為重症，對小鼠毒性強<br>-是否有輕症或無症狀感染情形不明 | -病毒毒性及疾病嚴重性仍待觀察 | 不明 |
| **治療與控制** | | | 低 |
| **1.疫苗使用** | 無 | | |
| **2.抗病毒藥劑** | -神經胺酸酶胺基酸位點未突變<br>-M2 蛋白胺基酸位點已突變 (Ser31Asn) | -對國內儲備之神經胺酸酶抑制劑無抗藥性。<br>-對 Adamantanes 具抗藥性 | |
| **3.防治政策** | 加強監測、禁止陳列、展示及販售活禽政策及抗病毒藥劑整備等防治作為 | 執行國內各項整備應變政策將可降低國內衝擊 | |

表十三、H7N9 流感疫情國內發生可能性之風險評估

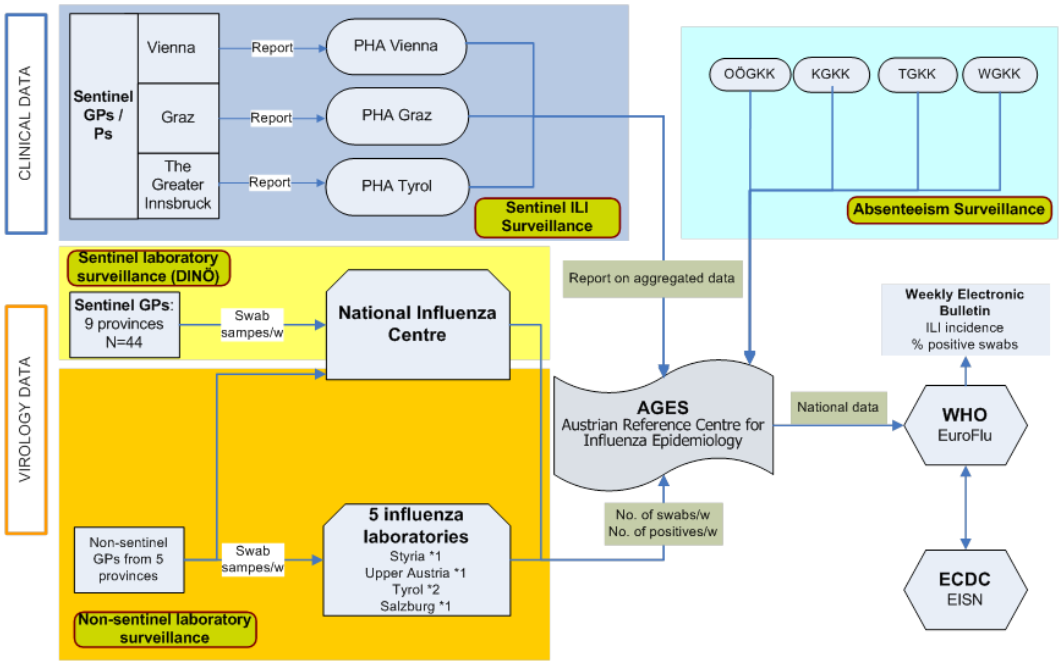
| 評定標準<br>（依重要性排序） | 風險等級<br>（低/中/高） | 證據 | 證據來源及品質 |
|---|---|---|---|
| **人類感染情形** | 中 | 禽傳人，人傳人證據不足 | 國際疫情報導等相關文獻。高 |
| **實驗動物傳染力** | 中 | H7N9 流感病毒可在多種哺乳動物宿主複製， 安徽株在雪貂可經呼吸道飛沫傳播 | 相關研究論文。高 |
| **病毒與宿主受體的結合度** | 中 | H7N9 病毒上海株可同時辨認禽類及哺乳類宿主細胞表面唾液酸接受體(α-2,3 and α-2,6 linked sialic acid) | 相關研究論文。高 |
| **民眾的抗體盛行率** | 高 | 無免疫力 | 疾管署發布資訊。高 |
| **動物的感染情形** | 低 | 我國野鳥曾檢出，家禽則未曾檢出 | 農委會發布資訊。高 |
| **病毒基因的變異性** | 高 | 多筆研究指出病毒具高突變率 | 相關研究論文。高 |
| **抗原與疫苗株的差異** | 中 | 疫苗仍於臨床試驗階段 | 相關研究論文及 WHO 報告。高。 |
| **感染動物全球分布** | 低 | 基因庫資料分析在野鳥之病毒盛行率極低[50]。家禽檢出僅限於中國大陸 | 病毒株分離分布資料及 WHO 報告。高 |
| **疾病嚴重度** | 高 | 疾病致死率為 30%，年齡分布主為青壯年及老人 | 國際疫情報導等相關文獻。高 |
| **抗病毒藥物的感受性** | 低 | 目前上海株對抗病毒藥劑，已產生部分抗藥性，但非主要流行株 | 國際疫情報導等相關文獻。高 |

圖一、2011 年奧地利薩爾斯堡職業學校諾羅病毒疫情趨勢

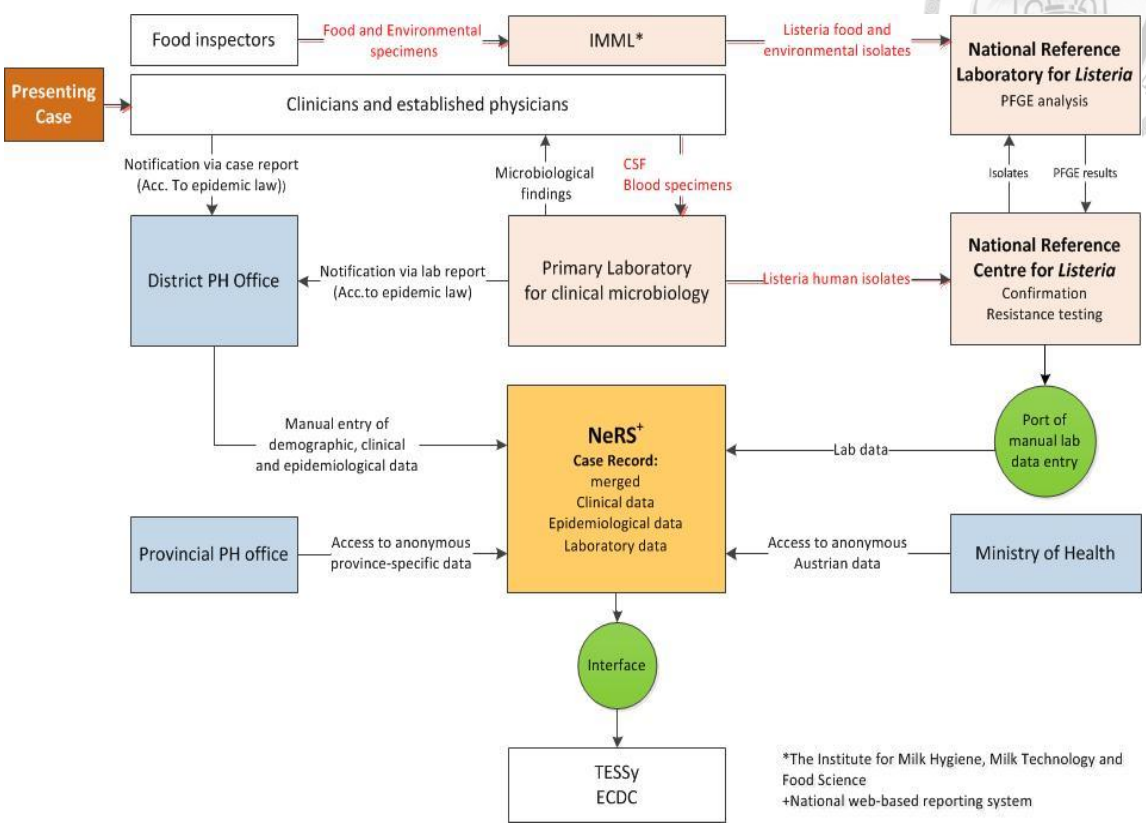
(n=41，7 名學生無症狀發生日資料) 1:學校環境清潔及提供手部消毒劑；2.學生餐廳及廚房關閉。



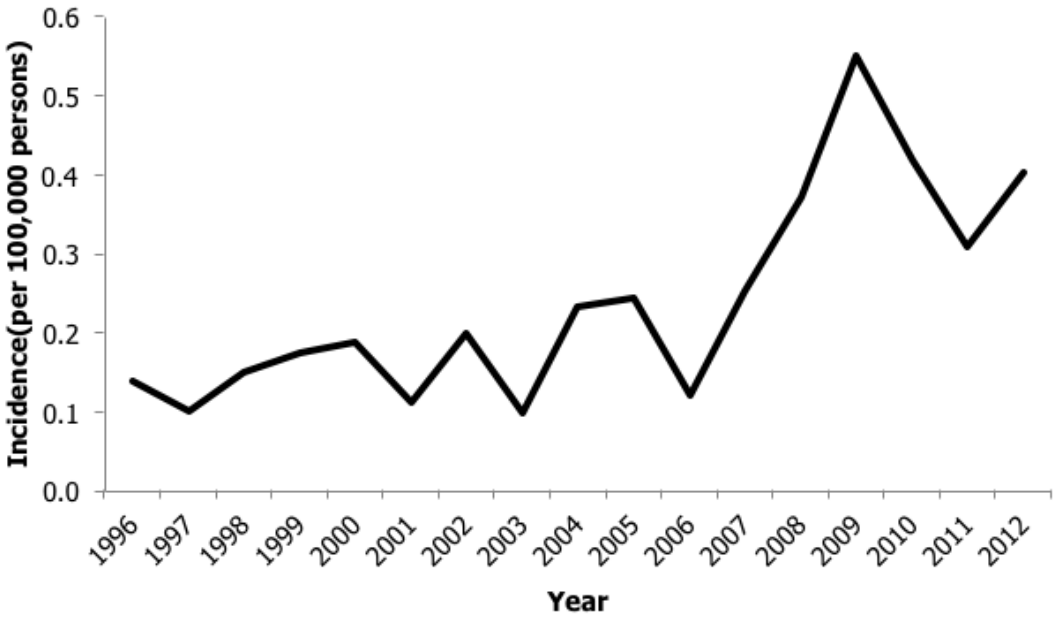

圖二、奧地利流行性感冒監測系統架構



圖三、奧地利李斯特菌監測系統架構

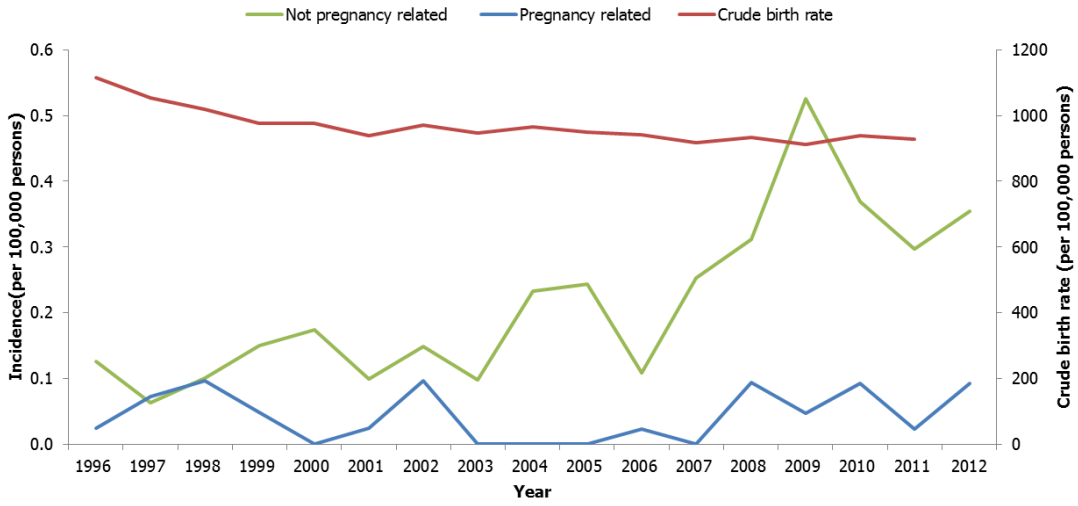



圖四、1996-2012 年奧地利李斯特菌症每十萬人口發生率

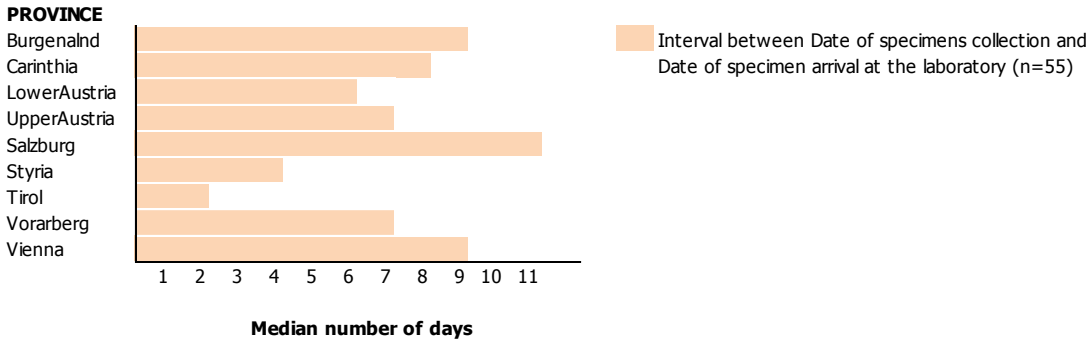


圖五、1996-2012 年奧地利李斯特菌症通報個案發生率

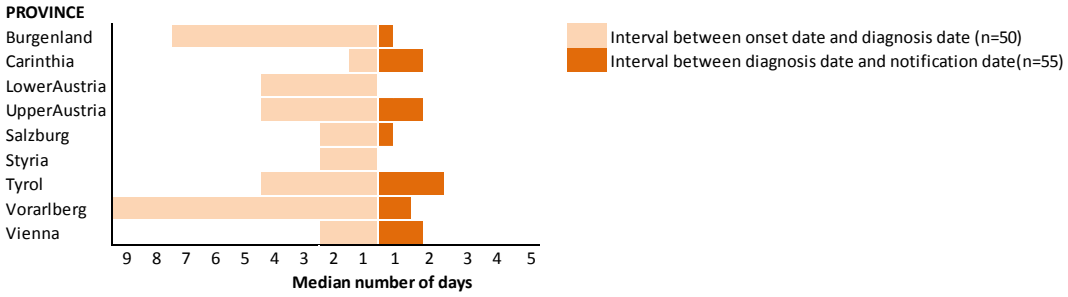
（綠：非懷孕病例、藍：懷孕病例、紅：粗出生率）



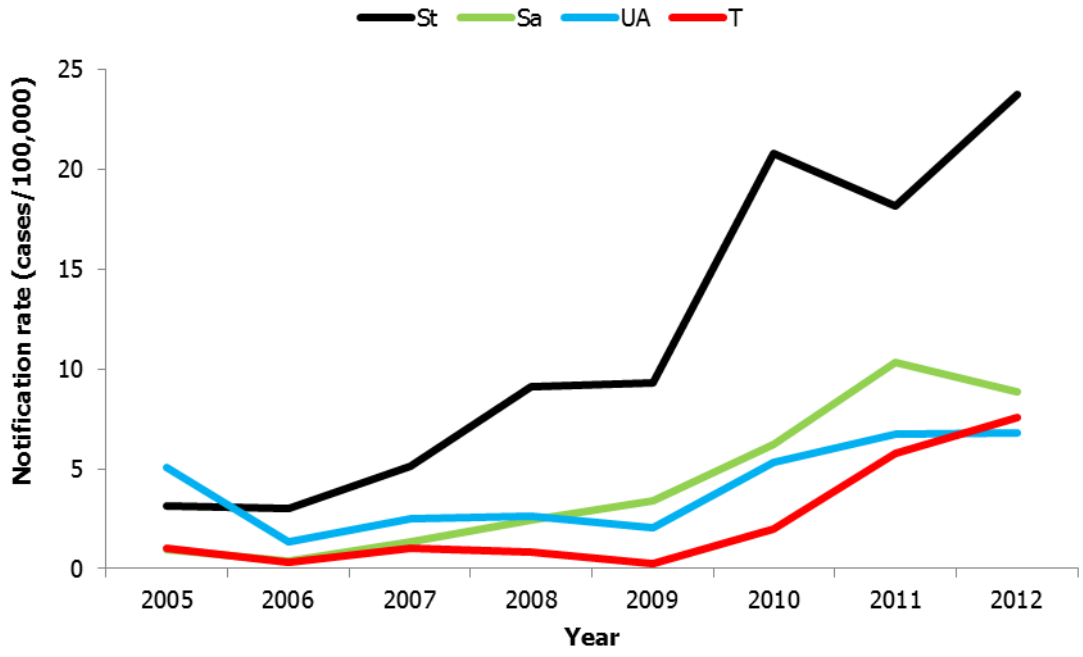

圖六、1996-2008 年奧地利各省市李斯特菌症個案採檢日至檢體收到日比較



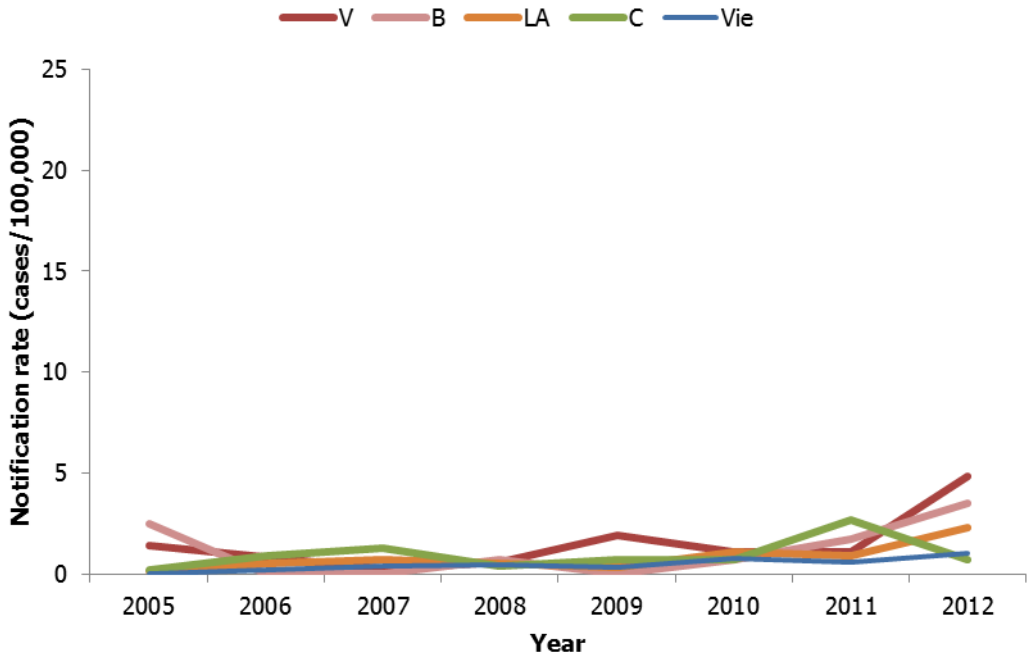

圖七、2009-2011 年奧地利各省市李斯特菌症個案發病日至診斷日及診斷日至通報日比較



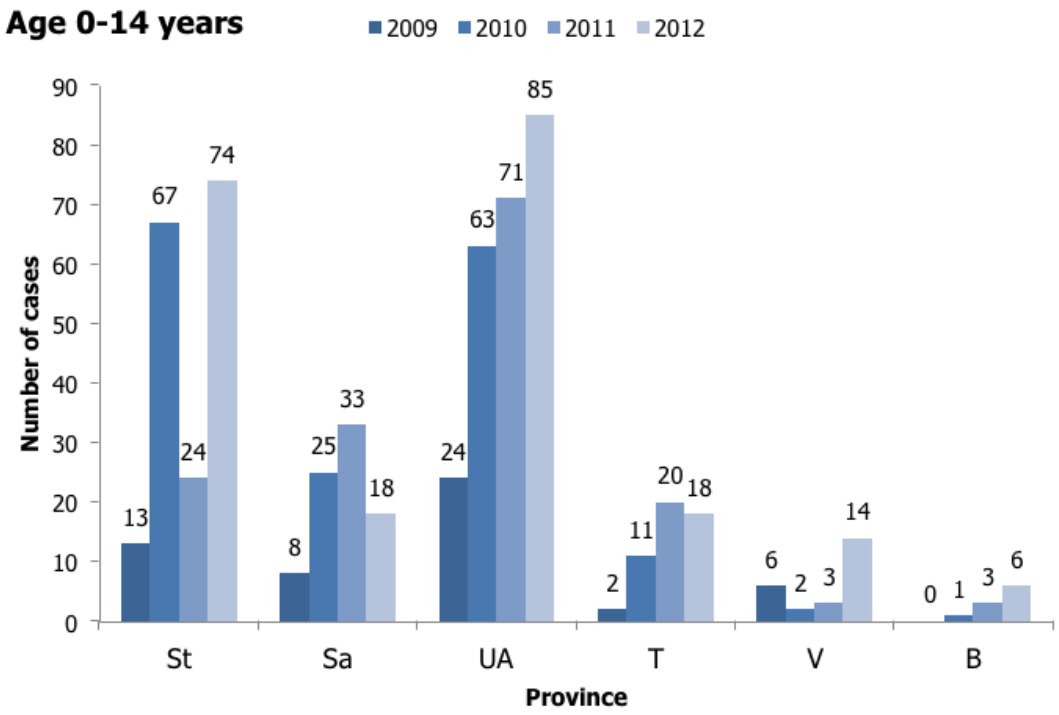
圖八-1、2005-2012 年奧地利 Styria、Salzburg、Upper Austria、及 Tyrol 省百日咳通報率趨勢




圖八-2、2005-2012 年奧地利 Vorarlberg、Burgenland、Lower Austria、Carinthia、Vienna 省百日咳通報率趨勢

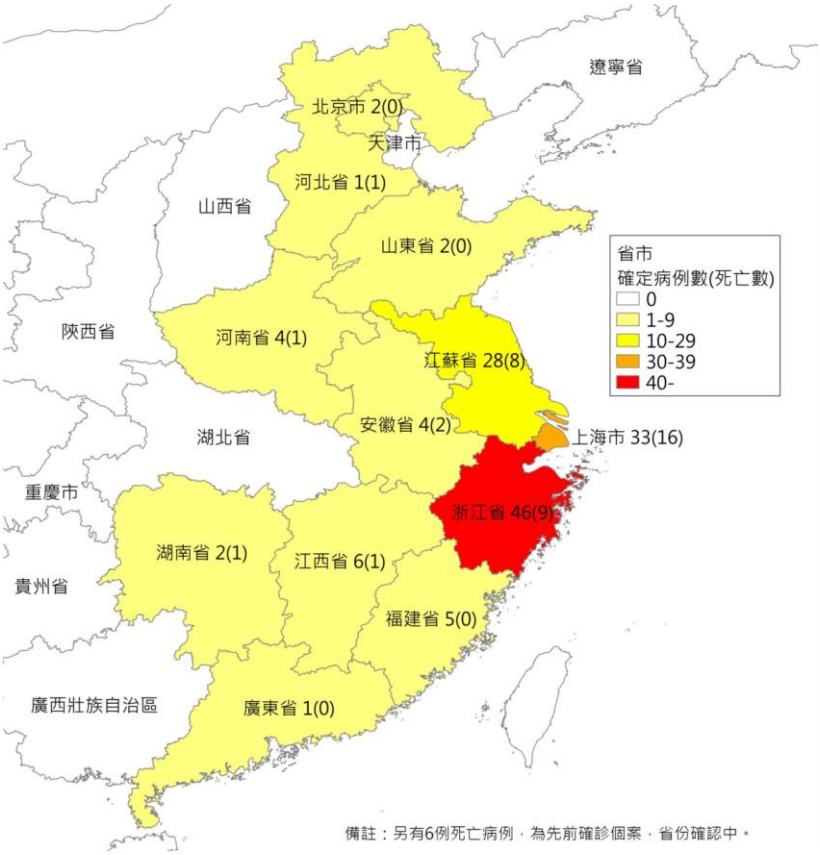


圖九、2009-2012 年奧地利各省市 0-14 歲孩童百日咳病例通報數比較

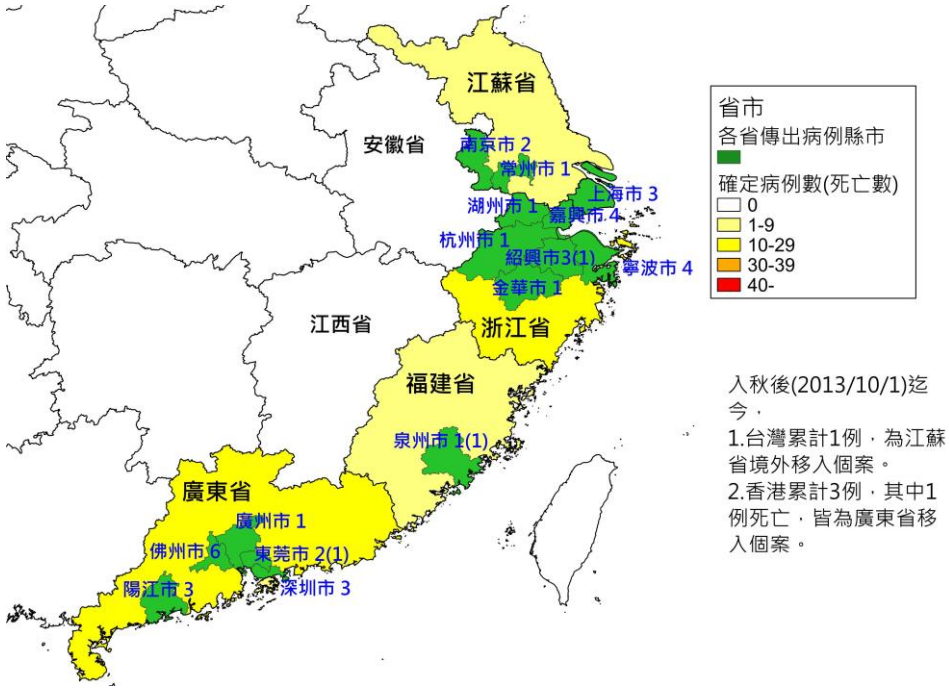



圖十、全球 H10N8 禽流感病毒檢出地理分布

圖十一、2013 年入秋前中國大陸各省市 H7N9 流感確定病例分布




圖十二、2013 年入秋後中國大陸各省市 H7N9 流感確定病例分布



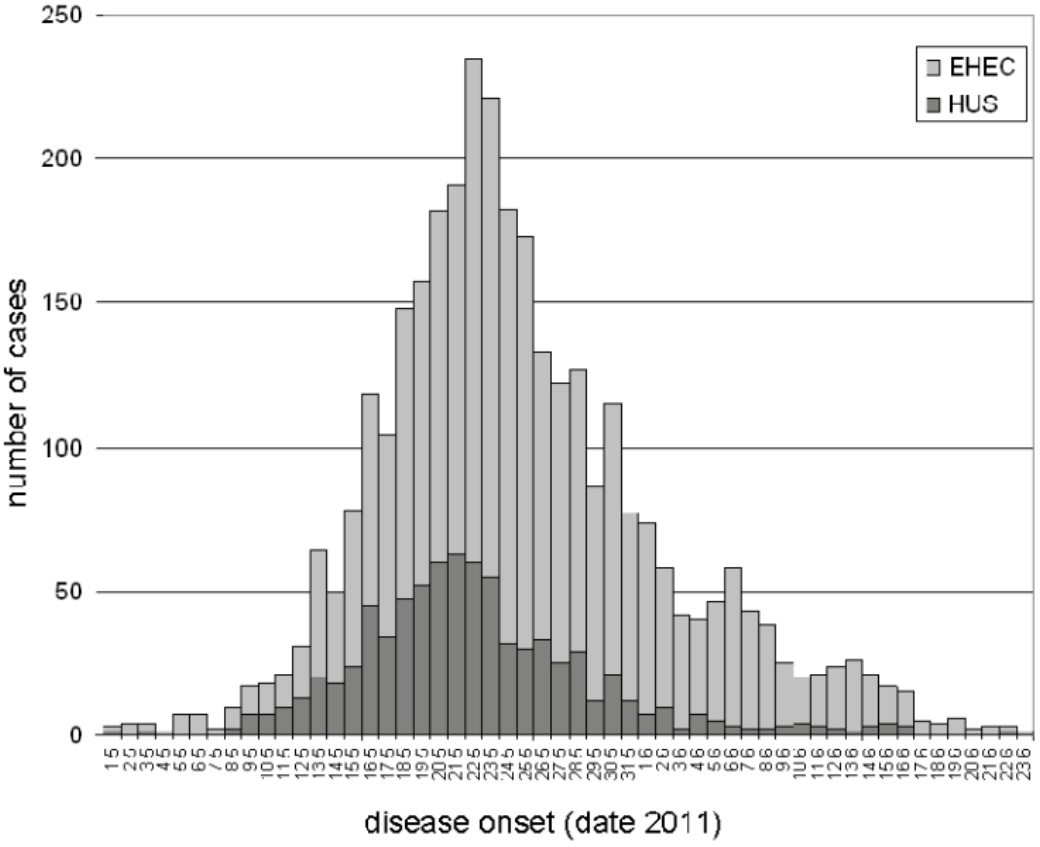
圖十三、WHO 公布 H7N9 流感病毒可用疫苗株

(2013 年 12 月 20 日公布)

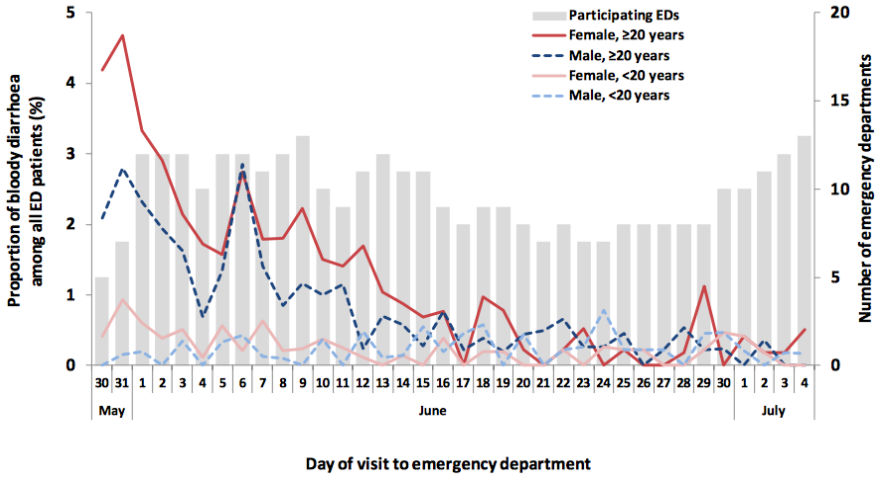
| Parent virus | Candidate vaccine virus | Type of virus or reassortant | Developing institute | Available from |
|---|---|---|---|---|
| A/Shanghai/2/2013 Synthetic HA&NA | IDCDC-RG32A* | Reverse genetics | CDC, USA | CDC, USA |
| | IDCDC-RG32A.3* | Reverse genetics | CDC, USA | CDC, USA |
| | NIBRG-267* | Reverse genetics | NIBSC, UK | NIBSC, UK |
| | CBER-RG4A* | Reverse genetics | CBER, USA | CBER, USA |
| A/Anhui/1/2013 | Wild type virus | | | WHO CCs |
| | NIBRG-268* | Reverse genetics | NIBSC, UK | NIBSC, UK |
| | NIIDRG-10.1* | Reverse genetics | NIID, Japan | NIID, Japan |
| | IDCDC-RG33A* | Reverse genetics | CDC, USA | CDC, USA |

圖十四、德國 2011 年 EHEC O104:H4 病例發病日之疫情趨勢

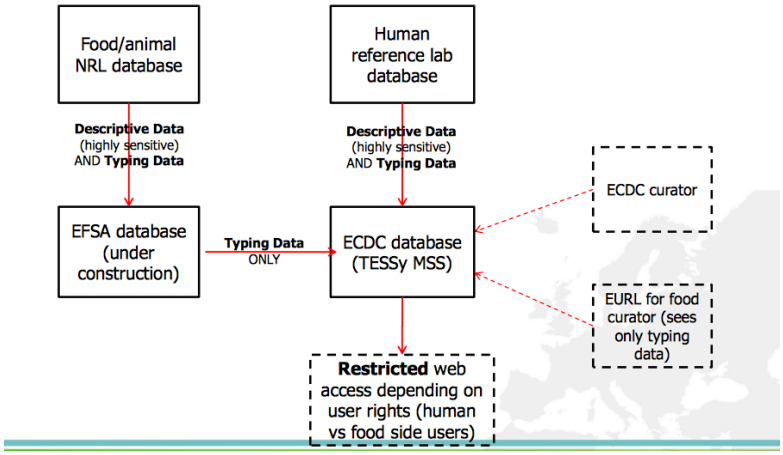
（$N_{HUS}$=773, $N_{EHEC}$＝2,507，截至 6 月 28 號）



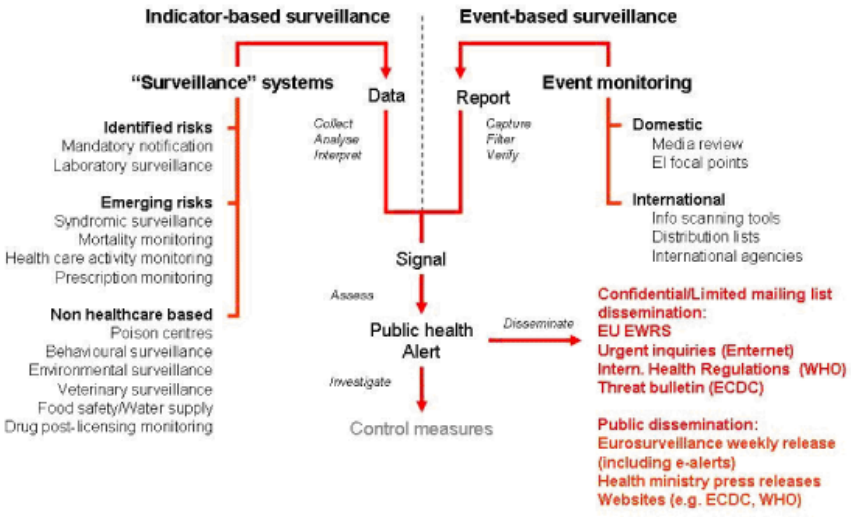
圖十五、2011 年 5-6 月德國醫院急診室血便症狀監測結果趨勢（n=1,021）




圖十六、ECDC 與 EFSA 病原體分子監測資料庫介接流程圖




圖十七、ECDC 傳染病疫情監測架構圖



圖十八、STATA 時間序列分析工具簡介圖

# A practical Stata tool for time series analysis

G Desve[2], E Kissling[2], I Devaux[1], F Hruba[1], F Luquero[2], C Quinten[1], J Gomes Dias[1], M Valenciano[2], B Ciancio[1]

1: European Centre for Disease Prevention and Control
2: EpiConcept, Paris, France

## Background

ECDC long term strategies for surveillance include analysis of trends of communicable disease of public health importance for EU and EEA Member States to guide public health action. The European Surveillance System (TESSy) holds data on 49 communicable diseases reported by 30 countries.

To simplify trend analysis using TESSy data, ECDC launched a **project to facilitate descriptive and routine time series analysis using a Stata TSA toolkit**.

## Methods

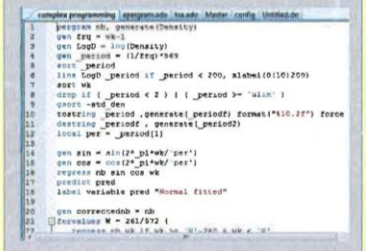
Protocols were developped for five diseases to specify
- hypotheses to be tested
- types and format of variables needed for TSA

A Stata dialogue box was designed with tabs corresponding to each step of the analysis plan. This allows users to carry out TSA from a comprehensive dialogue box without complex programming. In depth documentation forms part of the TSA toolkit and helps with its use and interpretation of outputs.
A TSA toolkit workshop was organised at ECDC and enabled feedback on the utility and user-friendliness of the tool.

## Results

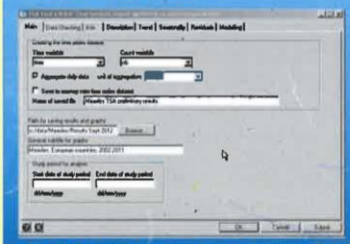
The Stata TSA toolkit enables data aggregation, data checking, data description, analysis of trends and seasonality, residual analysis, simple modelling and long-term forecasting. It incorporates generalised linear model regression, creates graphs and a log of the outputs. Feedback from the workshop showed the TSA toolkit enables a quick exploratory TSA even by non-Stata users who could focus on interpretation of results. However previous TSA knowledge is necessary to ensure appropriate analysis and meaningful interpretation of results.

**Before the TSA toolkit:**

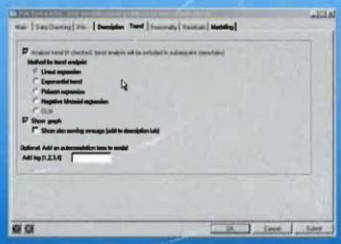


**Complex programming is needed in TSA**

**Now with the TSA tool:**

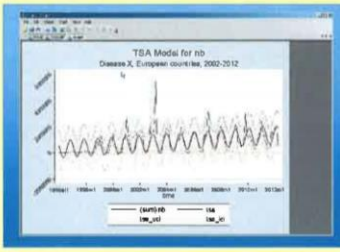


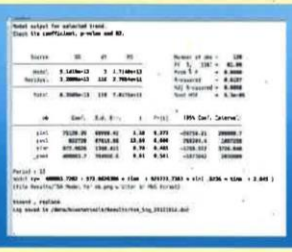
The TSA toolkit provides a dialogue box, where the complex programming is already done for you!



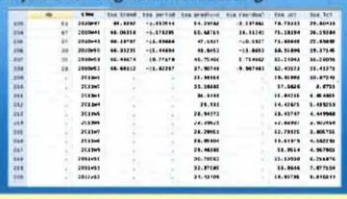
Each tab of the TSA toolkit takes you through a stepwise process for TSA

**TSA toolkit outputs are in graphs and onscreen:**



**The TSA toolkit provides datasets for further analysis and long-term forecasting:**



## Conclusions

Using the TSA toolkit
- Can save time and minimise programming errors
- Is supported by an in-depth documentation for TSA
- Avoids the need for complex programming
- Useful for rapid exploratory of epidemiological time series
- Useful during TSA teaching
- Sophisticated TSA still needs custom programming

## How to test the TSA tool

Further testing and training will be carried out before wide dissemination of the tool. But if you are interested in getting an installation package and full documentation please send a request to tsa@ecdc.europa.eu.

**Contact at ECDC**: firstname.lastname@ecdc.europa.eu Isabelle Devaux, Joana Gomes-Dias, Frantiska Hruba, Chantal Quinten
**Contact from EpiConcept**: tsa@epiconcept.fr Gilles Desvé, Esther Kissling

# 附錄

## 1. EPIET 訓練課程表

## European Programme for Intervention Epidemiology Training
## Course and module content

### EPIET/EUPHEM Introductory Course
### Mahon, Spain, 26 September – 14 October 2011

**Topics covered during the course (110 hours) included:**

- Methods of outbreak investigation
- Development and presentation of a study protocol
- Developing and evaluating surveillance systems and analysis of surveillance data
- Analytical epidemiological skills for data analysis
- Scientific communication
- Introduction to different pedagogical methods
- Introduction to public health microbiology

**Teaching methods included:**

- Lectures
- Group exercises and case studies based on real investigations
- Problem-based learning
- Pre-course study, and presentation by participant about a public health problem in own country
- Structured general and panel discussions

### Computer Tools for Outbreak Investigations Module
### Berlin, Germany, 05 - 09 December 2011

**Topics covered during the module (40 hours) included:**

- Creating a data entry file from a paper questionnaire
- Entering, validating and cleaning data, managing datasets
- Performing descriptive analysis
- Calculating study power and sample size for various study designs
- Randomly selecting controls
- Carrying out analysis for cohort and case-control studies, including stratified analysis
- Interpreting the results of the various analyses
- Communication of public health messages to different audiences
- Principles of abstract writing

**Software used:**

- EpiData 3.1
- Stata 12
- Microsoft Excel
- Episheet

**Teaching methods included:**

- Presentations and computerised demonstrations
- Computerised case studies
- Discussions
- Exercises on scientific communication

## Multivariable Analysis Module
## Madrid, Spain, 19 – 23 March 2012

**Topics covered during the module (40 hours) included:**

- Principles of multivariable analysis und its use in field epidemiology
- Types of stratified and multivariable analysis (linear, logistic, Poisson, regression)
- The appropriate use of regression models
- Interpretation of linear, logistic, Poisson regression
- Confounding and interactions in a logistic regression analysis, interpreting correctly the coefficients of each term
- How to build an optimal regression model
- Need, advantages and disadvantages of conditional logistic regression
- Need, advantages and disadvantages of Poisson regression
- Introduction to survival analysis
- Communication of the results of an analytical study: how to report and discuss findings in a manuscript

**Software used:**

- Stata 12

**Teaching methods included:**

- Presentations and computerised demonstrations
- Computerised case studies
- Discussions
- Exercises on scientific communication

## Times Series Analysis (Optional Module)
## Madrid, Spain, 26 – 30 March 2012

**Topics covered during the module (30 hours) included:**

- Features, objectives and applications of time series modeling
- Concepts of infectious disease dynamics
- Descriptive and statistical analysis of time series, including plots, aggregation, smoothing and regression techniques
- Decomposing and analyzing the main components of a time series: trend, seasonality, periodicity, and residuals
- Fundamentals of spectral analysis
- Fundamentals of autocorrelation and periodic regression
- Use of time series analysis techniques to design epidemic thresholds for notifications and make predictions
- Introduction to correlation between two independent time series

**Software used:**

- Stata 12
- Excel

**Teaching methods included:**

- Presentations and computerised demonstrations
- Computerised case studies
- Discussions

## Project Review Module
## Stockholm, Sweden, 27 August – 31 August 2012

**Topics covered during the module (35 hours) included:**

- Oral communication techniques
- Preparation of a scientific poster or an oral presentation
- Revision of epidemiological, microbiological, and statistical methods
- Critical appraisal of scientific presentation

**Teaching methods included:**

- Oral presentation
- Poster presentation
- Group discussion
- Lectures
- Review sessions

## Vaccination Module
## London, United Kingdom, 22 – 36 April 2013

**Topics covered during the module (40 hours) included:**

- Clinical and epidemiological characteristics of main vaccine preventable diseases and their current level of control in Europe
- Possible aims, methods of delivery and effects of vaccination programmes;
- Epidemiological and public health principles for the design of vaccination programmes incl. introduction of new vaccines
- Evaluation of vaccination programmes, using data on surveillance, vaccine uptake, vaccine safety, immune status and seroepidemiology, vaccine effectiveness, outbreak investigation
- Understanding the role of risk perception and communication in relation to vaccination programmes
- Key aspects of vaccine related immunology
- Become familiar with modelling and economic evaluation of vaccination programmes

**Software used:**

- STATA 12
- Microsoft Excel
- Berkley Madonna v8.3.18

**Teaching methods included:**

- Presentations and computerised demonstrations
- Lectures
- Case studies
- Discussions
- Hands on practical training

## Sampling Module
## Athens, Greece, 17 – 21 June 2013

**Topics covered during the module (30 hours) included:**

- Use surveys to address an applied public health research question
- Choose a sampling strategy that is adapted to the population to sample
- Select a sample that is as representative of the population as possible
- Estimate sample size
- Analyze surveys taking into account the sampling methods used
- Use the results of surveys to drive public health decisions

**Software used:**

- Stata 11-12
- Microsoft Excel

**Teaching methods included:**

- Presentations and computerized demonstrations
- Computerized case studies
- Discussions

## Rapid Health Assessment in Complex Emergency Situations & Mass Gathering (Optional Module)

## Athens & Skala, Greece, 24 – 28 June 2013

**Topics covered during the module (37 hours) included:**
**Rapid Health Assessment in Complex Emergency Situations:**

- Identify priorities in CES
- Know the national and international partners in CES
- Prepare for a CES international mission
- Comply with UN security requirements
- Know and use relevant indicators to monitor intervention in CES
- Identify source of information and implement data collection to monitor intervention
- Plan and conduct a survey in CES
- Use GPS for sampling and mapping
- Use appropriate methods for counting population

**Mass Gathering:**

- Justify needs for Mass Gathering surveillance
- Identify public health events for Mass Gathering surveillance
- Explore analytical tools and design surveillance to facilitate Public Health action

**Software used:**

- E-POP
- Quantum GIS

**Teaching methods included:**

- Presentations and lectures
- Video presentations
- Discussions
- Exercises and case studies
- Practical outdoor exercise for mapping and population estimation
- Participation in a real survey

## Project Review Module
## Stockholm, Sweden, 26 - 30 August 2013

**Topics covered during the module (40 hours) included:**

- Oral communication techniques
- Preparation of a scientific poster or an oral presentation
- Revision of epidemiological, microbiological, and statistical methods
- Critical appraisal of scientific presentation

**Teaching methods included:**

- Oral presentation
- Poster presentation
- Group discussion
- Lectures
- Review sessions

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**On behalf of the European Centre for Disease Prevention and Control**

# European Programme for Intervention Epidemiology Training

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

**We certify that:**

## Shu-Wan Jian

EPIET

**Has successfully completed 24 months of training at**

**Österreichische Agentur für Gesundheit, Austria**

The European Programme for Intervention Epidemiology Training (EPIET) provides training and practical experience in intervention epidemiology at national centres for surveillance and control of communicable diseases in the European Union (EU). The objectives of the programme are to strengthen the surveillance of infectious diseases in EU member states and at community level, develop response capacity at national and community level to meet communicable disease threats through rapid and effective field investigation and control, develop a European network of public health epidemiologists using standard methods, and sharing common objectives and contribute to the development of the community network for the surveillance and control of communicable diseases.

The full programme entails 24 months in a suitable training department in an EU/EEA member state. The practical training was interspersed with regular formal courses. During their attachment, fellows have been trained in surveillance, outbreak investigations, public health research, teaching and scientific communication.

Date: 18 September 2013

Marc Sprenger
Director, ECDC

Yvan Hutin
EPIET Chief Scientific Coordinator

Marion Muehlen
EPIET Frontline Coordinator

Daniela Schmid
Austria FETP
EPIET Associated Programme

# European Programme for Intervention Epidemiology Train

ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

EPIET

18 September 2013

*Austria*
*Belgium*
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*Croatia*
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*Germany*
*Greece*
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*Latvia*
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*Luxemburg*
*Malta*
*Norway*
*Poland*
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*United Kingdom*

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*Epicentre*

*www.epiet.org*
*www.ecdc.europa.eu*

I, the undersigned, certify that **Shu-Wan Jian** has successfully completed the following courses and modules during the EPIET fellowship:

- **EPIET/EUPHEM Introductory Course**
  Mahon, Spain, 26 September – 14 October 2011
- **Computer Tools for Outbreak Investigations Module**
  Berlin, Germany, 05 – 09 December 2011
- **Multivariable Analysis Module**
  Madrid, Spain, 19 – 23 March 2012
- **Times Series Analysis** (Optional Module)
  Madrid, Spain, 26 – 30 March 2012
- **Project Review Module**
  Stockholm, Sweden, 27 August – 31 August 2012
- **Sampling Module**
  Athens, Greece, 17 – 21 June 2013
- **Project Review Module**
  Stockholm, Sweden, 26 – 30 August 2013

**Yvan Hutin**

**EPIET Chief Scientific Coordinator**

# 3. 諾羅病毒腹瀉群聚事件論文發表

wtm Wiener Tierärztliche Monatsschrift – Veterinary Medicine Austria 99 (2012)

*From the Institute of Medical Microbiology and Hygiene[1], Austrian Agency for Health and Food Safety, (AGES) Vienna, Austria, the European Programme for Intervention Epidemiology Training (EPIET)[2] at the European Centre for Disease Prevention and Control, Stockholm, Sweden, and the Consiliary Laboratory for Norovirus[3], Robert Koch Institute, Berlin, Germany*

# A foodborne outbreak due to norovirus in a vocational school, Austria November 2011

S.-W. JIAN[1,2], E. SIMONS[1], I. LEDERER[1], M. HÖHNE[3], E. OFFNER[1], F. ALLERBERGER[1] and D. SCHMID[1]*

*received June 4, 2012*

*accepted for publication August 20, 2012,*

**Keywords:** gastroenteritis, vocational school, boarding school, kitchen worker, food.

**Schlüsselwörter:** Brechdurchfall, Berufsschule, Internat, Küchenangestellte, Lebensmittel.

## Summary

On 28th November 2011, a school physician informed the Austrian Agency for Health and Food Safety (AGES) of 40 cases of gastroenteritis that occurred on 24th and 25th November in a vocational school in the city of Salzburg, Austria. Two out of five students with gastroenteritis tested positive for norovirus (NV). A probable case involved diarrhoea or vomiting in a student, which occurred between 21st November and 5th December 2011. A confirmed case was a probable case with an NV-positive stool sample. Epidemiological findings led to suspect food items prepared by the school kitchen and consumed between 21st and 25th November as outbreak sources. All students at the school were eligible to be included in a retrospective cohort study. Forty-eight cases fulfilled the outbreak case definitions including three (6%) confirmed cases among a total of 351 responding students. The outbreak started on 23th November, peaked on 24th and ended on 5th December. The cohort study indicated a sour cream sauce (food-specific relative risk (RR): 16.1; 95% CI: 3.9–67.5) and a turkey-strip salad (RR: 5.2; 95% CI: 2.3–11.8) as the most likely sources, accounting for 85% of the 39 suspected foodborne cases.

## Zusammenfassung

**Ein Lebensmittel-bedingter Ausbruch von Norovirus in einer Berufsschule im November 2011 in Österreich**

Ende November kam es zu einer Häufung von Brechdurchfällen bei Schülern einer Berufsfachschule mit Internat in Salzburg Stadt. Von zwei der fünf untersuchten Schüler war die Stuhlprobe Norovirus (NV) positiv. Die AGES wurde mit der Aufklärung beauftragt. Ein Ausbruchfall war definiert als Brechdurchfall bei einem Schüler mit Erkrankungsbeginn zwischen 21. November und 5. Dezember; ein bestätigter Ausbruchfall hatte zusätzlich eine NV-positive Stuhlprobe. Die deskriptive Epidemiologie ließ Speisen, die von der Schulküche zubereitet und zwischen 21. und 25. November von den Schülern konsumiert wurden, als Ausbruchquelle(n) vermuten. Zur Prüfung dieser Hypothese wurde mit den 370 Schülern eine retrospektive Kohortenstudie durchgeführt. Informationen über die Speisenkonsumation der Schüler an den besagten Tagen erhoben wir mittels eines selbst auszufüllenden Fragebogens. Wir berechneten die Tages-spezifische Erkrankungs-Befallsrate für 21.–25. November und für jede Speise das relative Erkrankungs-Risiko. Wir identifizierten 48 Ausbruchsfälle (drei bestätigt) unter den 351 vollständig befragten Schülern. Der Ausbruch dauerte von 23. November bis 5. Dezember, mit einem Fallzahl-Gipfel am 24. November. Höchste Erkrankungs-Befallsraten wurden bei den Schülern beobachtet, die an den Tagen 22., 23. und 24. November Speisen der Schulküche konsumiert hatten (10 %, 12,4 %, 4,7 %). Eine Sauercremesauce (RR: 16,1; 95 % CI: 3,9–67,5) und ein Putenstreifensalat (RR: 5,2; 95% CI: 2,3–11,8) erwiesen sich als plausibelste Quellen des Ausbruchs. Insgesamt konnten mit diesen Speisen 85% der 39 suspekt Lebensmittel-assoziierten Fälle erklärt werden. Als Ausbruchsstamm wurde eine NV-Hybride von Genotyp GGII.7 und GGII.6 identifiziert. Die Art des NV-Eintrags in die Schulküche bleibt ungeklärt, da keine Stuhluntersuchungen bei den Küchenangestellten durchgeführt wurden. Ein HACCP-Konzept (i.e. Gefahrenanalyse und kritische Lenkungspunkte) war in der Schulküche nicht etabliert.

Abbreviations: HACCP = hazard analyses and critical control points; NV = Norovirus; nt = nucleotide; GGII = genogroup II; AR = Attack rate

Genotyping identified the hybrid GGII.7/GGII.6 as the virus causing the outbreak.

The mode of NV entry into the school kitchen remains unclear as stool samples from kitchen workers have not been tested. However, the lack of a hazard analysis critical control point system (HACCP) in the school kitchen might have caused the failure of food safety procedures and facilitated the contamination of kitchen surfaces and food items with NV.

## Intoduction

Norovirus (NV) is a single-stranded RNA virus that can cause acute gastroenteritis in humans. NV can spread via aerosolized vomit, contaminated food and environmental surfaces and directly from person to person via the faecal-oral route (KOOPMANS, 2008; DREYFUSS, 2009). The infectious dose is low, ranging between 10–100 viral particles and the incubation period lasts on average from 24 to 48 hours (KRONEMAN et al., 2008; TEUNIS et al., 2008). The virus is increasingly recognized as a leading cause of foodborne disease in Europe and is frequently reported to be associated with NV-excreting food handlers (LOPMAN et al., 2004; KRONEMAN et al., 2006; KOOPMANS, 2008; DREYFUSS, 2009).

The virus is classified molecularly into genogroups (GG) and genotypes. Genome sequencing followed by phylogenetic analysis is the most common method for genotyping (DINGLE, 2004). Most NV outbreaks reported in the last five years in Europe have been caused by the GGII.4 genotype.

In Austria, notification of foodborne NV gastroenteritis has been mandatory since 2006 (BMG, 2009). According to the 2012 update of the European NV molecular platform (Noronet) in which the Austrian NV reference laboratory has participated since 2008, 34 NV outbreaks were registered in Austria in 2008, 39 in 2009, 54 in 2010 and 21 in 2011 (SCHMID et al., 2005; FRETZ et al., 2009; KRAUSE, 2009). The two dominant GGII genotypes registered were GGII.4-2006b in 2008 and 2009 and GGII.4-2010 in 2010 and 2011.

On 28th November 2011, a school physician informed the Austrian Agency for Health and Food Safety (AGES) of 40 cases of gastroenteritis that had occurred on 24th and 25th November in a vocational school in the city of Salzburg. Two of five stool specimens collected from students with gastroenteritis were positive for NV. Insufficient hand hygiene among the students was initially cited as the reason for the outbreak, putting the blame on the students affected. On 30th November, the provincial public health authority of Salzburg commissioned AGES to investigate the outbreak.

## Material and Methods

We investigated a school outbreak of gastroenteritis due to NV and performed a retrospective cohort study among the students of the vocational school to identify the source(s).

### Descriptive epidemiology

We defined a probable outbreak case as diarrhoea or vomiting in a student of the vocational school with disease onset between 21th November and 5th December 2011. A confirmed outbreak case was a probable case with a stool sample positive for NV. A suspected foodborne case was defined as an outbreak case with disease onset not later than 28th November, considering the kitchen closure on 26th November. The outbreak team engaged the school teachers in active case-finding, asking them to ask students whether they had fallen sick with diarrhoea or vomiting in the time period of interest. For each identified case, we collected information on age, sex, date of disease onset, symptoms (diarrhoea, vomiting, fever, nausea, stomach ache, and cramps) and on laboratory testing of stool specimen. The school physician interviewed the first 20 patients on exposure to food prepared by the school kitchen facility and on exposure to a vomiting case in order to generate hypotheses about potential sources of infection.

### Analytical epidemiology

Epidemiological findings led us to suspect food items prepared in the school kitchen and consumed between 21th and 25th November as likely sources of infection with NV. All students registered at the school for the winter semester 2011/2012 and who had possibly consumed food prepared in the school kitchen facility were eligible to be included in the retrospective cohort study. Information on food items consumed at the school on any of the days of interest (21th–25th November) and at any meal (breakfast, lunch, dinner) was collected via self-administered questionnaires, together with information on boarding school status and demographics (age, sex). We entered data into the EpiInfo software version 7 and used Stata version 10 to calculate relative risks and 95% confidence intervals by chi-square test and Fisher's exact test.

To identify the date of risk of infection, we defined students exposed on specific days and day-specific cases. For the particular day under study, a day-specific case was a case exposed to any food item on that day and who fell sick within the following two days, taking into account the incubation period for NV of 24–48h (day-specific analysis) (SCHMID et al., 2007). In the second step, we compared for each food item the risk among exposed students with the risk among the unexposed per day (day-wise food-specific analyses), resulting in the food-specific relative risk (RR). We restricted these day-wise food-specific analyses to the days found to be associated with illness in the day-specific analysis. We conducted

stratified analyses to control for potential confounders or effects of modification of exposure to the different foods.

### Laboratory investigations

The National Consultant Laboratory for Norovirus in Germany tested the stool specimens available from outbreak cases for the presence of NV using a real-time PCR as described previously (MILLER et al., 2002). Characterization of NV by genogroup was performed by a nested multiplex RT-PCR. The genotype was identified by direct sequencing and a neighbour-joining tree analysis using a consensus region of 275 nt (nucleotides) in the RNA-dependent RNA polymerase gene open reading frame 1 (ORF1) and a consensus region of 140 nt in the capsid gene open reading frame 2 (ORF2) (OH et al., 2003).

### Environmental investigations

No staff in the school kitchen provided stool specimens for laboratory diagnostics. The public health authority did not collect food or environmental samples.

## Results

Forty-eight cases fulfilled the outbreak case definitions including three (6%) confirmed cases. Thirty-seven cases (77%) reported nausea, 31 (65%) vomiting, 29 (60%) stomach ache, 24 (50%) diarrhoea and 16 (33%) fever. The median age was 17 years (range: 14–20), 39 cases were male (81.3%) and 38 (80%) were boarding students. We identified consumption of food prepared in the school kitchen facility as the only common link among the 20 case students interviewed by trawling questionnaire. The outbreak started on 23th November, peaked on the 24th and ended on 5th December. The shape of the outbreak curve suggested sources of infection on the 21st, 22nd, 23rd, 24th and possibly 25th November, followed by non-foodborne transmission of NV on 26th, 27th, 28th November and 2nd and 5th December (Fig. 1).

### Analytical epidemiology

Of the 370 students registered at the school, including 207 boarding and 163 non-boarding students, we recruited 351 students for participation in the retrospective cohort study. These encompassed 196 boarding students (response rate: 94.7%) and 155 non-boarding students (response rate: 95.0%).

The overall disease attack rate was 14% (48/351). The median age of the cohort participants was 15 years (min 13; max 19) with a male: female ratio of 1:2. Males (RR: 2.2; 95% CI: 1.1–4.42) and boarding students (RR: 3.0; 95% CI: 1.5–5.8) were more likely to be a case. When stratified by boarding school status, males among the boarding students were more likely to be a case (RR: 3.4; 95% CI: 1.4–8.2, p=0.003). Of the 41 cases with available data on disease onset (for seven outbreak cases the onset of disease wasunknown), 39 were suspected to be foodborne cases and included in the day-specific analyses and subsequently in the day-wise food-specific analyses.

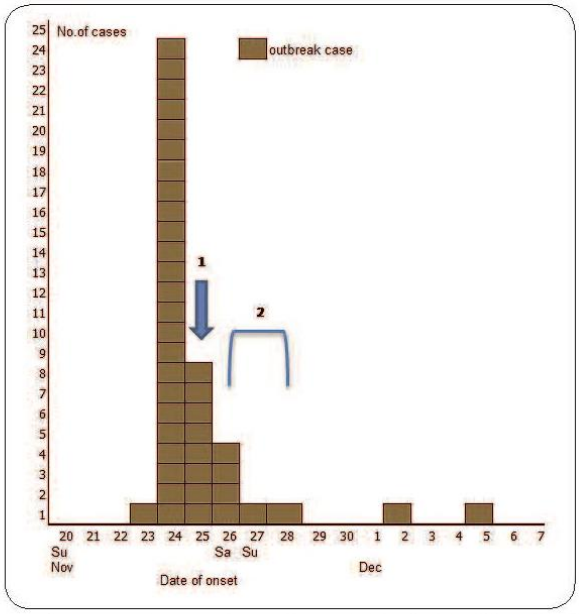


**Fig. 1:** Cases of an outbreak due to NV in Austria, November/December 2011 by date of clinical onset (n=41; in seven cases disease onset unknown); 1: indicates the day on which hand disinfectant effective against NV was provided and the school environment disinfected, 2: indicates period of kitchen closure

Highest disease attack rates (AR) were seen among the participants who had eaten any food on 22nd November and 23rd November (AR: 10%, 12.4%) (Tab. 1). Using 21st November – the day associated with the smallest AR (0.4%) – as reference, the day-specific relative risk (RR) of illness was 24.5 (95% CI: 3.3–179.6) for food consumption on 22nd November, 30.4 (95% CI: 4.2-220.9) for food consumption on 23rd November and 11.4 (95% CI: 1.5–88.3) for food consumption on 24th November. The AR associated with food exposure on 25th November did not differ significantly from the AR associated with food exposure on 21st November (1.7% versus 0.4%).

Based on these findings we restricted the day-wise food-specific analyses to 22th, 23th and 24th November. Compared with unexposed students, participants exposed on 22th November to the consumption of venison ragout, red cabbage/dumplings, cranberries, baked potatoes or sour-cream sauce were more likely to be a case (Tab. 2). After stratifying these food-specific analyses by exposure to sour-cream sauce, the food item with the highest relative risk and biological plausibility, consumption of venison ragout, red cabbage/dumplings, cranberries and baked potatoes was no longer associated with the risk of being a case (Tab. 3). Participants who consumed Wiener Schnitzel, potatoes or turkey-strip salad on 23th November were more likely to be a case than those who did not consume

these items (Tab. 2). After stratification of the food-specific analyses by consumption of turkey-strip salad, consumption of Wiener Schnitzel or potatoes was no longer associated with risk (Tab. 3). Of the 39 suspected foodborne cases, consumption of sour cream sauce on 22nd November or of turkey strip-salad on 23rd November can explain 33 (85%) cases, all of which occurred on 23rd–25th November. No food item consumed on 24th November was associated with the risk of being a case. The eight cases that occurred on 26th–28th November and on 2nd and 5th December are suspected to be secondary.

**Tab. 1:** Day-specific attack rate (AR%) of the days 21st–25th November 2011 in an Austrian NV outbreak in a vocational school

| Days of food exposure | Day-specific exposed student[1] ($N_{exp}$) | Day-specific case[2] n | AR (%) n/N (exp) |
|---|---|---|---|
| Nov 21 | 245 | 1 | 0.4 |
| Nov 22 | 240 | 24 | 10.0 |
| Nov 23 | 242 | 30 | 12.4 |
| Nov 24 | 215 | 10 | 4.7 |
| Nov 25 | 60 | 1 | 1.7 |

[1]Day-specific exposed student defined as a cohort participant with food exposure on the day under study; the decreasing numbers of the day-specific exposed participants is due to exclusion of participants who had fallen sick before or on the day under study;
[2]Day-specific case defined as a student who fell sick within the two days following the day of exposure to food

### Laboratory investigations

Three of seven stool specimens collected from student cases tested positive for NV genogroup (GG) II. Genotyping of the outbreak virus characterized the virus as a hybrid of the GGII.7 and GGII.6 genotypes. The hybrid showed high homology in the polymerase gene open reading frame 1 (ORF 1) (94.3%) to the GGII.7 genotype (GenBank acc. no. AB039777) and high homology in the capsid gene open reading frame 2 (ORF2) (94%) to the GGII.6 genotype (GenBank acc. no AJ277620).

### Environmental investigations

According to the school physician, no members of the kitchen staff had taken sick leave and there was no indication that kitchen workers with diarrhoea had continued work in the week prior to and during the outbreak. There was no hazard analysis critical control point (i.e. HACCP) concept for food safety in place in the school kitchen.

## Discussion

The epidemiological investigation of an outbreak of NV gastroenteritis including a total of 48 cases in an Austrian boarding school in November 2011 indicated a foodborne genesis for the majority of the cases. Insufficient hand hygiene of boarding school students may explain the few non-foodborne cases generated by person-to-person transmission.

Genotyping of NV from the outbreak cases identified the hybrid GGII.7/GGII.6 as the outbreak causing virus, which has not been previously reported in Austria. In Sweden, among 101 foodborne and waterborne NV outbreaks in 2002–2006, four of the foodborne outbreaks were also caused by this NV hybrid GGII.7/II.6a (LYSÉN et al., 2009). Most NV outbreaks reported in the last five years in Europe were caused by the GGI.3, I.4 and I.b genotypes and the GGII.4 genotype (SIEBENGA et al., 2008; VAN BEEK et al., 2012) but the spread of recombinant viruses such as hybrids of different polymerase and capsid genotypes has increased over the past five years (REUTER et al., 2006; LYSÉN et al., 2009). The public health impact of emerging recombinant NV strains is not yet known.

**Tab. 2:** Day-wise food-specific attack rate (AR%) and food-specific risk ratio (RR) for food items served on 22nd and 23rd November; 95% confidence intervals (CI) and p-values.

| Food items | Food exposed | | | Food unexposed | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Total | Cases | AR% | Total | Cases | AR% | RR | 95 % CI | P |
| 22nd November; N=344 | | | | | | | | | |
| Sour-cream sauce | 143 | 23 | 16.1 | 201 | 2 | 1.0 | 16.2 | 3.9–67.5 | <0.01 |
| Baked potatoes | 161 | 23 | 14.3 | 183 | 2 | 1.1 | 13.1 | 3.1–54.6 | <0.01 |
| Ragout of venison | 199 | 22 | 11.1 | 145 | 3 | 2.1 | 5.3 | 1.6–17.5 | <0.01 |
| Red cabbage/dumpling | 184 | 19 | 10.3 | 160 | 6 | 3.8 | 2.8 | 1.1–6.7 | 0.02 |
| Cranberries | 137 | 15 | 11.0 | 207 | 10 | 4.8 | 2.3 | 1.1–4.9 | 0.03 |
| 23rd November; N=343 | | | | | | | | | |
| Wiener Schnitzel | 230 | 30 | 13.0 | 113 | 2 | 1.8 | 7.37 | 1.8–30.3 | <0.01 |
| Turkey-strip salad | 139 | 25 | 18.0 | 204 | 7 | 3.4 | 5.24 | 2.3–11.8 | <0.01 |
| Potatoes | 220 | 27 | 12.3 | 123 | 5 | 4.1 | 3.02 | 1.2–7.6 | 0.01 |

**Tab. 3:** Stratified analyses: Food-specific risk ratio (RR) for food items served on 22nd and 23rd November stratified by the two food items that are the most microbiologically plausible vehicles for NV (i.e. sour-cream sauce, turkey-strip salad); 95% CI

| Exposures | Crude analyses | Stratified analyses | |
|---|---|---|---|
| | RR (95% CI) | RR (95% CI) | RR (95% CI) |
| 22nd November | | exposed to sour-cream sauce | not exposed to sour-cream sauce |
| Baked potato | 13.1 (3.1–54.6) | ∞ | 0.0 |
| Ragout of venison | 5.3 (1.6–17.5) | 1.9 (0.5–7.6) | 1.6 (0.1–24.9) |
| Red cabbage/ dumpling | 2.8 (1.1–6.7) | 1.0 (0.4–2.4) | 1.8 (0.1–28.8) |
| Cranberry | 2.3 (1.1–4.9) | 1.2 (0.5–2.6) | 0.0 |
| 23rd November | | exposed to turkey-strip salad | not exposed to turkey-strip salad |
| Wiener Schnitzel | 7.4 (1.8–30.3) | ∞ | 2.8 (0.6–13.9) |
| Potatoes | 3.0 (1.2–7.6) | 0.9 (0.3–2.6) | 2.8 (0.6–14.2) |

As described in previously published NV outbreaks, defining outbreak cases for each day of exposure under study according to the incubation period of infection increases the likelihood of identifying probable sources of infection with a pathogen with such a short incubation period as NV (SCHMID et al., 2007; SCHMID et al., 2011a). Two dishes implicated by our findings - the sour cream sauce and the turkey-strip salad - are biologically plausible sources of infection with NV. The other food items also implicated by the findings of the day-wise food specific analyses such as baked potatoes or Wiener Schnitzel are rather biologically non-plausible as NV vehicles. This was confirmed by the findings of the stratified analyses, which indicated the two biologically plausible food items as effect modifiers for the others. Boarding students were more likely to be cases, which can be explained by the fact that sour-cream sauce and turkey-strip salad were served for dinner.

Preparation of cold meals not requiring heating has been repeatedly reported to be associated with foodborne outbreaks of NV (KOOPMANS and DUIZER, 2004; SCHMID et al., 2007; SHOWELL et al., 2007).

NV can easily enter kitchen facilities of schools, accommodations and health-care facilities via symptomatic and asymptomatic kitchen workers (SCHMID et al., 2007; MOE, 2009; MARSHALL and BRUGGINK, 2011). Up to 20% of people infected with NV do not have symptoms of gastroenteritis and may continue to work and to have contact with food (MOE, 2009; MARSHALL and BRUGGINK, 2011). A study in Japan showed that the mean viral load in stools found in asymptomatic food handlers was similar to that of symptomatic individuals (OZAWA et al., 2007). Foodborne outbreaks due to asymptomatic NV excretors among kitchen staff have been repeatedly reported. In Ireland in 2009, sandwiches, which were epidemiologically identified as the source of an outbreak, were suspected to have been contaminated by asymptomatic, NV-excreting food handlers (NICOLAY et al., 2011). In Austria in 2009, an outbreak of NV in a healthcare facility was traced back to asymptomatic kitchen staff excreting NV (SCHMID et al., 2011a). Another mode of spread of NV into kitchen facilities could be via kitchen workers, in whose households somebody had fallen sick from an NV infection. This was reported in an outbreak due to NV at a university cafeteria in Texas in 1998 (DANIELS et al., 2000) and in an outbreak among attendees of a party in Austria in 2007 (KUO et al., 2009). A study of NV viability indicated that NV can remain infectious for up to 28 days at 20 °C on the surface of a kitchen (LAMHOUJEB et al., 2009). The lack of a hazard analysis critical control point system (HACCP) in the school kitchen might be responsible for the failure of food safety and have facilitated the contamination of kitchen surfaces and food items by kitchen workers excreting NV. However, as no stool samples from the disease-free kitchen workers, no food or environmental samples and no information on the disease status of the kitchen workers' household members were available, the mode of entry of NV into the school kitchen remains unclear.

On 25th November (outbreak day 3), the school cleaning staff cleaned and disinfected the surfaces of the classrooms, toilets and public areas. On 26th November, the kitchen was closed for two days for cleaning and disinfection. The school physician trained students and kitchen workers in hand hygiene by use of a hand disinfectant effective against NV (Bode Sterilium Virugard®, Hartmann, Heidenheim, Germany), which was provided in toilets and in the kitchen facility. Only two further cases were reported after November 28th (outbreak day 6).

We recommended implementation of an HACCP system, which is required by law in Austria but hard to control in boarding schools due to the lack of personnel resources. We advise school directors to comply with the Austrian guidelines for the control and prevention of NV outbreaks (SCHMID et al., 2011b).

## References


DANIELS, N.A., BERGMIRE-SWEAT, D.A., SCHWAB, K.J., HENDRICKS, K.A., REDDY, S., ROWE, S.M., FANKHAUSER, R.L., MONROE, S.S., ATMAR, R.L., GLASS, R.I., MEAD, P. (2000): A foodborne outbreak of gastroenteritis associated with Norwalk-like viruses: first molecular traceback to deli sandwiches contaminated during preparation. J Infect Dis **181**, 1467–1470.

DINGLE, K.E. (2004): Mutation in a Lordsdale Norovirus Epidemic Strain as a Potential Indicator of Transmission Routes. J Clin Microbiol **42**, 3950–3957.

DREYFUSS, M.S. (2009): Is norovirus a foodborne or pandemic pathogen? An analysis of the transmission of norovirus-associated gastroenteritis and the roles of food and food handlers. Foodborne Pathog Dis **6**, 1219–1228.

FRETZ, R., SCHMID, D., JELOVCAN, S., TSCHERTOU, R., KRASSNITZER, E., SCHIRMER, M., HELL, M., ALLERBERGER, F. (2009): An outbreak of norovirus gastroenteritis in an Austrian hospital, winter 2006-2007. Wien Klin Wochenschr **121**, 137–143.

KOOPMANS, M. (2008): Progress in understanding norovirus epidemiology. Curr Opin Infect Dis **21**, 544–552.

KOOPMANS, M., DUIZER, E. (2004): Foodborne viruses: an emerging problem. Int J Food Microbiol **90**, 23–41.

KRAUSE, G. (2009): Ausbruchsabklärung: medizinische Notwendigkeit oder akademische Spielerei? Wien Klin Wochenschr **121**, 69–72.

KRONEMAN, A., HARRIS, J., VENNEMA, H., DUIZER, E., DUYNHOVEN, Y. VAN, GRAY, J., ITURRIZA, M., BOTTIGER, B., FALKENHORST, G., JOHNSEN, C., BONSDORFF, C.-H. VON, MAUNULA, L., KUUSI, M., POTHIER, P., GALLAY, A., SCHREIER, E., KOCH, J., SZUCS, G., REUTER, G., KRISZTALOVICS, K., LYNCH, M., MCKEOWN, P., FOLEY, B., COUGHLAN, S., RUGGERI, F.M., BARTOLO, I. DI, VAINIO, K., ISAKBAEVA, E., POLJSAK-PRIJATELJ, M., GROM, A.H., BOSCH, A., BUESA, J., FAUQUIER, A.S., HERNANDEZ-PEZZI, G., HEDLUND, K.-O., KOOPMANS, M. (2008): Data quality of 5 years of central norovirus outbreak reporting in the European Network for food-borne viruses. Journal of Public Health **30**, 82–90.

KRONEMAN, A., VENNEMA, H., HARRIS, J., REUTER, G., BONSDORFF, C.H. VON, HEDLUND, K.O., VAINIO, K., JACKSON, V., POTHIER, P., KOCH, J., SCHREIER, E., BÖTTIGER, B.E., KOOPMANS, M. (2006): Increase in norovirus activity reported in Europe. Euro Surveill **11**, E061214.1.

KUO, H.-W., SCHMID, D., JELOVCAN, S., PICHLER, A.-M., MAGNET, E., REICHART, S., ALLERBERGER, F. (2009): A foodborne outbreak due to norovirus in Austria, 2007. J Food Prot **72**, 193–196.

LAMHOUJEB, S., FLISS, I., NGAZOA, S.E., JEAN, J. (2009): Molecular study of the persistence of infectious human norovirus on food-contact surfaces. Food Environ Virol **1**, 51–56.

LOPMAN, B., VENNEMA, H., KOHLI, E., POTHIER, P., SANCHEZ, A., NEGREDO, A., BUESA, J., SCHREIER, E., REACHER, M., BROWN, D., GRAY, J., ITURRIZA, M., GALLIMORE, C., BOTTIGER, B., HEDLUND, K.-O., TORVÉN, M., BONSDORFF, C.-H. VON, MAUNULA, L., POLJSAK-PRIJATELJ, M., ZIMSEK, J., REUTER, G., SZÜCS, G., MELEGH, B., SVENNSON, L., DUIJNHOVEN, Y. VAN, KOOPMANS, M. (2004): Increase in viral gastroenteritis outbreaks in Europe and epidemic spread of new norovirus variant. Lancet **363**, 682–688.

LYSÉN, M., THORHAGEN, M., BRYTTING, M., HJERTQVIST, M., ANDERSSON, Y., HEDLUND, K.-O. (2009): Genetic diversity among food-borne and waterborne norovirus strains causing outbreaks in Sweden. J Clin Microbiol **47**, 2411–2418.

MARSHALL, J.A., BRUGGINK, L.D. (2011): The dynamics of norovirus outbreak epidemics: recent insights. Int J of Environ Res Public Health **8**, 1141–1149.

MILLER, I., GUNSON, R., CARMAN, W.F. (2002): Norwalk like virus by light cycler PCR. J Clin Virol **25**, 231–232.

MOE, C.L. (2009): Preventing norovirus transmission: How should we handle food handlers? Clin Infect Dis **48**, 38–40.

NICOLAY, N., MCDERMOTT, R., KELLY, M., GORBY, M., PRENDERGAST, T., TUITE, G., COUGHLAN, S., MCKEOWN, P., SAYERS, G. (2011): Potential role of asymptomatic kitchen food handlers during a food-borne outbreak of norovirus infection, Dublin, Ireland, March 2009. Euro Surveill **16**, pii: 19931.

OH, D.-Y., GAEDICKE, G., SCHREIER, E. (2003): Viral agents of acute gastroenteritis in German children: prevalence and molecular diversity. J Med Virol **71**, 82–93.

OZAWA, K., OKA, T., TAKEDA, N., HANSMAN, G.S. (2007): Norovirus infections in symptomatic and asymptomatic food handlers in Japan. J Clin Microbiol **45**, 3996–4005.

REUTER, G., VENNEMA, H., KOOPMANS, M., SZÜCS, G. (2006): Epidemic spread of recombinant noroviruses with four capsid types in Hungary. J Clin Virol **35**, 84–88.

SCHMID, D., LEDERER, I., PICHLER, A.-M., BERGHOLD, C., SCHREIER, E., ALLERBERGER, F. (2005): An outbreak of Norovirus infection affecting an Austrian nursing home and a hospital. Wien Klin Wochenschr **117**, 802–808.

SCHMID, D., STÜGER, H.P., LEDERER, I., PICHLER, A.-M., KAINZ-ARNFELSER, G., SCHREIER, E., ALLERBERGER F., (2007): A foodborne norovirus outbreak due to manually prepared salad, Austria 2006. Infection **35**, 232–239.

SCHMID, D., KUO, H.-W., HELL, M., KASPER, S., LEDERER, I., MIKULA, C., SPRINGER, B., ALLERBERGER, F. (2011a): Foodborne gastroenteritis outbreak in an Austrian healthcare facility caused by asymptomatic, norovirus-excreting kitchen staff. J Hosp Infect **77**, 237–241.

SCHMID, D., LEDERER, I., JELOVCAN, S., KASPER, S., PICHLER, J., MANN, M., LADSTÄTTER, J., WEWALKA, G., CROCE, U., SUMANN G., ECKER, C., HRABCIK, H., LUCKNER-HORNISCHER, A., JURIK, K., HELL, M., SPRINGER, B., ALLERBERGER, F. (2011b) Vorgehen bei Gastroenteritisausbrüchen durch Norovirus in Gemeinschaftseinrichtungen, auf Personenschiffen, in Beherbergungsbetrieben, Schulen und anderen Gemeinschaftseinrichtungen. Österreichische Agentur für Gesundheit und Ernährungssicherheit (AGES), Wien. Available under: http://www.ages.at/ ages/gesundheit/mensch/noroviren/, last accessed May, 2012.

SHOWELL, D., SUNDKVIST, T., REACHER, M., GRAY, J. (2007): Norovirus outbreak associated with canteen salad in Suffolk, United Kingdom. Euro Surveill **12**, E071129.6.

SIEBENGA, J., KRONEMAN, A., VENNEMA, H., DUIZER, E., KOOPMANS, M. (2008): Food-borne viruses in Europe network report: the norovirus GII.4 2006b (for US named Minerva-like, for Japan Kobe034-like, for UK V6) variant now dominant in early seasonal surveillance. Euro Surveill **13**, pii: 8009 .

TEUNIS, P.F.M., MOE, C.L., LIU, P., MILLER, S.E., LINDESMITH, L., BARIC, R.S., PENDU, J. LE, CALDERON, R.L. (2008): Norwalk virus: how infectious is it? J Med Virol **80**, 1468–1476.

VAN BEEK J., BASS, D., KRONEMAN, A., VENNEMA, H., KOOPMANS, M. (2012): Noronet update, April 2012. National Institute for Public Health and the environment, Bilthoven, the Netherlands. http://www.noronet.nl/noronet/, last accessed April 2012.

**Legal regulations**

Bundesministerium für Gesundheit: Anzeigepflichtige Krankheiten gem. Epidemiegesetz 1950, BGBl. Nr. 186/1950 idgF, und der Verordnung des Bundesministers für Gesundheit betreffend anzeigepflichtige übertragbare Krankheiten 2009, BGBl. II Nr. 359/2009 idgF, http://bmg.gv.at/home/Schwerpunkte/Krankheiten/Uebertragbare_Krankheiten/Epidemiologie/Meldepflichtige_uebertragbare_Krankheiten_in_Oesterreich, accessed 14th February, 2012.



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# 4. 諾羅病毒腹瀉群聚事件壁報

# A foodborne outbreak due to norovirus in a vocational school, Austria, November 2011

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## Background

- According to the 2012 update of noronet (European NV molecular platform), there were for Austria 34 registered in 2008, 39 in 2009, 54 in 2010, and 21 NV outbreaks in 2011. The 2 dominant GGII genotypes were GGII.4 2006b in 2008/2009, and GGII.4 2010 in 2010/ 2011.
- On 28 Nov: school physician informed AGES about 40 cases of gastroenteritis
- Cases occurred on 24-25 Nov in a vocational school in city Salzburg
- 3/7 stool specimens from diarrhea case-students were positive for NV
- On 30 Nov, the provincial public health authority Salzburg mandated AGES to investigate the outbreak.

## Methods

**Descriptive epidemiology:** active case finding by school teachers, description of cases by place, time and person; collection of information on food exposure and exposure to vomiting case
Outbreak Case definition: a probable outbreak case is diarrhea/vomiting in a student of affected school with disease onset between 21 Nov- 5 Dec 2011; a confirmed outbreak case is probable case with NV positive stool sample; a suspected foodborne outbreak case is a outbreak case with disease onset not later than 28 Nov, considering date of kitchen closure on 26 Nov.

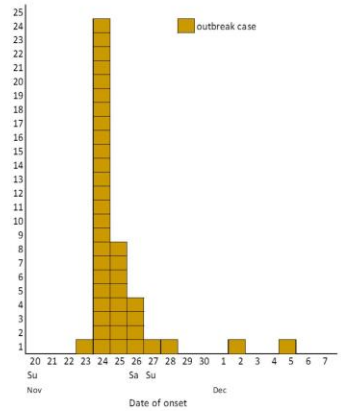
**Analytical epidemiology:** cohort study
Cohort of interest: 370 students registered at the school for 2011/2012 and a possible consumer of food prepared in school kitchen facility for on days 21-25 Nov, 2011.
Data collection: Information on food items consumed at school on 21-25 Nov collected via self-administered questionnaire.
Plan of analyses: I: day-specific analysis yielding day-specific attack rates (AR%),, II: day-wise food-specific analyses yielding food-specific risk ratios.
Day-wise food-specific analyses were restricted to these days found associated with illness in day-specific analysis.
Stratified analyses: to control for potential confounding or effect modification of the different food exposures.

## Results

### Descriptive epidemiology

48 cases fulfilled outbreak case definitions consumption of food prepared in the school kitchen facility was only common link among case-students interviewed by trawling questionnaire. Shape of the outbreak curve suggested sources of infection on the days 21, 22, 23, 24 and possibly on 25 November, followed by non-foodborne transmission of NV on 26, 27, 28 Nov, 2 and 5 Dec (Figure 1).

Figure 1; cases by date of onset of an outbreak due to NV in Austria, November 2011 (n=41)




### Analytical epidemiology I

Day-specific analysis

Using Nov. 21 with the smallest AR% as reference for computing day-specific risk ratios for 22-25 Nov. (Table 1).

Table 1; Day-specific attack rate (AR) and risk ratio (RR) of 21-25 November

| Days of exposure | Day-specific exposed ($N_{exp}$) | Day-specific case n | AR (%) | RR | 95% CI |
|---|---|---|---|---|---|
| 21 Nov | 245 | 1 | 0.4 | Reference | |
| 22 Nov | 240 | 24 | 10.0 | 24.5 | 3.3-179.6 |
| 23 Nov | 242 | 30 | 12.4 | 30.4 | 4.2-220.9 |
| 24 Nov | 215 | 10 | 4.7 | 11.4 | 1.5-88.3 |
| 25 Nov | 60 | 1 | 1.7 | 4.1 | 0.3-64.3 |

Highest attack rates (ARs) and risk ratios (RRs) were seen among students, who have eaten any food on 22 and 23 Nov.
No significant difference was found in day-specific attack rate between the two days 21 Nov and 25 Nov.

### Laboratory investigation

Genotyping of the outbreak virus characterized the virus as a hybrid of GGII.7 genotype and GGII.6 genotype. The hybrid showed high homology in the polymerase gene open reading frame 1 (ORF 1) (94.3%) to the GGII.7 genotype and high homology in the capsid gene open reading frame 2 (ORF2) (94 %) to the GGII.6 genotype.

### Analytical epidemiology II

Day-wise food-specific analyses

Table 2; Food-specific risk ratios (RR) for 22 and 23 Nov; 95% confidence interval (CI) and p-value.

| Food items | Total | RR | 95%CI | P |
|---|---|---|---|---|
| 22 November; N=344 | | | | |
| Sour cream sauce | 143 | 16.2 | 3.9-67.5 | 0.00 |
| Baked potato | 161 | 13.1 | 3.1-54.6 | 0.00 |
| Ragout of venison | 199 | 5.3 | 1.6-17.5 | 0.00 |
| Red cabbage/ dumpling | 184 | 2.8 | 1.1-6.7 | 0.02 |
| Cranberry | 137 | 2.3 | 1.1-4.9 | 0.03 |
| 23 November; N=343 | | | | |
| Wiener Schnitzel | 230 | 7.37 | 1.8-30.3 | 0.00 |
| Turkey strip salad | 139 | 5.24 | 2.3-11.8 | 0.00 |
| Potatoes | 220 | 3.02 | 1.2-7.6 | 0.01 |

Students who consumed venison ragout, red cabbage/dumplings, cranberries, baked potato or sour cream sauce on 22 Nov,
Students who consumed Wiener Schnitzel, potatoes or turkey strip salad on 23 Nov were more likely to be a case (Table 2)

Stratified analyse indicated two items independently associated with the disease risk:
Sour cream sauce: 16.2 (95%CI:3.9-67.5)
Turkey strip salad: 5.2 (95%CI:2.3-11.8)

**Outbreak control measures:** On 25 Nov (outbreak day 3), the school cleaning staff cleaned and disinfected the environmental surfaces of the classrooms, toilets, and public areas. On 26-27 Nov the kitchen was closed for cleaning and disinfection.

## Conclusions

- Epidemiological findings indicated two biologically plausible outbreak sources: sour cream sauce and turkey strip salad.
- Genotyping of the outbreak NV identified a hybrid - GGII.7/GGII.6, which has not been reported before in Austria.
- Lacking a HACCP in the school kitchen might have facilitated contamination of kitchen surfaces and food items.
- The mode, how NV entered school kitchen, remained unclear due to lacking information on presence of asymptomatic excreting kitchen workers, and disease status of kitchen workers' household members.
- We recommend implementation of a HACCP, which is required by law in Austria, but hardly to be controlled in boarding school due to lack of personal resources.
- We advise the school director to comply with the AGES guidelines for control and prevention of NV outbreaks.

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**Österreichische Agentur für Gesundheit und Ernährungssicherheit GmbH** www.ages.at

5. 諾羅病毒腹瀉群聚事件口頭報告投影片

## Methods
### Case Definition

**Probable case**

- Primary case
  - vomiting/ diarrhoea in a student of the school with disease onset between **21 Nov - 27 Nov 2011**
- Secondary case
  - vomiting / diarrhoea in a student of the school with disease onset after **27 Nov 2011** and contact to a primary case

**Confirmed case**

Primary or secondary case of RT-PCR confirmed NV infection

4

## EPIET

# A foodborne norovirus outbreak in a boarding school, Austria, November 2011

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Austrian Agency for Health and Food Safety (AGES)
Oct 25, 2012

www.ages.at Österreichische Agentur für Gesundheit und Ernährungssicherheit GmbH

## Retrospective cohort study

- Population of interest
  - 370 students registered at the school for 2011/2012
- Self-administered questionnaire
  - Demographics, clinical onset, symptoms, duration of illness, hospitalization and food exposure
  - Breakfast, lunch, dinner on 21-25 Nov included 70 food items
- Plan of analyses

  Primary cases were included
  - **Univariate** analysis

    Day-specific analysis, food-day-specific analysis
  - **Stratified** analyses

5

## Background

- 24-25 Nov: 40 students of a boarding school fell sick with gastroenteritis
- 26 Nov: closure of school kitchen
- 28 Nov: report to local PH authority
- 30 Nov: AGES started investigation

- School: 370 students including 207 boarding students
- Student: Age 13-20 years, Male : female=1.9
- School kitchen: preparing 3 meals/day, 5 kitchen workers

2

## Environmental & Laboratory investigation

- Laboratory investigation
  - Genogroup (GG): nested multiplex RT-PCR
  - Genotype: direct sequencing and analysis
- Environmental Investigation
  - Inspection of the school kitchen
  - Interviews of kitchen staff on disease status
  - PH authority did not collect food or environmental samples

6

## Objectives

- To describe the outbreak
- To identify the possible sources of the infection
- To prevent further outbreaks of gastroenteritis in schools

3

## Thank you for your listening



## Conclusion

- Sour cream sauce and Turkey-strip salad most likely sources of NV-outbreak
  - Both manually prepared without heating
- Hypothesis on food contamination with NV
  - I: Kitchen staff – excretor
  - II: Purchased food items contaminated with NV -> contamination of kitchen environment
  - No microbiological evidence



## Stratified analyses II

- Other risk factors for being a case: Male, boarding student

| characteristic | Crude RR (95%CI) |
|---|---|
| male | 2.2 (1.1-4.4) |
| positive boarding status | 3.0 (1.6-5.8) |

**Exposure to sources of infection stratified by gender**

| Source of infection | male Risk difference (95%CI) | female Risk difference (95%CI) |
|---|---|---|
| Sour cream sauce | 0.18 (0.10-0.26) | 0.09 (0.01-0.17) |
| Turkey-strip salad | 0.20 (0.10-0.30) | 0.07 (0-0.14) |



## Recommendation

- Reinforced the implementation of HACCP in the kitchen
- No HACCP may cause food safety failure
- HACCP concept implementation is required by law in Austria
- Comply with Austrian guidelines for control and prevention of NV outbreaks
- Facilitate the collection of specimens in suspected foodborne disease outbreak
- Food leftovers
- Any food handlers involved



## Food day specific analysis

| Day-by-day food-specific analysis | Food Eaten | | | Food not eaten | | | | |
|---|---|---|---|---|---|---|---|---|
| Wednesday, November 21 | Total | Cases | AR% | Total | Cases | AR% | RR | 95%CI | P |
| Lunch | | | | | | | | | |
| Wildragout | 199 | 22 | 11.06 | 145 | 3 | 2.07 | 5.34 | [1.63-17.51] | 0.002 |
| rotkraut, serviettenknodel (menu1) | 184 | 19 | 10.33 | 160 | 6 | 3.75 | 2.75 | [1.13-6.73] | 0.010 |
| preiselbeeren (menu1) | 137 | 15 | 10.95 | 207 | 10 | 4.83 | 2.27 | [1.05-4.98] | 0.032 |
| kohlrabisuppe (menu2) | 14 | 2 | 14.29 | 330 | 23 | 6.97 | 2.05 | [0.54-7.85] | 0.302 |
| kohlrabisuppe (menu1) | 87 | 8 | 9.20 | 257 | 17 | 6.61 | 1.39 | [0.62-3.11] | 0.423 |
| salat (menu2) | 26 | 2 | 7.69 | 318 | 23 | 7.23 | 1.06 | [0.27-4.26] | 0.931 |
| ger. kraidel mit Ei (menu1) | 28 | 2 | 7.14 | 316 | 23 | 7.28 | 0.98 | [0.24-3.95] | 0.978 |
| Dinner | | | | | | | | | |
| Sauerrahmsauce | 141 | 23 | 16.31 | 201 | 2 | 1.00 | 16.31 | [3.87-67.47] | 0.000 |
| pfefferkartoffel mit Schnittlauch | 161 | 23 | 14.29 | 181 | 2 | 1.09 | 13.07 | [3.13-54.58] | 0.000 |
| Gemüse | 156 | 22 | 14.10 | 188 | 3 | 1.60 | 8.84 | [2.70-28.98] | 0.000 |

| Day-by-day food-specific analysis | Food Eaten | | | Food not eaten | | | | |
|---|---|---|---|---|---|---|---|---|
| Wednesday, November 21 | Total | Cases | AR% | Total | Cases | AR% | RR | 95%CI | P |
| Lunch | | | | | | | | | |
| wienerschnitzel(menu1) | 231 | 30 | 12.99 | 113 | 2 | 1.77 | 7.34 | [1.79-30.16] | 0.001 |
| kartoffeln(menu1) | 221 | 27 | 12.22 | 123 | 5 | 4.07 | 3.01 | [1.19-7.61] | 0.013 |
| kartoffelsuppe(menu1) | 102 | 10 | 11.73 | 152 | 13 | 7.14 | 1.64 | [0.84-3.22] | 0.144 |
| salat(menu1) | 132 | 15 | 11.36 | 212 | 17 | 8.02 | 1.42 | [0.73-2.74] | 0.299 |
| gemüseschnitzel(menu2) | 8 | 0 | 0.00 | 336 | 32 | 9.52 | 0 | [-,-] | 0.359 |
| salat(menu2) | 8 | 0 | 0.00 | 336 | 32 | 9.52 | 0 | [-,-] | 0.359 |
| kartoffeln(menu2) | 8 | 0 | 0.00 | 336 | 32 | 9.52 | 0 | [-,-] | 0.359 |
| ka kaiserschmarrn(menu1) | 7 | 0 | 0.00 | 337 | 32 | 9.50 | 0 | [-,-] | 0.392 |
| Dinner | | | | | | | | | |
| salatgurkenstreifen | 140 | 25 | 17.86 | 204 | 7 | 3.43 | 5.21 | [2.31-11.78] | 0 |
| getränk | 143 | 24 | 16.78 | 201 | 8 | 3.98 | 4.22 | [1.95-9.12] | 0 |
| getränk | 146 | 24 | 16.44 | 198 | 8 | 4.04 | 4.07 | [1.80-9.20] | 0 |

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## Acknowledgement


- AGES
- School physician: Dr. Offner
- Consiliary Laboratory for Norovirus, RKI, Germany
- EPIET2010 & 2011 fellows, coordinators and facilitators

6. 奧地利李斯特菌監測系統評估報告

# Listeriosis in Austria

# An Evaluation of the Austrian *Listeria* Surveillance System

On behalf of the Chief Medical Officer
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2012-2013

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# Introduction/Background

## Introduction to the Disease

Listeriosis is a rare but potentially serious infectious disease caused by *Listeria monocytogenes*. *L. monocytogenes* is a Gram-positive bacteria that occurs ubiquitously in nature. Many ruminant animals (e.g. cow, goats) excrete the bacteria via faeces. Listeria serotypes are based on the two antigens O and H. Currently, there are twelve serotypes of L. monocytogenes (1/2a, 1/2b, 1/2c, 3a, 3b, 3c, 4a, 4b, 4c, 4d, 4e, and 7) recognized, of which three (1/2a, 1/2b, and 4b) cause the majority of human cases (95%); serotype 4b is most commonly associated with outbreaks. Most cases of human listeriosis are foodborne, related to contaminated raw food and undercooked food. Risk groups of listeriosis are pregnant women, newborns, and adults with a weakened immune system (1). A person with listeriosis usually has fever and muscle aches, sometimes preceded by diarrhea or other gastrointestinal symptoms. Symptoms in pregnant women include mild flu-like symptoms, headaches, muscle aches, fever, nausea, and vomiting. Most reported cases of invasive listeriosis present with life-threatening illness such as materno-fetal listeriosis or neonatal listeriosis, blood stream infection, and meningoencephalitis.

## Listeriosis in Austria, until 2012

*National Surveillance Data - Data Sources*

From 1996-2006 data on the annual number of cases were provided by the National Reference Laboratory for Listeria, Innsbruck, Tyrol. Since 2007 the National Reference Centre and since 2010 the National Reference Laboratory for Listeria have been estalished by AGES, providing all laboratory case data. Since 2005 data on monthly and annual number of confirmed cases of listeriosis has been published at the website of the MoH.

From 1996 to 2005 the annual incidence increased from 0.14 to 0.24/100,000 with a total of 131 cases within the 10 years (1996: 11 cases; 2005: 20 cases). The rate decreased thereafter to 0.12/100,000 in 2006 (n=10). There was a steep increase to 0.55/100,000 persons in 2009 due to a multinational listeriosis outbreak (n=46) (figure 1).

The incidence of pregnancy-related listeriosis from 1996 to 2012 ranged between 0 and 0.1/100,000 population with peaks in 1998, 2002, 2008 and 2010 (Figure 3).

Serotype 4b and 1/2a accounted for the majority of cases from 1997- 2012 (data not shown).

## Outbreaks 2003-2012

According to the annual surveillance report of listeriosis in Austria, there were no outbreaks reported from 2003 to 2007. From 2008 until 2012 a total of 4 outbreaks have been detected and investigated.

2008: a foodborne was outbreak associated with jellied pork contaminated with *Listeria monocytogenes* including 14 cases with onset of gastroenteritis within 1 week following dinner at a wine tavern on September 6.

2009/2010: A multinational Listeriosis outbreak with a total of 34 cases (25 Austrian cases) including five deaths. The microbiologically identified outbreak source was an acid curd cheese 'Quargel', produced in Austria.

2010: An outbreak of three cases was detected in May (source unknown)

2012: An outbreak of three cases was detected (source unknown) (figure 2).

**Figure 1.** Annual incidence of invasive listeriosis disease /100,000 persons, Austria, 1996–2012; Source: National surveillance data

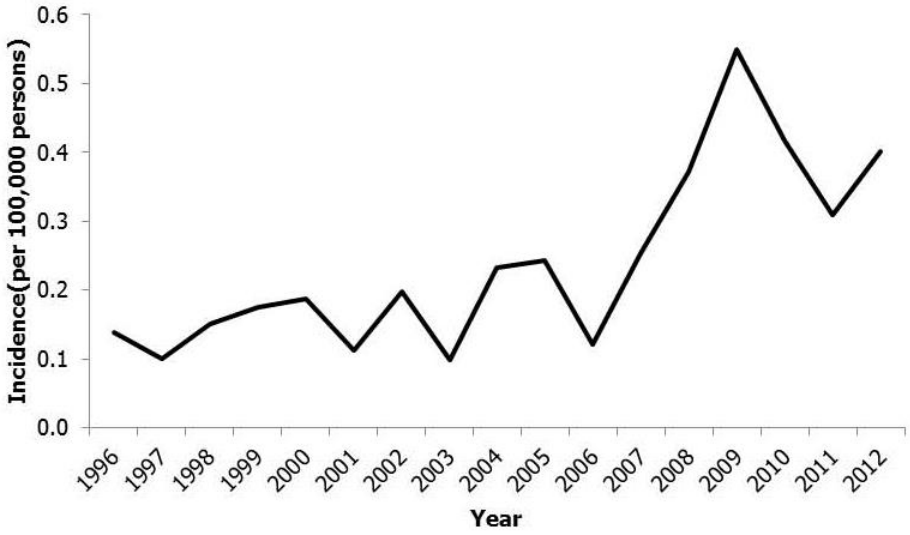
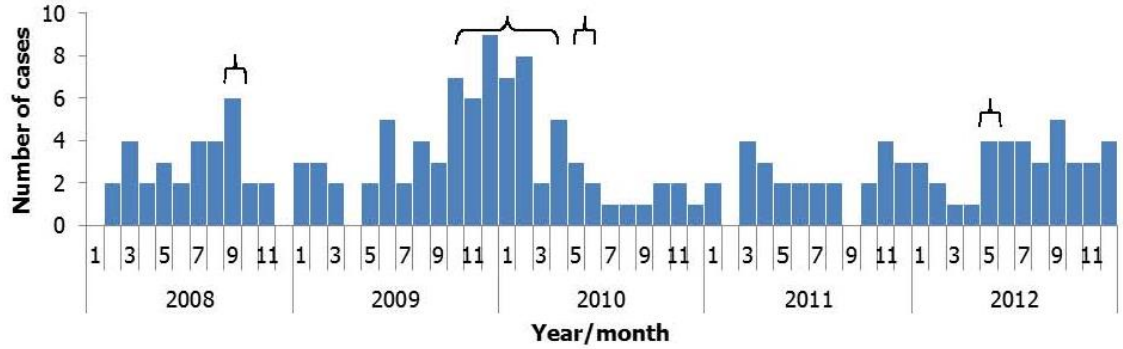
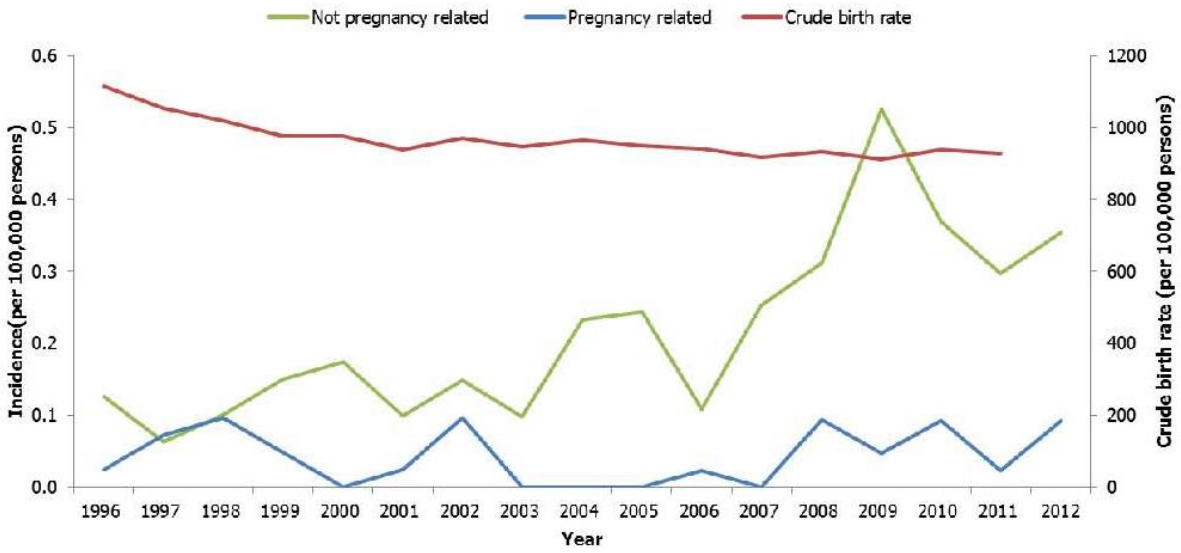


**Figure 2.** Number of invasive listeriosis disease by month of diagnosis, Austria, 2008-2012 (the bracket indicated cases within an outbreak)




The incidence of pregnancy-related and non-pregnancy related Listeriosis is illustrated in Figure 3. The incidence of non-pregnancy related Listeriosis increased since 2006 and reached a peak in 2009, the year in which the "Quargel" associated outbreak occurred.

**Figure 3.** Annual number of listeriosis cases in non-pregnant adults and children > 1 month of age (green line) and listeriosis cases in pregnant adults (blue lines), Austria, 1996–2012, Source: National surveillance data




The number of live births in 2012 is not available at the moment.

The number of invasive listeriosis disease cases and percentage of all the cases by province from 2008 to 2012 was given in the Figure 4.

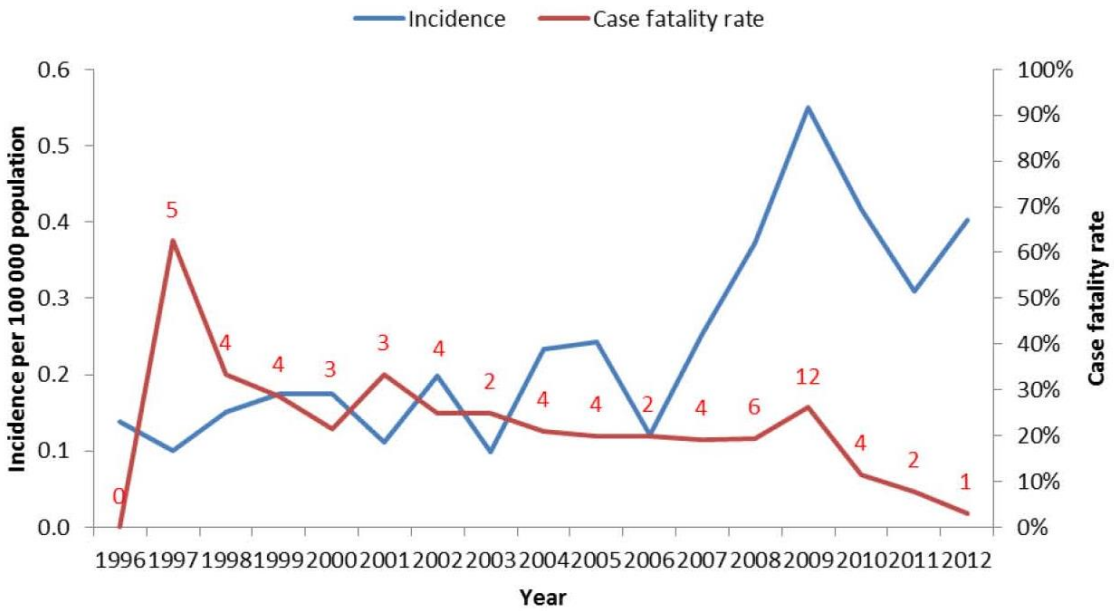
**Figure 4.** Annual incidence of invasive listeriosis disease (per 100,000 persons), number and percentage of cases by province, Austria, 2008-2012 (Source: National Reference Laboratory for *Listeria)*

| | | Province n (%) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Year | Annual incidence | B | K | NÖ | OÖ | S | ST | T | V | W |
| 2008 | 0.37 | 1(3) | 1(3) | 7(23) | 4(13) | 4(13) | 5(16) | 2(6) | 1(3) | 6(19) |
| 2009 | 0.55 | 1(2) | 4(9) | 8(17) | 3(7) | 4(9) | 5(11) | 3(7) | 1(2) | 17(37) |
| 2010 | 0.42 | 0 | 1(3) | 10(29) | 4(11) | 5(14) | 6(17) | 1(3) | 0 | 8(23) |
| 2011 | 0.31 | 2(8) | 4(15) | 8(31) | 3(12) | 1(4) | 4(15) | 0 | 2(8) | 2(8) |
| 2012 | 0.40 | 2(5) | 3(8) | 5(14) | 7(19) | 7(19) | 2(5) | 3(8) | 2(5) | 6(16) |

The color in red displayed the province with highest number of cases during 2008-2012

The trend of case fatality rate (CFR) decreased despite the incidence increase, the peak of increased CFR in 2009 was the year of the international outbreak (Figure 5).

**Figure 5.** Annual incience and case fatality, Austria, 1996-2012 (the number displayed the annual number of deaths)



## Prevention and control of listeriosis

General recommendations to prevent an infection with *Listeria* include proper washing and handling food, cook meat and poultry thoroughly, store foods safely and choose safer food (e.g. pasteurized milk). Higher risk group such as pregnant women and immunocompromised individuals should avoid consumption of foods such as not well-cooked hot dogs, delicatessen meats, soft cheese and smoked seafood, which can be contaminated with *Listeria* (1). In addition, the utilities used in the kitchen such as knives, countertops, and cutting boards, and refrigerators should clean up often to avoid cross-contamination.

In public health perspectives, promptly detect and investigate cluster of listeriosis through effective *listeria* surveillance system is crucial in order to take public health actions and interventions.

The control measure is aimed at the farm and food-processing level, in order to prevent contamination of food products. To avoid raw milk contamination at farm, good farm practices (e.g. animal and waste management, water treatment, good hygienic conditions during milking and mastitis control) are essential to prevent the accumulation, survival, and transmission of pathogens. At the processing factories, in order to prevent colonization of the processing environment by *L. monocytogenes*, plant layout and equipment should be designed to be more hygienic, such as without edges, crevices and dead spaces to facilitate good working routines and to ensure an effective sanitation process (2).

## Standard prevention and control strategies in Austria

Austrian Agency for Health and Food Safety (AGES) has published Zoonoses Community Summary Report and listeriosis annual report for disseminating epidemiological data, standard prevention and control strategies. Emphasize kitchen hygiene and rules to minimise the risk of foodborne infection include cooking meat and fish thoroughly, boiling raw milk, and no consumption of raw meat and regular washing of hands.

The Austrian guidelines on microbiological critereia for milk and milk production are based on Directive 92/46/EEC of the EU commission (Discussion paper on strategy for setting microbiological criteria for foodstuffs in Community legislation). Detailed criteria regarding milk and milk products proposed by the Scientific Committee on Veterinary Measures relating to Public Health (SCVPH) in 2005 are given in Appendix 2.

## Microbiological criteria for foodstuff on sampling and testing

The microbiological criteria according to EU investigation regulation (EC) No 2073/2005 valid since Jan 2006 on microbiological criteria for foodstuffs (e.g. dairy products and ready-to-eat food) are used for verification of good hygiene practices and HACCP-based procedures which are mandatory for the food business apply in Austria (3). The regulation differs in terms of food safety criterion for *L. monocytogenes* which classified into three food categories for ready to eat food and gives an overview of the appropriate sampling plans (Appendix 3).

Samples shall be taken from processing areas and equipment used in food production, when such sampling is necessary for ensuring that the criteria are met. In that sampling the ISO standard 18593 shall be used as a reference method. Food business operators manufacturing ready-to-eat foods and dairy products, which may pose a *L. monocytogenes* risk for public health, shall sample the processing areas (e.g. water, grease, salt bath) and equipment for *L. monocytogenes* as part of their sampling scheme.

The analytical reference method for detection and enrichment of *L. monocytogenes* is according to the European Committee for Standardization EN/ ISO 11290-1 and 11290-2 standard operating procedures. In Austria, the food and environmental specimens are examined in the laboratory of IMML base on the standard operating procedures (4).

# Description of the surveillance system

## Objective of the surveillance system

We identified five objectives of the Austrian Listeria surveillance system determined in the Epidemic Act (Epidemiegesetz, BGBL. Nr. 186/1950) and Zoonoses Act (Zoonosengesetz, BGBl. I Nr. 128/2005), which has been adapted to the goals for the Surveillance of Communicable Diseases in the EU (7) (the laws are illustrated in Appendix1).

1. Monitor trends in listeriosis incidence in order to assess the present situation in real-time to respond to rises above warning thresholds and to facilitate appropriate evidence-based action;

2. Detect and monitor any listeriosis outbreaks with respect to source, time, population and place, in order to provide a rationale for public health action;

3. Identify population groups at risk and in need for targeted prevention measures;

4. Generate hypotheses on (new) sources, modes of transmission and groups most at risk and identify needs for research and development and for pilot projects;

5. Report Austrian Listeria data to TESSy according to Decision No 2119/98/EC (6).

## Population under surveillance

We consulted the federal institute Statistics Austria for information on the population under surveillance including age, sex and province of residence. The role of Statistics Austria is to provide reliably collected and expertly analyzed political, social and economic information in Austria and is owned by the state.
The comprehensive surveillance system includes the entire Austrian population under surveillance (8,489,482 in 2013). The Federal Republic of Austria lies in central Europe and covers an area of 83,870 sq km. Austria is surrounded by the Czech Republic, Germany, Hungary, Italy, Liechtenstein, Slovakia, Slovenia, and Switzerland. Austria is divided into nine provinces: Burgenland, Carinthia, Lower Austria, Upper Austria, Salzburg, Styria, Tyrol, Vorarlberg, and Vienna. The official national language is German although Croatian, Hungarian and Slovenian are recognized as regional languages. Austria is divided into a total of 106 district PH offices within the 9 provinces.

## Case definitions

The surveillance system applies the case definition of listeriosis given by WHO until 2008. Since 2009, the case definitions comply with the new EU case definition (Decision No 2119/98/EC of the European Parliament and of the Council).

### Table 1. Case definitions, EU

| **Case Definition** | | |
|---|---|---|
| **Clinical Criteria** | Stillbirth | |
| | the first month of life:<br>at least 1 of the 5 following symptoms | • Granulomatosis infantiseptica<br>• Meningitis or meningoencephalitis<br>• Septicaemia<br>• Dyspnoea<br>• Lesions on skin, mucosal membranes or conjunctivae |
| | Pregnancy:<br>at least 1 of the 3 following symptoms | • Abortion, miscarriage, stillbirth or premature birth<br>• Fever<br>• Influenza-like symptoms |
| | Other:<br>at least 1 of the 4 following symptoms | • Fever<br>• Meningitis or meningoencephalitis<br>• Septicaemia<br>• Localised infections such as arthritis, endocarditis, and abscesses |
| **Laboratory Criteria**<br>At least 1 of the following 2 | • Isolation of Listeria monocytogenes from a normally sterile site<br>• Isolation of Listeria monocytogenes from a normally non-sterile site in a foetus, stillborn, newborn or the mother at or within 24 hours of birth | |
| **Epidemiological Criteria**<br>At least 1 of the following 3 epidemiological links | • Exposure to a common source<br>• Human to human transmission (vertical transmission)<br>• Exposure to contaminated food/drinking water | |
| **Additional information** | • Incubation period 3-70 days, most often 21 days | |
| **Case Classification** | Possible case | Not applicable |
| | Probable case | Any person meeting the clinical criteria and with an epidemiological link |
| | Confirmed case | Any person meeting the laboratory criteria<br>OR<br>Any mother with a laboratory confirmed listeriosis infection in her foetus, stillborn or newborn |

## Type of the surveillance system

Since 1996 a compulsory, comprehensive, passive, case-based surveillance system for zoonoses and zoonotic agents has been in place. The Zoonoses Act (Bundesgesetz zur Überwachung von Zoonosen und Zoonoseerregern, BGBl I Nr. 128/2005) in 2005 re-defined the zoonoses and antibiotic resistance surveillance systems and the National Reference Centres for zoonotic agents (7).

## Data Structure

Detailed description about data structure of the current case-based surveillance system for *listeria* is given in the chapter of evaluation result of simplicity (Figure 6).

For detection of food and environmental specimens with listeria contamination, the food inspectors collect specimens and submitted to the Institute for Milk Hygiene, Milk Technology and Food science (IMML) for further diagnosis. The isolates of *Listeria* were submitted to National Reference Laboratory for PFGE analysis. The laboratory data of both food and human specimens were generated by the National Reference Centre for *Listeria*. The notification data and the laboratory data are merged into one case record located in the National electronic web-based reporting system (NeRS). This dataset is uploaded regularly to TESSy by the Federal Ministry of Health (MoH).

## The role of National Reference Laboratory for Listeria

The National Reference Laboratory for *Listeria* is located within the AGES at the Center for Foodborne infectious diseases, Institute for Medical Microbiology and Hygiene, Graz.
The designation was based on the EU Regulation (EC) Nr.882/2004 that each Member State is required to designate the relevant reference laboratories for specific tests of foods and human specimens. The jurisdiction of the National Listeria Reference Laboratory included for the test of human specimens and food products such as dairy products to detect infection or contamination of *Listeria monocytogenes.* The role and request form for the submission of isolates of *Listeria monocytogenes* were according to Food Safety and Consumer Protection Act (LMSVG) § 38 Abs. 1-6, § 74 and §75.

## The role of the Institute for Milk Hygiene, Milk Technology and Food Science

The Institute for Milk Hygiene, Milk Technology and Food Science (IMML) is a teaching, research and food-sample testing institute at Department of Animal Production and Public Health in Veterinary Medicine, University of Vienna. IMML organize platforms for knowledge transfer, training events and lectures at conferences on current issues in food safety in Austria. In addition, IMML have also involved in the environment monitoring and product contamination chain investigations. IMML offers the interdisciplinary entanglement of activities with other universities and risk assessment bodies such as the Austrian Agency for Food and Food Safety (AGES) and other responsible authorities (8). The research of the IMML is organized into five working groups:

Innovative methods of detection,

Molecular epidemiology,

Adaptation of pathogenic microorganisms

Global aspects of food safety and

Food-associated Zoonotic Ecology (post-doctoral program of the University of Veterinary Medicine Vienna)

In addition to IMML, the Federal Institute for Alpine Dairy Farming (Bundesanstalt für Alpenländische Milchwirtschaft, abbreviated as BAM redwood) also monitors *Listeria* in dairy products since 2004 in Austria. BAM redwood also provides hygiene training and education courses for cheese technological information include control of *Listeria* (9).

## Indicators

The indicators of the surveillance system are the monthly and annual number of cases at the MoH website and the annual incidence/100,000 population total and by age, sex, and province, the annual number of cases by serotype and PFGE (pulse filed gel-electrophoresis) type, 28-days mortality/100,000 population, case fatality and the annual number of registered outbreaks provided in the annual surveillance report of the National Reference laboratory.

## Feedback

The annual report "Report on Zoonoses and Zoonotic agents" published by Ministry of Health and Austrian Agency for Health and Food Safety (AGES) is to disseminate information of surveillance of zoonoses in Austria, which include *listeria* infection. The MoH also publishes the number of *Listeria* cases online each month: "Monatliche Statistik meldepflichtiger Infektionskrankheiten" since 2005. The MoH has published the number of Listeria cases that are reported to the National electronic web-based reporting system (NeRS) each month on the "Monatliche Statistik meldepflichtiger Infektionskrankheiten", with a lag of one month. This is generated by National Reference Centre for *Listeria* and reported to MoH or directly extracted from NeRS by MoH since 2009. The annual report of Annual statistics of notifiable infectious diseases (Statistik meldepflichtiger Infektionskrankheiten vorläufiger Jahresbericht) has been published as the news letters by MoH, which includes listeriosis.

On the provincial public health directorate level, the provincial PH director is assigned the task of overseeing *Listeria*-surveillance and also supports the coordination of province-border-crossing outbreaks together with the Federal Zoonoses Commission. The provincial PH director has access to anonymous province-specific data within the NeRS in order to monitor the epidemiological trends. At the start of the following year, the total number of *Listeria* cases is made available only provisionally as the numbers are then corrected and confirmed over the course of the year. One additional advantage is that the *Listeria* data that is collected in the NeRS can also be submitted to TESSy via the MoH directly. Furthermore, the binational cooperation for *listeria* via Binational Consulting Laboratory for Listeria Germany / Austria established the bond between the Institute for Medical Microbiology and Hygiene, AGES and Robert Koch Institute to encourage the European network in German-speaking countries, with the consistent aim and better resources to control rare infectious disease such as listeriosis.

## Action taken

The binational Austrian-German Consiliar Laboratory for Listeria in Vienna noticed a cluster of human isolates of *L.monocytogenes* serotype 1/2a in August 2009. Fourteen cases with onset of disease ranged from June 2009 to January 2010. An epidemiological investigation revealed 'Quargel' cheese produced by an Austrian manufacturer as the source of infection. The product was withdrawn from the Austrian, German, Slovakian and Czech markets on 23 January 2010 according to MoH (10). This was criticized as too long to recall the incriminated products. During that time, Austrian law illustrated that before any public health reaction such as food product recall, microbiological evidence of identical pathogen in the food product is required. As a direct influence of this outbreak, since 21 April 2010, the Austrian government amended its Food Safety and Consumer Protection Act (LMSVG) to enable products recall announcing by health authorities base on epidemiological evidence before microbiological evidence being confirmed (11).
Another room for improvement from the experience of this outbreak is risk communication to the public, especially if hard-to-reach group (e.g. the elderly) is involved. There were at least two additional cases associated to consumption of the contaminated Quargel after date of product recall, which means the information is not well disseminated to all the public at risk or some people reluctant to dispose of food even though information has been informed. House visit of the patient is important to be able to obtain possible food leftover and to advise other family members on precautionary procedures.

# Methods of the evaluation of the Surveillance System

## Goal

To assess whether the objectives of the surveillance system for Listeriosis are fulfilled

## Aim

The aim of the evaluation of the surveillance system will be to assess whether the system has the appropriate simplicity and timeliness to reach the following objectives of the system:

> Detect and monitor any listeriosis outbreaks with respect to source, time, population and place, in order to provide a rationale for public health action.

## Evaluation of the surveillance system

In the following we describe method/materials on the simplicity and timeliness before and after implementation of NeRS in 2009 (Table 2).

**Table 2.** Methods used for evaluation of the two selected attributes (simplicity and timeliness)

| Attribute | Method |
|---|---|
| **Simplicity** | **Study objective:** To assess the simplicity of the *Listeria* surveillance system through identifying and comparing the number of components and data pathways, and the mode of data analysis before and after implementation of the National electronic web-based reporting system (NeRS) for statutorily notifiable diseases in Austria<br>**Study design:** Before - After Intervention Study<br>**Study population:** The whole population of Austria<br>**Outcome:** The difference in the number of components and data transfer pathways before and after the implementation of NeRS<br>**Data analysis plan:** Personal interviews will be performed with AGES Department of Infectious Disease Epidemiology and National Reference Centre for *Listeria* to compare the number of components and number of data transfers before and after the implementation of NeRS include<br>·Number of stakeholders involved in data production e.g. physicians, primary laboratories and the reference laboratories<br>·Document used to collect data<br>·Interface used to transfer data<br>·Stakeholders involved in data transfer (senders and receivers)<br>·Software used for data managing and data analysis (e.g. MS Excel and Epi info) |
| **Timeliness** | **Study objective:** To assess the timeliness of the *Listeria* surveillance system by measuring the median time of delivery process include from date of onset to blood or CSF specimen receipt at primary laboratories until the last step of case record entry into the NeRS<br>**Study design:** Before - After Intervention Study<br>**Study population:** The surveillance system before (-2008)and after the implementation of NeRS (2009-)<br>**Outcome:** Median length of time between<br>·the interval between date of specimen collection and date of specimen arrival at the laboratory for the Listeria surveillance system, 1996-2008<br>·date of onset, date of diagnosis and date of notification since 2009<br>**Data analysis plan:** Calculation of the median length of time mentioned above |

# Results of the Evaluation of the surveillance system

## Simplicity

The number of components, data pathways, and the mode of data analysis were compared before (-2008) and after (2009-2011) implementation of the National electronic web-based reporting system (NeRS) in Austria (Figures 5). The implementation of the NeRS eliminated two steps in the case data reporting process between local and national level due to the direct entry of case data at local level. Previously, the data transfer step between the district public health office to the provincial public health department and the step between the provincial PH directorates to the Ministry of Health had been conducted on a monthly schedule to transfer case records to the national level. In addition, the National Reference Centre for *Listeria* no longer needs to provide the MoH with the data monthly and annually. The MoH is able to access Austrian dataset of listeriosis from the NeRS anonymously. The National Reference Laboratory for *Listeria* also entry the results of food and environmental samples through NeRS, in order to response and investigate possible foodborne listeriosis outbreaks promptly. The implementation of NeRS does simplify the surveillance system for *Listeria* in humans and animals (Figure 6).

**Figure 6.** Data flow in the case-based surveillance system for Listeria **after** the implementation of NeRS in Austria

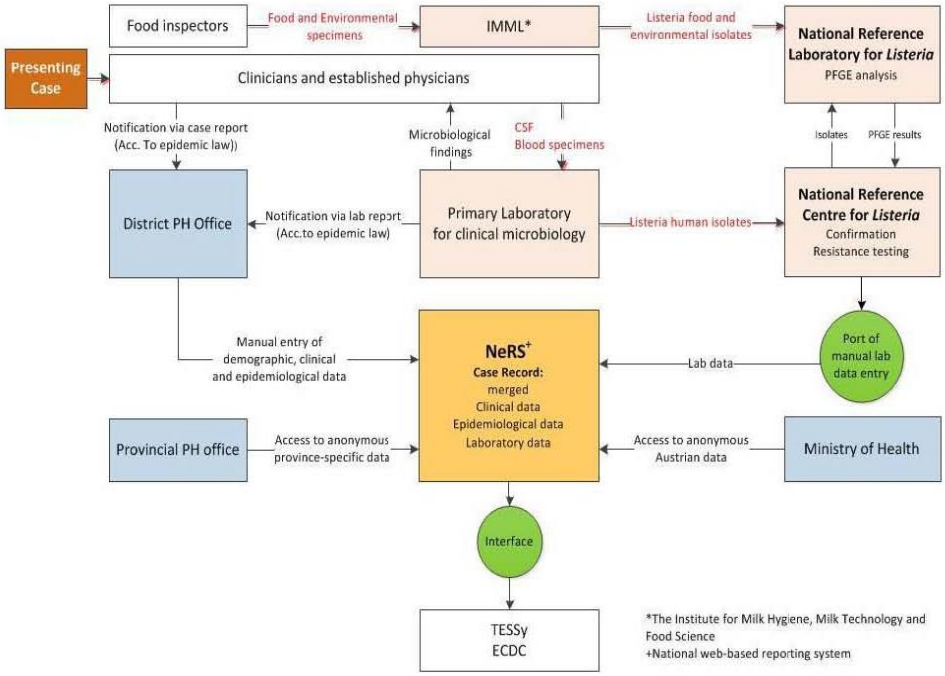


Figure 6 provides a detailed view on the current system case data generating components, data collection and transition. Arrows indicate the direction of the data transition, squares indicate the components participating in the surveillance system and circles indicate the mode of data entry into the National electronic web-based reporting system (NeRS) and TESSy.

The current structure of the case-based *Listeria* surveillance system has been in place since 2009, when the Ministry of Health implemented the National electronic web-based reporting system (NeRS). There are six main components which participate in the Listeria surveillance system for human in Austria: the Listeria-case-detecting clinicians and physicians with praxis, the district PH office, the primary laboratory, the National Reference Centre for *Listeria*, the National Reference Laboratory for Listeria, the National electronic web-based reporting system (NeRS) and the Ministry of Health.

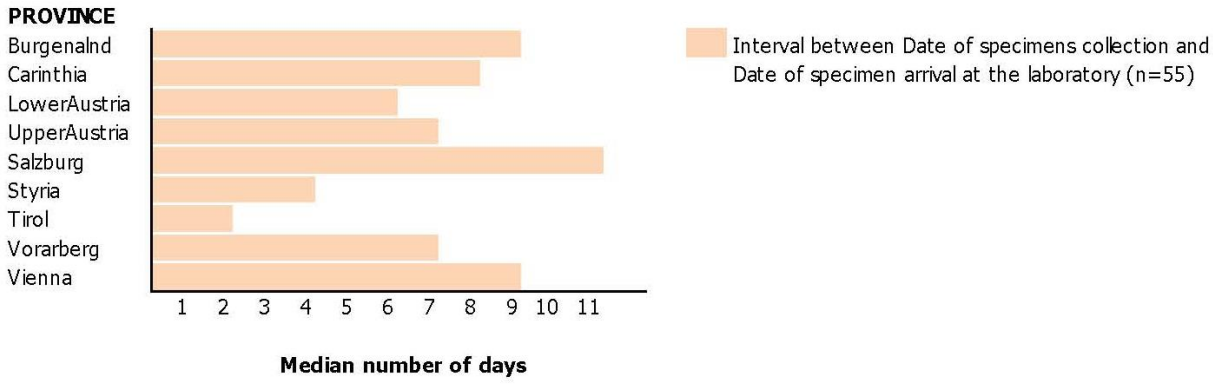
## Timeliness

Monthly and annual report of notifiable communicable diseases (Monatliche Statistik meldepflichtiger übertragbarer Infektionskrankheiten and Jahresstatistik meldepflichtiger Infektionskrankheiten) have been uploaded on the official website of Ministry of Health included the number of cases for listeriosis since 2005 (12). Before 2005, listeriosis was not included in the annual surveillance report. However, the case-based information of listeriosis in Austria from the National Reference Laboratory of *Listeria* or the National Reference Centre for *Listeria* was available since 1997 onwards.

Timeliness of the Listeria surveillance system to compare prior to and after implementing National electronic web-based reporting system (NeRS) was calculated by measuring the median time of time-related information available in the dataset. From 1996 to 2008, date of specimen collection and date of specimen arrival at the primary laboratories are the only information available to calculate timeliness. The date of specimen arrival refers to the date when the CSF or blood specimens are received at the primary laboratories for clinical microbiology.

A total of 55 out of 172 cases with both information on the sampling date and date of specimens arrival at the primary laboratories available from 1996-2008, the period before NeRS has been implemented (Figure 7). The median days of the interval between date of specimen collected and date of specimens arrival at the primary laboratories are 6 days (Max: 688, Min: 0).

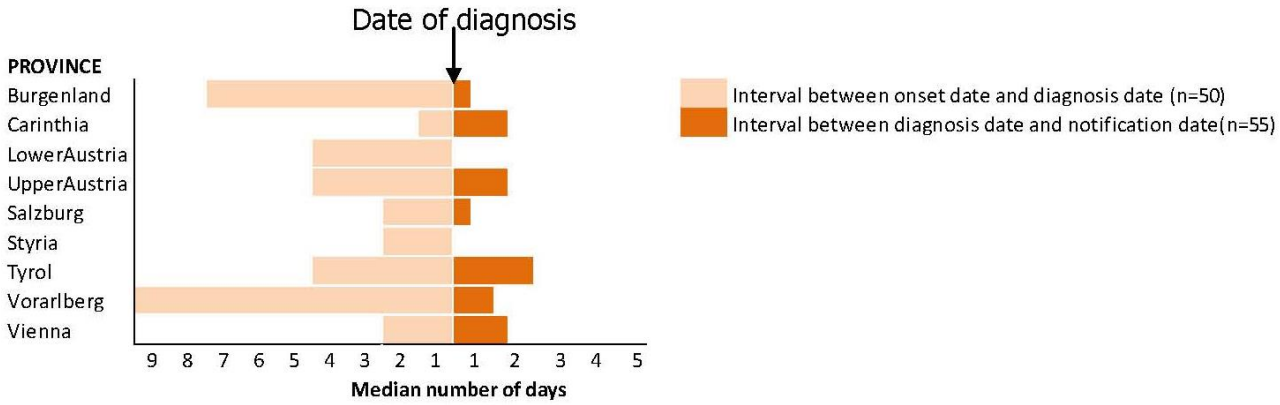
**Figure 7.** The median interval between date of specimen collection and date of specimen arrival at the primary laboratories for the *Listeria* surveillance system, 1996-2008, Austria




After the NeRS has implemented, there were three date variables that were used to calculate timeliness from *Listeria* case records from 2009 to 2011 (2012 not available): date of onset, date of diagnosis and date of notification.

A total of 96 out of 107 cases with the information on both the onset date and the diagnosis date available, the medians days of intervals from 2009-2011 are two days (Max: 17, Min: 0). A total of 101 out of 107 cases with the information on both the diagnosis date and the notification date available, the medians days of intervals from 2009-2011 are one day (Max: 28, Min: 0). Compare to the interval before the NeRS has been implemented, data transmission efficiency has improved. The information of cases with data available on both time-related variables and reported province were given in Figure 8. The median time between date of onset and date and diagnosis among the Austrian provinces range from 1.5 days in Carinthia to nine days in Vorarlberg during 2009 and 2011. The intervals between date of diagnosis and date of notification range from zero days in Styria to 2.5 days in Tyrol.

**Figure 8.** The median time between date of disease onset, date of diagnosis and date of notification among cases reported to NeRS within the *Listeria* surveillance system by province, 2009-2011



# Discussion

Through establishing the surveillance system for listeriosis according to the Epidemic and Zoonoses Act, the incidence of listeriosis has been monitored to detect any possible cluster or outbreak. In combination with the result from food and environmental specimens, the surveillance system is able to detect and monitor any listeriosis outbreaks with respect to source, time, population and place, in order to provide a rationale for public health action.
The implementation of the NeRS enables the MoH to ransfer data to TESSy on a regular basis.

Based on the results from the attribute simplicity, the implementation of the NeRS eliminated two steps from the data reporting process. The NeRS provided the district, province and national levels of the surveillance system with direct access to analyse and monitor the trends of listeriosis in real-time. The NeRS also reduced the time needed between case identification and case reporting compared to the previous surveillance system structure. The results of the calculation of the timeliness of this step in the reporting process enables observation of the listeriosis trends in real-time in order to provide a rationale for public health action.

The limited date variables available in the former surveillance system provided limited information on the evaluation of timeliness of the system prior to implementation of the NeRS. Without the variables date of diagnosis and date of notification, we could not calculate timeliness when the data was made available at the national level.
One recommendation for further investigation would be to include attributes such as sensitivity and completeness, which have not yet been assessed, and thus a comprehensive conclusion whether system achieves all objectives is still pending.

# References


1. Allerberger F, Wagner M. Listeriosis: a resurgent foodborne infection. Clin. Microbiol. Infect. 2010 Jan;16(1):16–23.

2. Kousta M, Mataragas M, Skandamis P, Drosinos EH. Prevalence and sources of cheese contamination with pathogens at farm and processing levels. Food Control. 2010 Jun;21(6):805–15.

3. EUROPA - Food Safety - Biological Safety of Food - Salmonella and Food-borne Diseases - Microbiological Criteria [Internet]. [cited 2013 Apr 10]. Available from: http://ec.europa.eu/food/food/biosafety/salmonella/microbio_en.htm

4. University of Veterinary Medicine Vienna - Research portal [Internet]. [cited 2013 Apr 10]. Available from: http://vmutpp.vu-wien.ac.at/vuw/fodok/suche.publikationen_suchergebnis

5. Surveillance objectives [Internet]. [cited 2013 Jan 8]. Available from: http://ecdc.europa.eu/en/activities/surveillance/strategies_principles/Pages/surveillance_objectives.aspx

6. EUR-Lex - 31998D2119 - EN [Internet]. [cited 2013 Jan 8]. Available from: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31998D2119:EN:NOT

7. RIS - Gesamte Rechtsvorschrift für Epidemiegesetz 1950 - Bundesrecht konsolidiert, Fassung vom 03.11.2011 [Internet]. [cited 2011 Nov 3]. Available from: http://www.ris.bka.gv.at/GeltendeFassung.wxe?Abfrage=Bundesnormen&Gesetzesnummer=10010265&ShowPrintPreview=True

8. Vetmeduni Vienna : Institut für Milchhygiene : Über uns [Internet]. [cited 2013 Apr 10]. Available from: http://www.vetmeduni.ac.at/de/milchhygiene/ueber-uns/

9. willkommen-bei-der-bam-rotholz | home [Internet]. [cited 2013 Apr 10]. Available from: http://www.bam-rotholz.at/

10. Fretz R, Pichler J, Sagel U, Much P, Ruppitsch W, Pietzka AT, et al. Update: Multinational listeriosis outbreak due to 'Quargel', a sour milk curd cheese, caused by two different L. monocytogenes serotype 1/2a strains, 2009-2010. Euro Surveill. 2010 Apr 22;15(16).

11. Pichler J, Appl G, Pietzka A, Allerberger F. Lessons to be Learned from an Outbreak of Foodborne Listeriosis, Austria 2009–2010. Food Protection Trends. 2011 May;31(5):16–21.

12. Monatliche Statistik meldepflichtiger übertragbarer Infektionskrankheiten 2012 [Internet]. [cited 2012 Aug 13]. Available from: http://bmg.gv.at/home/Schwerpunkte/Krankheiten/Uebertragbare_Krankheiten/Statistiken/Monatliche_Statistik_meldepflichtiger_uebertragbarer_Infektionskrankheiten_2012

# Appendix

## 1. The objective of surveillance system for *Listeria*

1 Monitor trends in listeriosis incidence in order to assess the present situation in real-time to respond to rises above warning thresholds and to facilitate appropriate evidence-based action;

ZOONOSES ACT–

i. §1 (1) and §3 (1) – goals for methodological surveillance established

ii. §8 and Annex 3 – Zoonoses report requirements

EPIDEMIC ACT –

iii. §2 (1) – all notifiable diseases are required to be reported to the appropriate district PH office within 24 hours

iv. §3 (2) – duties of federal zoonoses commission for zoonoses surveillance

v. §4 (8) – within framework of epidemiological surveillance, access to personal data of cases allowed

2 Detect and monitor any listeriosis outbreaks with respect to source, time, population and place, in order to provide a rationale for public health action;

ZOONOSES ACT–

i. §4 (1) – established outbreak response duties for provincial governors

ii. §7 – Data required to be collected in foodborne outbreaks

EPIDEMIC ACT –

iii. §26a (1) – all isolates must be sent to National Reference Laboratories for confirmation

3 Identify population groups at risk and in need for targeted prevention measures;

ZOONOSES ACT–

i. §5 (1) – general regulations of zoonoses surveillance include recognition, description and evaluation of potential health hazards

EPIDEMIC ACT

ii. §4 (4) – all data collected in the registry for notifiable diseases must also include prevention measures implemented

4 Generate hypotheses on (new) sources, modes of transmission and groups most at risk and identify needs for research and development and for pilot projects;

ZOONOSES ACT

i. §3 (2)– integrated risk assessment within zoonoses surveillance

5 Report Austrian Listeria data to TESSy according to Decision No 2119/98/EC.

## 2. The interim criteria proposed by the Scientific Committee on Veterinary Measures relating to Public Health (SCVPH), 2005

| Food category | Criteria in current Community legislation | Interim criteria proposed in the opinion of the SCVPH | Other opinions or comments from the SCVPH |
|---|---|---|---|
| Cheeses made from raw milk and from thermized milk (Dir. 92/46/EEC) | *Listeria monocytogenes* | Retain (not concerning hard cheese) | |
| | *Salmonella* | Retain (not concerning hard cheese) | |
| Soft cheese (made from heat-treated milk) (Dir.92/46/EEC) | *Listeria monocytogenes* | Standard | |
| | *Salmonella* | Deletion | |
| | *S. aureus*, guideline | Standard | |
| | *E. coli*, guideline | Deletion | |
| | Coliforms, guideline | Replace with *Enterobacteriacae* | |
| Fresh cheese (Dir. 92/46/EEC) | *Listeria monocytogenes* | Standard for cheeses made from raw/thermised milk | |
| | *Salmonella* | Standard for cheeses made from raw/thermised milk | |
| | *S. aureus*, guideline | Deletion in cheese produced by fermentation | |
| Other cheeses than those mentioned above (Directive 92/46/EEC) | *Listeria monocytogenes* | Deletion | |
| | *Salmonella* | Deletion | |
| Butter (Dir. 92/46/EEC) | *Listeria monocytogenes* | Deletion | |
| | *Salmonella* | Deletion | |
| | Coliforms, guideline | Deletion | |
| Powdered milk (Dir. 92/46/EEC) | *Salmonella* | Standard | |
| | *Listeria monocytogenes* | Deletion | |
| | S. aureus, guideline | Deletion | |
| Frozen milk-based products (Dir. 92/46/EEC) | *Salmonella* | Deletion | |
| | *Listeria monocytogenes* | Deletion | |
| | *S. aureus*, guideline | None | |
| | Coliforms, guideline | Replace with *Enterobacteriacae* | |
| | Aerobic plate count, guideline | Deletion | |
| Liquid milk-based products and powdered milk-based products (Dir. 92/46/EEC) | *Salmonella* | Standard only for products made from raw/thermised milk | |
| | *Listeria monocytogenes* | Standard only for products made from raw/thermised milk | |
| | Coliforms, guideline | Replace with *Enterobacteriacae* | |
| | Aerobic plate count (for liquid heat-treated unfermented milk based products) | Guideline | |

## 3. Sampling plans for *Listeria monocytogenes* according to Regulation (EC) 2073/2005

| | Food category | Micro-organisms/their toxins, metabolites | Sampling plan (1) | | Limits (2) | | Analytical reference method (3) | Stage where the criterion applies |
|---|---|---|---|---|---|---|---|---|
| | | | n | c | m | M | | |
| 1.1 | Ready-to-eat foods intended for infants and ready-to-eat foods for special medical purposes (4) | *Listeria monocytogenes* | 10 | 0 | Absence in 25 g | | EN/ISO 11290-1 | Products placed on the market during their shelf-life |
| 1.2 | Ready-to-eat foods able to support the growth of *L. monocytogenes*, other than those intended for infants and for special medical purposes | *Listeria monocytogenes* | 5 | 0 | 100 cfu/g (5) | | EN/ISO 11290-2 (6) | Products placed on the market during their shelf-life |
| | | | 5 | 0 | Absence in 25 g (7) | | EN/ISO 11290-1 | Before the food has left the immediate control of the food business operator, who has produced it |
| 1.3 | Ready-to-eat foods unable to support the growth of *L. monocytogenes*, other than those intended for infants and for special medical purposes (4) (8) | *Listeria monocytogenes* | 5 | 0 | 100 cfu/g | | EN/ISO 11290-2 (6) | Products placed on the market during their shelf-life |

(1) n = number of units comprising the sample; c = number of sample units giving values between m and M.
(2) For points 1.1-1.25 m = M.
(3) The most recent edition of the standard shall be used.
(4) Regular testing against the criterion is not required in normal circumstances for the following ready-to-eat foods:—
those which have received heat treatment or other processing effective to eliminate *L. monocytogenes*, when recontamination is not possible after this treatment (for example, products heat treated in their final package),
— fresh, uncut and unprocessed vegetables and fruits, excluding sprouted seeds,
— bread, biscuits and similar products,
— bottled or packed waters, soft drinks, beer, cider, wine, spirits and similar products,
— sugar, honey and confectionery, including cocoa and chocolate products,
— live bivalve molluscs.
(5) This criterion shall apply if the manufacturer is able to demonstrate, to the satisfaction of the competent authority, that the product will not exceed the limit 100 cfu/g throughout the shelf-life. The operator may fix intermediate limits during the process that must be low enough to guarantee that the limit of 100 cfu/g is not exceeded at the end of shelf-life.
(6) 1 ml of inoculum is plated on a Petri dish of 140 mm diameter or on three Petri dishes of 90 mm diameter.
(7) This criterion shall apply to products before they have left the immediate control of the producing food business operator, when he is not able to demonstrate, to the satisfaction of the competent authority, that the product will not exceed the limit of 100 cfu/g throughout the shelf-life.
(8) Products with pH ≤ 4,4 or $a_w$ ≤ 0,92, products with pH ≤ 5,0 and $a_w$ ≤ 0,94, products with a shelf-life of less than five days shall be automatically considered to belong to this category. Other categories of products can also belong to this category, subject to scientific justification.

# 7. 奧地利百日咳 2005 至 2011 年趨勢報告壁報

Poster No. 21.147

## Increasing incidence of pertussis in Austria, 2005-2011

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### Background

- Within the previous 3-5 years, a substantial rise in reported cases of pertussis has been noticed in two of the nine Austrian provinces
- The Federal Ministry of Health mandated the AGES to assess the observed different trends and to generate hypotheses on possible reasons for the findings on trend differences among the provinces
- Since 2010, primary pertussis vaccine series have been recommended among infants aged 3mo, 5mo and 12mo

### Methods

- National surveillance data were used: monthly aggregated data for 2005-2008; cased-based data for 2009-2011
- Case definition used: WHO recommendation until 2008; EU/ECDC recommendation since 2009 onwards
- From 2005-2011: Annual incidence of total Austrian population by province
- From 2009-2011: Annual incidence by age-group and age-group specific proportional distribution by onset month

Province-specific proportional distribution of cases by case classification (possible, probable, confirmed)

### Results

- From 2006-2011; in 3/9 provinces incidence increased :
  **St**yria: by 3.5/100,000/y, **Sa**lzburg: by 1.9/100,000/y, **UA**: by 1.0/100,000/y
- From 2009-2011; in province **T**yrol increase from 0.3-5.8/100,000.
- The other 5 provinces showed stable incidences ("low/stable incidence provinces")
- In 3 of the 4 "high-incidence provinces", age-group 0-14 y only affected
- In 1 of the 4 "high-incidence provinces", both age-groups 0-14 y und ≥15 y affected (Fig. 1, 2 and 4).

**Fig.1.** Pertussis incidence in the nine provinces of Austria, 2005-2011

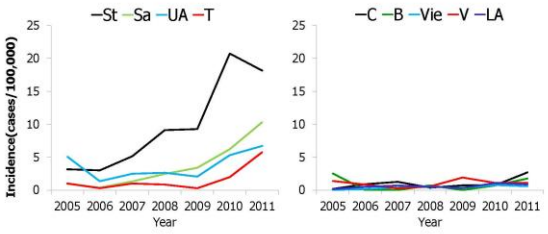
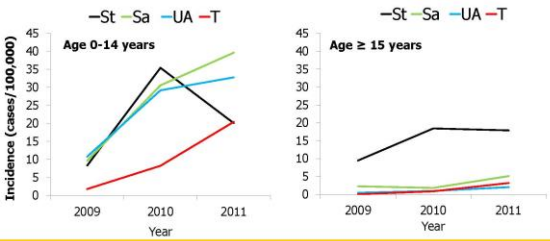
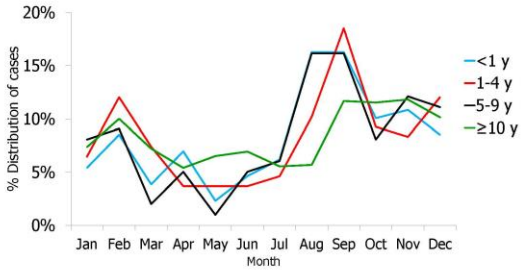



**Fig. 2.** Pertussis disease incidence by age group, Austria, 2009-2011




- In the 0-9 years old: cases (10-19%) peaked in Aug/Sep and in February (9-12%)
- In the ≥ 10 years old, cases peaked (10-12 %) from Sep - Dec (Fig. 3)

**Fig. 3.** Proprotional case distribution by age and month of onset, 2009-2011




- No significant difference in the case distribution by classification between "high-incidence provinces" and "low/stable incidence provinces" (p=0.639) during 2009-2011

**Fig. 4.** Geographical location of the four "high-incidence provinces" (in grey) and the five "low/stable incidence provinces" (in white) in Austria


### Conclusions

- Based on the national surveillance data we found four provinces, which experienced a considerable increase within the past 3-5 years (= high incidence provinces)
- The other five provinces showed stable incidence or decreasing trend (=low/stable incidence provinces)
- In one of the four "high incidence provinces" all age groups were affected: Styria
- The hypotheses on reasons for the provincial differences in the annual incidence trend:
  - Different notification behaviour of physicians
  - Clinical misclassification of cases
  - Laboratory misclassification of cases
  - Different province specific vaccine coverage of primary or booster immunisation

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8. 奧地利百日咳流行病學分析研究—橫斷式 KAP 調查

# Knowledge, practices and attitudes on pertussis among physicians in Austria, 2013

A cross sectional study among

general practitioners, pediatricians and pulmonologists

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2012-2013

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# Background

## Epidemiology in Austria

The "Österreichische Gesellschaft für Pneumologie" (The Austrian Society of Pulmonology) raised the concern of an increasing trend in the pertussis notification rate since 2006 in Styria, one of the nine Austrian provinces based on national surveillance data. The provincial public health authority of the province Tyrol reported an increase in the notification rate of pertussis since 2009. The Chief Public Health Officer at the Austrian Federal Ministry of Health, PhD Dr. P. Rendi-Wagner mandated the Austrian Agency for Health and Food Safety (AGES) to investigate and identify potential reasons for these observations.

We analyzed the national surveillance data on pertussis cases for the time period 1990 to 2012 to describe the trends of annual notification rate of pertussis among the total Austrian population, by the nine Austrian provinces and by the age groups. Findings indicate that, after a period of decreasing and stable trend in the annual notification rate in the total Austrian population (Figure 1), there was increasing annual notification rate in four of the nine provinces including Styria (3.0-23.7/100,000), Upper Austria (1.4-6.8/100,000), Salzburg (0.4-8.9/100,000) from 2006 to 2012 and Tyrol from 2009 to 2012 (0.3-7.6/100,000) (Figure2a). In the other five Austrian provinces decreasing, stable or slightly increasing annual notification rate was observed from 1990-2012: Vienna (2.7-1.0/100,000), Carinthia (3.7-0.7/100,000), Lower Austria (1.9-2.3/100,000), Vorarlberg (2.1-4.8/100,000) and Burgenland (1.8-3.5/100,000) (Figure 2b).

**Figure 1**. Annual notification rate of pertussis in Austria, 1990-2012

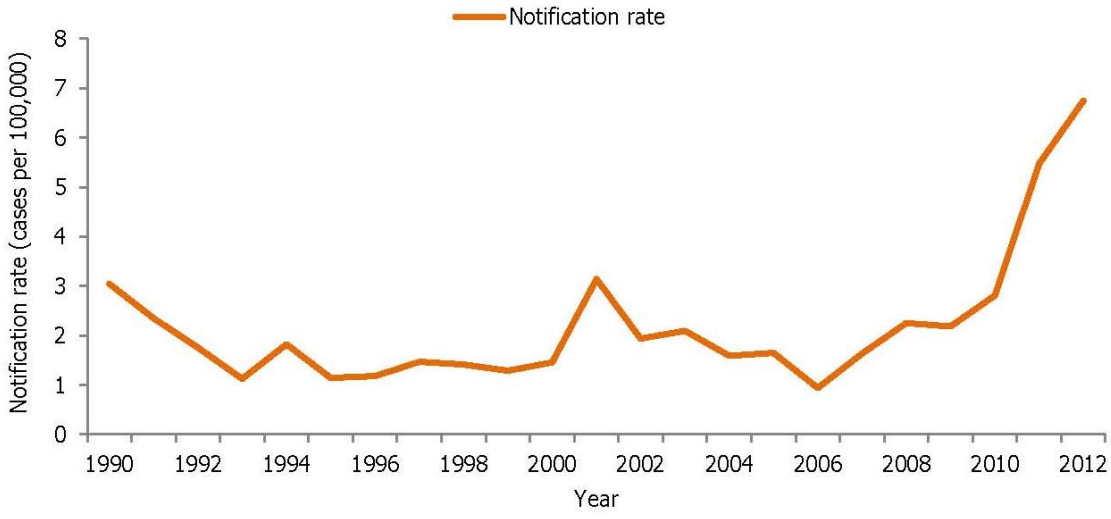


**Figure2a.** Annual notification rate of pertussis in Styria, Salzburg, Upper Austria and Tyrol (defined as high notification rate provinces), 2005-2012

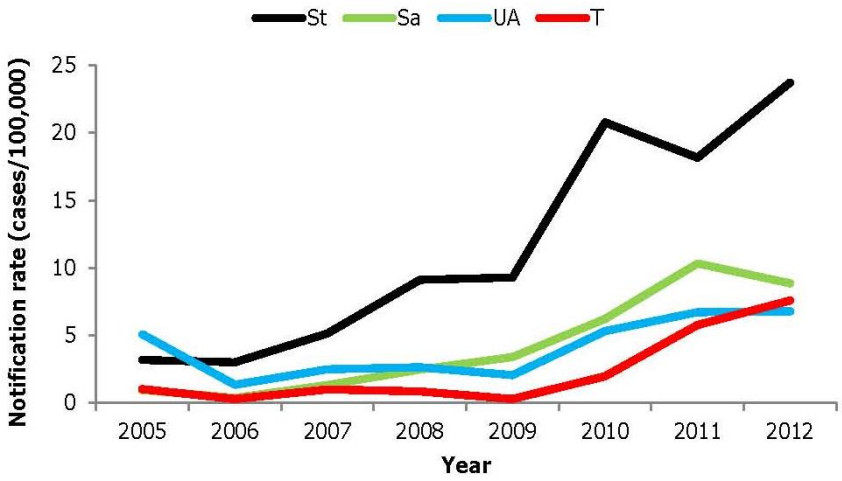
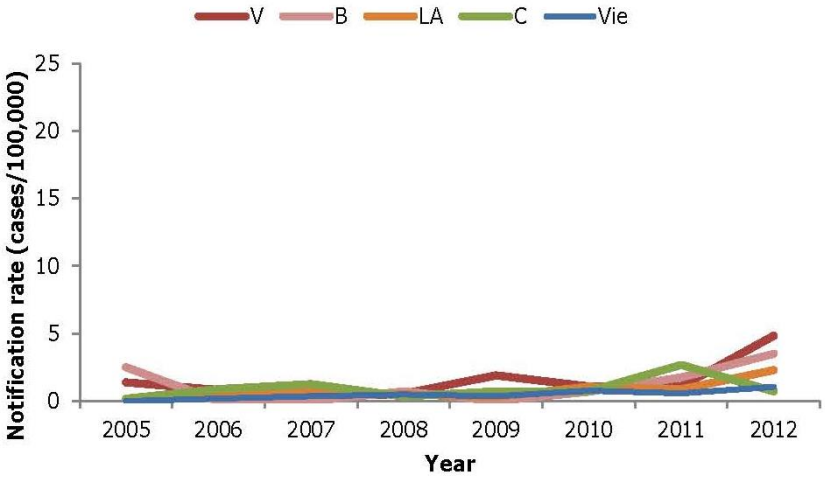



**Figure2b.** Annual notification rate of pertussis in Vorarlberg, Burgenland, Lower Austria, Carinthia and Vienna (defined as stable notification rate provinces), 2005-2012




Based on the data of the national electronic infectious disease reporting system (Elektronisches Epidemiologisches Meldesystem, EMS) from 2009-2012, we estimated the annual notification rate of pertussis by age group and assessed proportion of laboratory confirmed cases.

The age group <1 and 1-4 years showed a steep increase in the annual notification rate from 2009 (39.3/100,000; 3.5/100,000) to 2010 (66.3/100,000; 15.5/100,000) followed by a slight decrease in 2011 (61.3/100,000; 15.2/100,000) then peaked in 2012 (96.6/100,000; 25.2/100,000). The 5-9 and 10-14 years experienced a three to four times increase in the

annual notification rate from 2009 (2.5/100,000; 3.3/100,000) to 2011 (11.3/100,000; 11.6/100,000) then decreased in 2012 (10.9/100,000; 10.0/100,000). The 15-29 years old experienced only a slight increase since 2009. The notification rate among the ≥ 30 years increased more than double from 2009 (1.8/100,000) to 2012 (5.0/100,000). When grouping into the aged 0-14 and ≥15 years, we observed a considerable increase in the annual notification rate for the aged 0-14 years and only a marginal increase in the ≥ 15 years for the provinces of high notification rate including Upper Austria (10.8/100,000 to 39.7 /100,000), Salzburg (9.6/100,000 to 22.5/ 100,000) and Tyrol (1.8/100,000 to 16.9/ 100,000) from 2009-2012. In 2012, increase was also observed among aged 0-14 years in Burgenland (15.8/100,000) and Vorarlberg (23.0/100,000). In Styria, increased was observed in both age groups from 2009 through 2012 (0-14y: 7.7-45.5/100,000; ≥15 y: 9.6-20.3/100,000) (Figure3).

The majority (74%) of cases reported to the EMS were without laboratory confirmation. In 2012, a total of 334 (58%) cases classified as confirmed and 219 (38%) cases belonged to unknown or missing information on case classification.

**Figure 3a**. Annual notification rate of pertussis in the aged 0-14 years in Styria, Salzburg, Upper Austria, Tyrol, Vorarlberg and Burgenland, 2009-2012

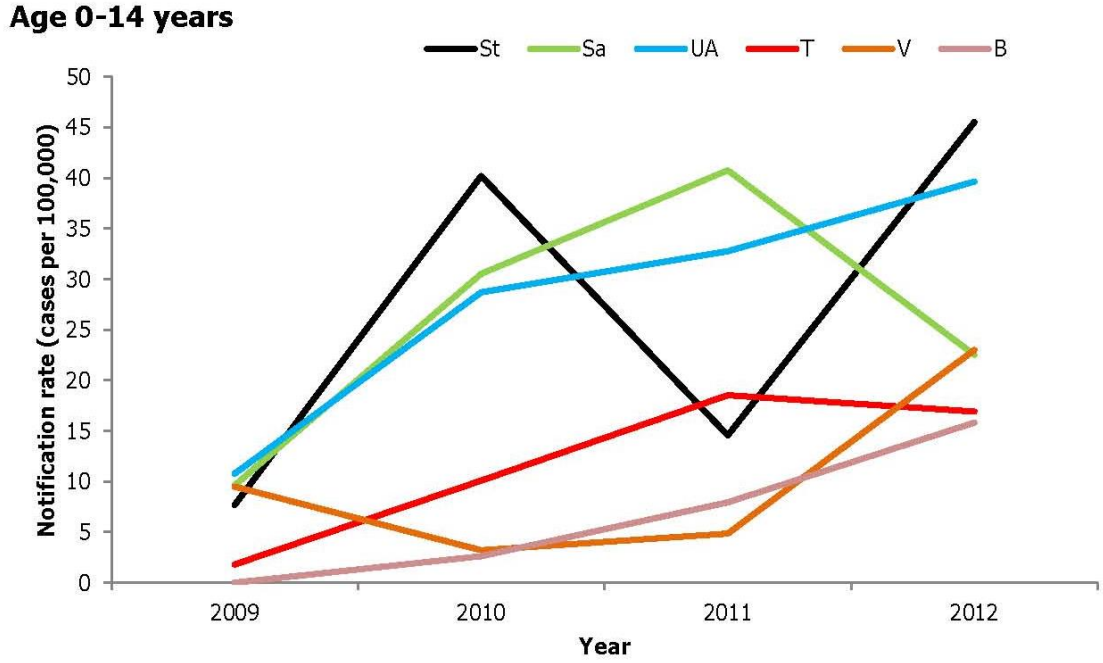


**Figure 3b.** Annual number of pertussis cases in the aged 0-14 years in Styria, Salzburg, Upper Austria, Tyrol, Vorarlberg and Burgenland, 2009-2012

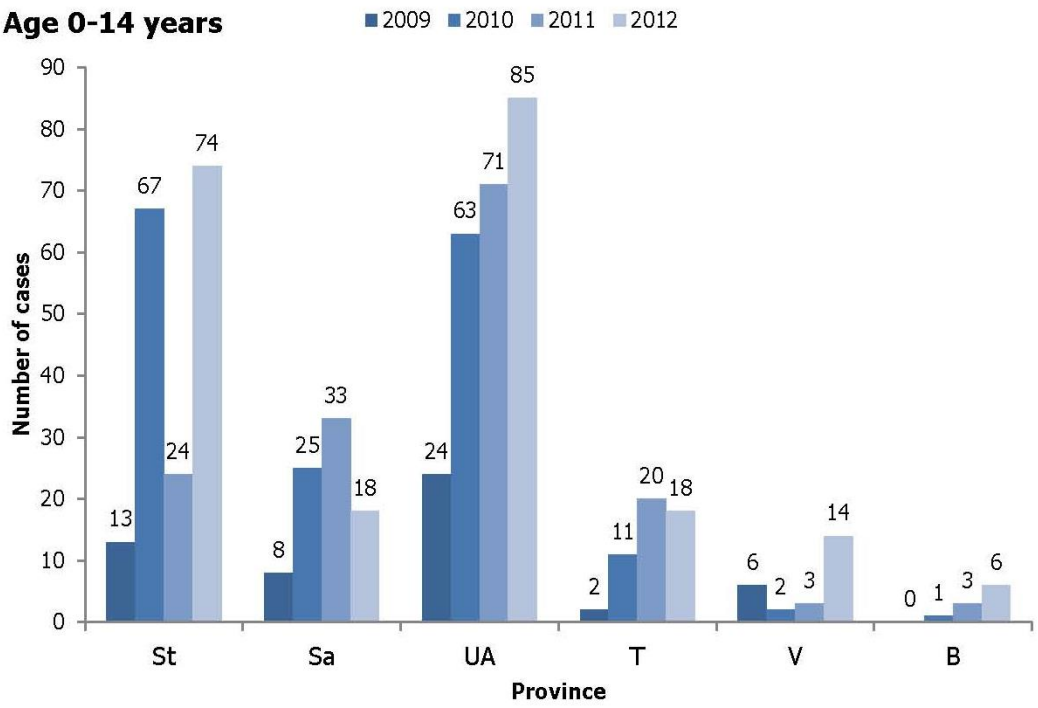
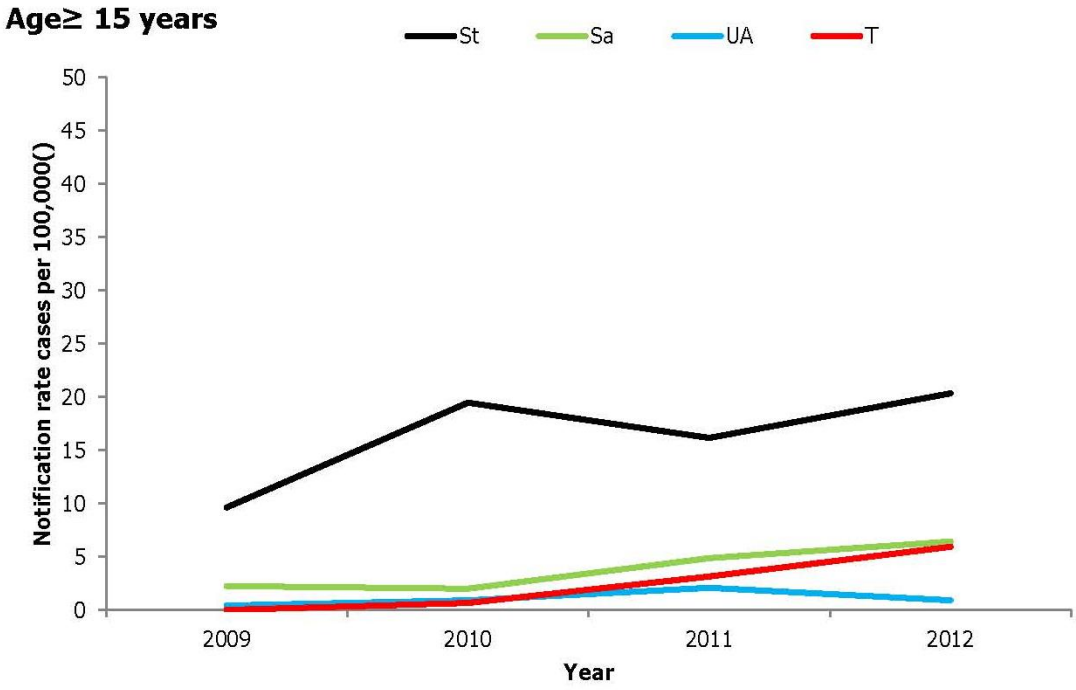



**Figure 3c.** Annual notification rate of pertussis in the aged ≥ 15 years in Styria, Salzburg, Upper Austria and Tyrol, 2009-2012



## Clinical signs and symptoms of pertussis by age group

Base on the fact that signs and symptoms of pertussis differ by age, the Global Pertussis Initiative 2011 developed a useful algorithm that tailors criteria for clinical diagnosis of pertussis in 3 different age cohorts: 0–3 months, 4 months-9 years, and ≥10 years (figure 4a), recently published in the Journal of Clinical Infectious Diseases. Key indicators of the clinical manifestation of pertussis in infants aged 0-3 months are afebrile non-productive cough, which does not improve and may be accompanied with post-tussive emesis, apnea, cyanosis or seizure. In children aged 4 months-9 years, the typical clinical picture of pertussis is characterized by paroxysmal non-productive cough with whoop lasting ≥ 7 days. Pertussis in age group ≥10 years including adolescents and adults is characterized by a non-productive cough lasting ≥ 14 days with or without the typical paroxysmal pattern. Figure 4b gives in detail signs and symptoms defined for clinical case definition for surveillance purposes (1).

**Figure 4a.** Symptoms and signs for clinical diagnosis of pertussis among three age groups (0–3 months, 4 months-9 years and ≥10 years), source: Global Pertussis Initiative Roundtable Meeting 2011

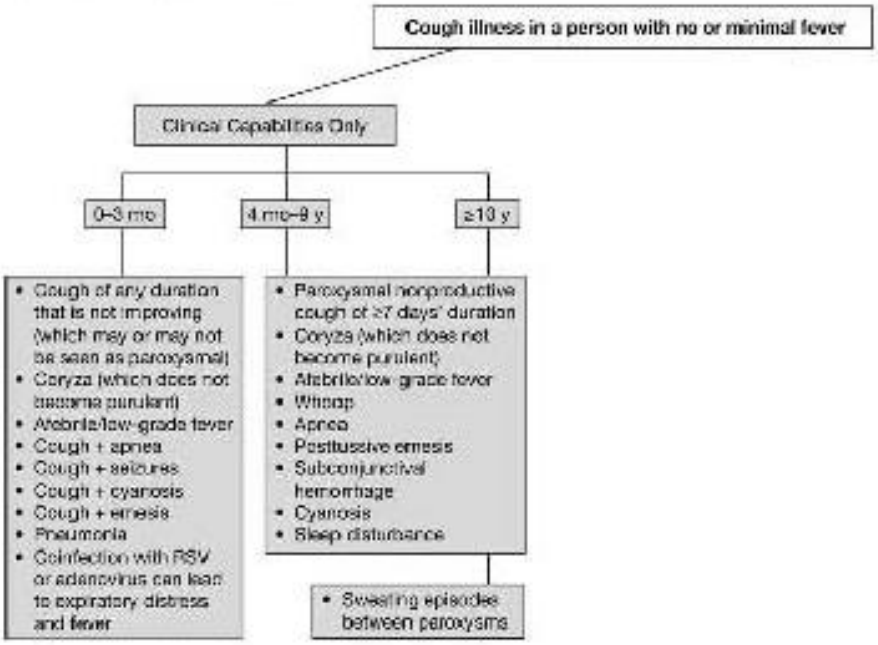
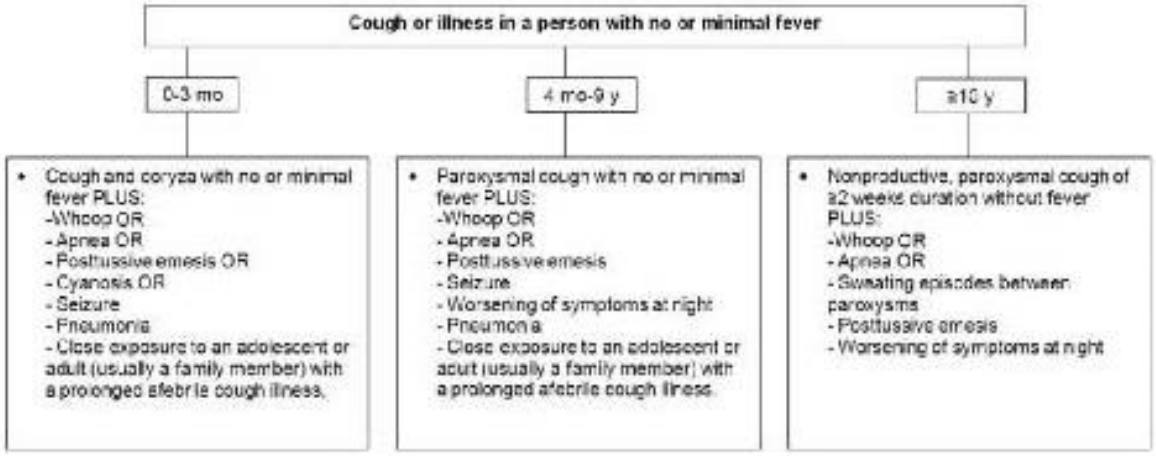


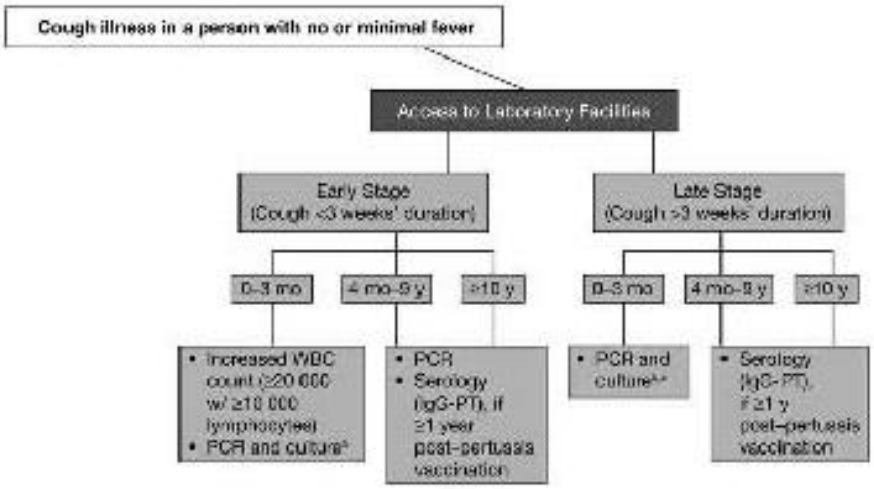
**Figure 4b.** Clinical case definition of pertussis for surveillance purposes, source: Global Pertussis Initiative Roundtable Meeting 2011




**International recommendations for laboratory diagnostics of pertussis**

The criteria for the laboratory diagnostic procedure also tailored to the age group 0–3 months, 4 months-9 years, and ≥10 years, developed by the Global Pertussis Initiative (figure 5).

**Figure 5.** Age group and disease stage specific criteria for the laboratory diagnosis of pertussis recommended by the Global Pertussis Initiative (GPI), source: Global Pertussis Initiative Roundtable meeting 2011



One differentiates between early and late disease stage based on the duration of cough (less/more than 3 weeks). In infants aged 0-3 months, the tests of choice are pertussis-specific PCR and culture for *Bordetella pertussis*. For infants, adolescents and adults (age group discrimination: 4 months-9 year; ≥10 years) presenting in the early disease stage, PCR and serological tests are appropriate. Most adolescents and adults present with late stage of disease therefore serology diagnosis is the only feasible diagnostic test. The measurement of IgG-anti-Pertussis Toxin (PT) is recommended; the cut-off value for seropositivity in a single serum sample is given between 60 IU/ml and 75 IU/ml (2); additionally the determination of the IgA anti-PT titer is advisable (cut-off value: 10-20 IU/ml). If the serum sample shows antibody-levels above the cut-off for single sample serology, the result can be interpreted as evidence of recent infection with *B. pertussis*. According to the clinical manifestations, if the diagnosis still cannot be confirmed by only single serum, the antibodies should be measured in a convalescent serum sample at 2-4 weeks interval. A dual cut-off between 62-125 IU/ml is used to define a recent infection for patients who were not vaccinated during the last 12 months(2).

**Public Health rationale of the study**

The resurgence of pertussis in Austria, as also observed in Europe (3), and the observed difference in the pertussis epidemiology between the Austrian provinces might be due to (a) increasing use of more sensitive clinical and/or laboratory diagnostic procedures, with differences between the provinces

(b) increasing case reporting by the diagnosing physicians, with differences between the provinces

(c) increasing awareness of pertussis among physicians, when examining a patient with respiratory symptoms (4), with differences between the provinces

(d) decreasing basic or booster vaccination coverage, and hereby true increase of transmission (the latter issue will not be covered by this survey)

The public health rationale of this *knowledge, attitude and practice survey* is to understand the particular epidemiological situation on pertussis in Austria, where a considerably increasing notification rate trends were observed in four provinces (referred as to high notification rate provinces) within the past 4-7 years. The other five Austrian provinces

(referred as to stable notification rate provinces) were observed stable level notification rate since 1990 or slightly increased notification rate within the past 1-2 years.

The overall aim of the survey is to assess the knowledge on pertussis, the attitudes towards case notification and the practice on laboratory diagnosis among general practitioners, pediatricians and pulmonologists. Secondly is to assess whether these factors differ between pertussis high notification rate provinces and pertussis stable notification rate provinces.

Based on our findings, appropriate measures are planned to be set by the Ministry of Health: these may include investment in encouraging the positive attitude towards case notification, increasing the practice on laboratory case confirmation and elevating the overall knowledge level on pertussis among physicians in Austria by education programs.

Further related projects currently on ongoing include the assessment of the laboratory capacity for diagnosis of *B. pertussis* infection in Austria and to assess the pertussis vaccination coverage by age.

The laboratory capacity of pertussis diagnostics in each province of Austria showed no significant differences on diagnostic criteria of pertussis. The primary vaccine coverage of pertussis in birth cohort 2000-2010 was not significantly different within provinces. The results of the two surveys revealed the differences of province-specific notification rate of pertussis were not associated with different diagnostic criteria for pertussis or different vaccine coverage of primary series among the provinces.

## Objectives

### Primary Objectives

To assess

- notification behavior/practice for pertussis,

- knowledge on clinical manifestation and laboratory diagnostic methods for pertussis, and

- attitude towards seeking laboratory confirmation for suspected pertussis cases

among general practitioners (GPs), pediatricians (Ps) and pulmonologists (Puls) in Austria (from now on in the study protocol collectively referred to as "physicians")

### Secondary objectives

To determine whether there is a difference

- in the notification behavior/practice for pertussis between "physicians" of high notification rate provinces (1) and "physicians" of stable notification rate provinces (2),

- in the level of knowledge on pertussis (including clinical manifestation and laboratory diagnostic methods) between physicians of high notification rate provinces (as given above) and physicians of stable notification rate provinces, and

- in the attitude towards seeking laboratory confirmation for suspected pertussis cases between physicians of high notification rate provinces (as given above) and physicians of stable notification rate provinces

## Hypotheses

Knowledge on pertussis, notification behavior/practice of pertussis cases and the attitude towards seeking laboratory confirmation differ between "physicians" of high notification rate provinces (I) and "physicians" of stable notification rate provinces (II)

(I) High notification rate provinces: defined as provinces with increasing pertussis annual notification rate from 2006 to 2012 or from 2009 to 2012 (i.e. Styria, Upper Austria, Salzburg and Tyrol)

(II) stable notification rate provinces: defined as provinces with stable or slightly increasing annual notification rate from 1990-2011, still at low level (i.e. Vienna, Lower Austria, Carinthia, Vorarlberg and Burgenland)

# Method

**Study design**

A Descriptive and analytical cross-sectional study

The descriptive part of the cross-sectional study will measure a convenience sample of "physicians" including GPs, pediatricians, and pulmonologists registered in Austria.

- The quality of the notification behavior /practice (detailed definition see below)
- The level of knowledge on clinical manifestation (definition see below) and laboratory diagnostic procedures (definition see below)
- The frequency of laboratory confirmation seeking behavior (definition see below)

The analytical part of the cross-sectional study will measure whether there are differences in

- the quality of notification behavior/practice,
- the level of knowledge on clinical manifestations and laboratory diagnostic procedures,
- and the frequency of seeking laboratory confirmation in a clinically suspected case of pertussis

  between physicians of high notification rate provinces and physicians of stable notification rate provinces

We will ascertain the exposure factors knowledge, notification practice and laboratory confirmation seeking behavior among Austrian physicians within a cross-sectional study. The results on the distribution of these exposure factors among the participating physicians across the nine provinces may help to explain the differences in the province-specific annual notification rate within the previous 4-7 years (until 2012).

Limitations related to this approach are explored in the paragraph study limitation.

**Source population**

The source population refers to the total of registered general practitioners (GPs), established and hospital pulmonologists, and pediatricians (Ps) in Austria, listed at the Austrian Chamber of Medical Doctors (Table 1). These professions are selected as they are most commonly involved in the consultation of a patient with *B. pertussis* infection. The list of the "physicians" was provided by the chamber.

**Table1.** Source population by province and professions (GPs, Pediatricians and Pulmonologists) in absolute number and number of physicians per 100,000 population

| **Source population** | **Province*** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Occupation | **B** | **CA** | **LA** | **UA** | **SA** | **ST** | **T** | **V** | **Vie** | **Total** |
| GPs N ( n per 100,000 population) | 145 (50.5) | 230 (41.3) | 741 (45.6) | 718 (50.5) | 231 (43.0) | 576 (47.4) | 309 (43.0) | 150 (40.0) | 772 (44.1) | 3872 (45.6) |
| Pediatricians N ( n per 100,000 population) | 22 (7.7) | 44 (7.9) | 153 (9.4) | 150 (10.5) | 65 (12.1) | 132 (10.9) | 100 (13.9) | 42 (11.2) | 361 (20.6) | 1069 (12.6) |
| Pulmonologists N ( n per 100,000 population) | 5 (1.7) | 18 (3.2) | 45 (2.8) | 58 (4.1) | 16 (3.0) | 61 (5.0) | 23 (3.2) | 9 (2.4) | 122 (7.0) | 357 (4.2) |
| **Total N (%)** | **172 (3)** | **292 (6)** | **939 (18)** | **926 (17)** | **312 (6)** | **769 (15)** | **432 (8)** | **201 (4)** | **1255 (24)** | **5298** |
| **% Distribution of Austrian population** | **3%** | **7%** | **19%** | **17%** | **6%** | **14%** | **8%** | **4%** | **21%** | **-** |

*B: Burgenland, CA: Carinthia, LA: Lower Austria, UA: Upper Austria, SA: Salzburg, St: Styria, T: Tyrol, V: Vorarlberg, Vie: Vienna

**Study sample/Study population**

**Convenience sampling**

The response rate of prior single random sampling was not satisfactory (<20%). To increase the response rate, the task force of pertussis project decided to collect trawling questionnaires by convenience sampling.

**Sample size calculation**

The sample size calculation for a descriptive study using a hypothesized frequency of 50% for the expected proportion, a precision of 0.05, a significance level of 0.95, a correction for finite population revealed required sample size of 283 paediatricians, 350 general practitioners and 186 pulmonologists respectively. In the analytical cross-sectional study, we calculated the sample size for the analytical cross-sectional study in each specialty. 276 respondents in each medical specialty were aimed to be recruited base on the following prerequisite.

- 50% of the unexposed (low level of knowledge, unsatisfactory notification behaviour, unsatisfactory laboratory diagnostic seeking behaviour) with outcome (being a physician in high notification rate provinces);

- A ratio of unexposed / exposed = 1;
- Significance level =95 %;
- Power = 80%;
- Min. PR = 1.3;

In order to both describe and analyse the cross-sectional study with sufficient sample size, we aimed at recruiting 283 paediatricians, 350 general practitioners and 276 pulmonologists into the study. The distribution of the study sample by province is given in Table2.

**Table2.** Study sample by province in each specialty

| | | Province n/N (%) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Medical specialty | **Total** | B | CA | LA | UA | S | St | T | V | Vie |
| GPs | **350** | 13 | 21 | 67 | 65 | 21 | 52 | 28 | 14 | 69 |
| Paediatricians | **283** | 6 | 12 | 41 | 40 | 17 | 35 | 26 | 11 | 95 |
| Pulmonologists | **276** | 4 | 14 | 35 | 45 | 12 | 47 | 18 | 7 | 94 |

**Pilot study**

The final version of the questionnaire has been decided by the pertussis task force who represent involved medical societies. The decision from the task force was not to conduct a pilot study for validating the questionnaire.

**Data collection**

Information was collected by a self-administered questionnaire online or by telephone. We developed a 32-questions questionnaire in cooperation with the Austrian Society of Pulmonology (ÖGP), the Austrian Society of Pediatrics and Adolescent Medicine (ÖGKJ) and Austrian Society of General Practice and Family Medicine (ÖGAM) to describe the notification behavior, the knowledge on clinical manifestation and laboratory diagnosis, and the laboratory confirmation seeking behavior among the physicians. Additionally information will be collected on physician's professions, place of practice and the catchment area. The majority of questions are fixed-response questions. For ascertaining the laboratories, to which the specimens for pertussis confirmation are sent, and for ascertaining physicians' procedure of obtaining a nasopharyngeal swab, open questions was used (Table 10 in Appendix). The online questionnaire system (Question Pro) will close the questionnaire within 30 minutes to avoid answering the questionnaire with help of library consultation. The KAP questionnaire, except for demographic characteristics, was structured into four attributes:

(1) Notification behaviour/practice. The eight questions including 1-3, 8-11 and 31 with binary (Yes/No) answers were to describe and analyze the satisfactory notification behaviour/practice.

(2) Level of knowledge on clinical manifestation of pertussis. The nine questions including 4-7 and 14 with single or multiple choices were used to describe level of knowledge on clinical manifestation of pertussis. Two required questions including question 4 and 5 were applied to analyze high level of knowledge on clinical manifestation of pertussis. In question 4, high level of knowledge was defined by a cumulative score of 7-9 points from nine multiple choices.

(3) Level of knowledge on laboratory diagnostic procedure of pertussis. The 12 questions including 15-17, 19, 21-26, 28 and 30 were used to describe the level of knowledge on laboratory diagnostic procedure of pertussis. The seven required questions including 15-17, 19, 23-24 and 28 will be used to analyze level of knowledge on laboratory diagnostic procedure of pertussis. High level of knowledge on laboratory diagnostic procedure was defined by a cumulative score of distribution of ≥75 percentile out of 17 points in the seven required questions.

(4) Laboratory confirmation seeking behaviour of pertussis. Two questions including question 12 and 13 were used to describe laboratory confirmation seeking behaviour of pertussis. Satisfactory laboratory confirmation seeking behaviour of pertussis was defined as the frequency of a physician seeks laboratory diagnosis in a patient clinically suspected with *B. pertussis* infection was ≥75%.

Please see appendix for the detail of the questionnaire design.

**Definitions**

Definition of the outcome

1. Being a physician in one of the high notification rate provinces defined as a physician whose place of practice is in a province with increase in the annual notification rate of pertussis within the previous 4-7 years (i.e. Styria, Salzburg, Tirol and Upper Austria, until 2012) was observed.

2. A physician who report a laboratory confirmed case of pertussis

Definition of exposure factors under study

The exposure factors under study are:

Satisfactory **notification behaviour/practice**

High level of **knowledge on clinical manifestation** of pertussis

High level of **knowledge on laboratory diagnostic procedure** of pertussis

Satisfactory **laboratory confirmation seeking behaviour** of pertussis

**Data analysis plan**

After questionnaires are retrieved each survey participant will receive a unique identification number. All data will be analyzed anonymously. Employees of the Department of Infectious Disease Epidemiology at AGES will generate spreadsheet in MS Excel extracted from the software of online questionnaire called QuestionPro and perform data validation and cleaning. The sampling weight will be considered for each respondent based on the response rate of each province.

In the descriptive cross-sectional study, survey responses from participating physicians will be described on the proportion of physicians replied correct answers in each question and frequency of satisfactory notification practice, high knowledge level and satisfactory laboratory seeking behaviour in the respondents obtained from convenience sampling. (Table 4).

In the analytical cross-sectional study, we will compare satisfactory notification behavior, high level of knowledge on clinical manifestation and laboratory diagnosis, and satisfactory laboratory confirmation seeking behavior between "physicians" (as defined above) of high notification rate provinces and "physicians" of stable notification rate provinces (Table 5). For bivariate analyses chi square test for contingency tables will be used. Data analyses will be performed by using STATA version 11.

Secondary, we analyzed the respondents' knowledge of clinical manifestation and laboratory diagnosis and satisfactory laboratory confirmation seeking behavior between "physicians" who notified a laboratory confirmed case and those who did not notify a laboratory confirmed case by calculating the prevalence ratio (PR) and 95% confidence interval

**Ethical considerations**

Creation of the protocol does not include the collection of potentially identifiable or sensitive data on individuals. Any data analysis undertaken as part of the investigations to inform the protocol construction will be presented in aggregated form.

**Project management**

The list of study population would be provided by The Austrian Society of Pulmonology (ÖGP), the Austrian Society of Pediatrics and Adolescent Medicine (ÖGKJ) and Austrian Society of General Practice and Family Medicine (ÖGAM). The primary investigators at AGES are Dr. Shu-Wan Jian (EPIET fellow, Austrian FETP) and Dr. Daniela Schmid (Head of Department for Infectious Disease Epidemiology, AGES). All the received questionnaires will be owned by the Department for Infectious Disease Epidemiology at AGES.

# Results

## Study participants' description

The response rate of pediatricians is the highest of the three specialties, accounting for 53%. There were only 78 GPs out of all registered 3872 GPs responded the online questionnaire. We only described data of GPs but not analyzed the data due to its 2% respondents of the source population.

**Table 3.** Description of the response rate of the study sample in physicians by nine provinces (as of 30.09.2013)

| | **n/N (%)** | High-rate provinces n/N (%) | | | | Stable-rate provinces n/N (%) | | | | | P value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Medical specialty | **Total** | UA | Sa | St | T | B | Ca | LA | V | Vie | |
| GPs | 78/350 (22) | 12/65 (18) | 4/21 (19) | 21/52 (40) | 9/28 (32) | 2/13 (15) | 2/21 (10) | 15/67 (22) | 2/14 (14) | 11/69 (16) | 0.06 |
| Pediatricians | 150/283 (53) | 28/40 (70) | 11/17 (65) | 19/35 (54) | 11/26 (42) | 6/6 (100) | 9/12 (75) | 21/41 (51) | 8/11 (73) | 37/95 (39) | 0.48 |
| Pulmonologists | 42/276 (15) | 8/45 (18) | 1/12 (8) | 13/47 (28) | 1/18 (6) | 1/4 (25) | 0/14 (0) | 3/35 (9) | 1/7 (14) | 13/94 (14) | 0.70 |

## Descriptive cross-sectional study

We described knowledge on pertussis, the attitudes towards case notification and the attitude of seeking laboratory diagnosis among physicians by their specialty. The weighted proportion allows for sample weights within provinces to be representative in provincial distribution of the three specialties.

**Table 4.** Frequency of notification practice, knowledge on clinical manifestations and laboratory procedures and laboratory confirmation seeking behaviour in the total study population

| Question no. and contents | **n/N ( weighted %)** | | |
|---|---|---|---|
| | GPs (Ntotal= 78 ) | Pediatricians (Ntotal= 150) | Pulmonologists (Ntotal= 42) |
| **Notification practice (8 required questions)** | | | |
| 1. Awareness of pertussis as a notifiable disease | 69/77 (90) | 142/147 (96) | 40/42 (93) |
| 2. Awareness of notifying a pertussis case to PH authorities. | 72/72 (100) | 138/138 (100) | 39/39 (100) |
| 2a. Awareness of notifying a pertussis case to district PH authorities | 57/72 (74) | 86/138 (63) | 19/39 (49) |
| 3. Use the standardized notification form provided by MoH | 49/76 (68) | 110/142 (77) | 30/40 (78) |
| 8. Use an official case definition | 22/73 (30) | 39/144 (28) | 13/40 (34) |
| 9. Awareness of the ECDC case definition of pertussis | 3/73 (4) | 5/125 (4) | 0/34 (0) |

| | | | |
|---|---|---|---|
| 10. Notify a pertussis case based on the ECDC case definition | 2/36 (5) | 5/70 (8) | 0/17 (0) |
| 11. Notify a clinically suspected case | 10/73 (16) | 13/140 (8) | 2/37 (5) |
| 31. Notify a clinical suspected case again after having received a laboratory confirmation (report a lab. confirmed case) | 41/64 (65) | 100/135 (74) | 20/32 (63) |
| **Level of knowledge on clinical manifestation of pertussis (2 required questions )** | | | |
| 4. High level of knowledge on clinical signs and symptoms of pertussis infection ( gained 7-9 points from total 9 points) | 26/77 (34) | 102/149 (67) | 18/41 (40) |
| 5. Differentiate the clinical signs and symptoms by age (1 point) | 46/77 (59) | 137/149 (91) | 27/39 (69) |
| 6.1. Duration of cough in children aged ≤ 3 months | 51/73 (73) | 129/142 (91) | 23/30 (74) |
| 6.2. Cough-related symptoms of pertussis in children between 4 months - 9 years | 53/72 (74) | 99/137 (72) | 19/31 (69) |
| 6.3. Duration of cough in children aged ≥ 10 years | 64/73 (90) | 125/142 (87) | 26/34 (83) |
| 7.1. High level of knowledge on the clinical case definition in young children ≤ 3 months (gained 7-10 points from total 10 points) | 34/72 (44) | 58/135 (41) | 5/30 (12) |
| 7.2. High level of knowledge on the clinical case definition in children between 4 months - 9 years (gained 7-10 points from total 10 points) | 15/70 (20) | 40/131 (32) | 9/30 (31) |
| 7.3. High level of knowledge on the clinical case definition in children aged ≥ 10 years and adults (gained 7-10 points from total 10 points) | 31/71 (42) | 64/130 (49) | 17/34 (44) |
| 14. Three weeks threshold between early stage and late stage of pertussis infection | 41/73 (57) | 60/127 (46) | 17/31 (59) |
| **Level of knowledge on laboratory diagnosis (8 required questions )** | | | |
| 15. Chose correct tests for laboratory confirmation in the aged ≤ 3 months with clinically suspected B. pertussis infection (three points) | 15/67 (20) | 36/139 (25) | 11/34 (27) |
| 16. Chose correct diagnostic tests to confirm a clinical cases in children aged > 3 months, adolescents and adults (three points) | 10/68 (14) | 35/143 (26) | 7/36 (25) |
| 17. Chose correct diagnostic tests to confirm a clinical case in a cough duration of ≥ 3 weeks (three points) | 21/68 (29) | 26/140 (17) | 6/37 (20) |
| 19. Chose correct immunoglobulin(s) for serological testing (IgM alone is an incorrect answer) (three points) | 47/67 (67) | 104/135 (78) | 23/34 (61) |
| 23. Chose correct answer on the duration of not using IgG for diagnosis of pertussis in patients following pertussis vaccination (one point) | 43/60 (76) | 70/117 (59) | 18/30 (63) |
| 24. Chose we cannot use IgG-titer to discriminate recent | 41/65 (63) | 120/134 (90) | 27/33 (80) |

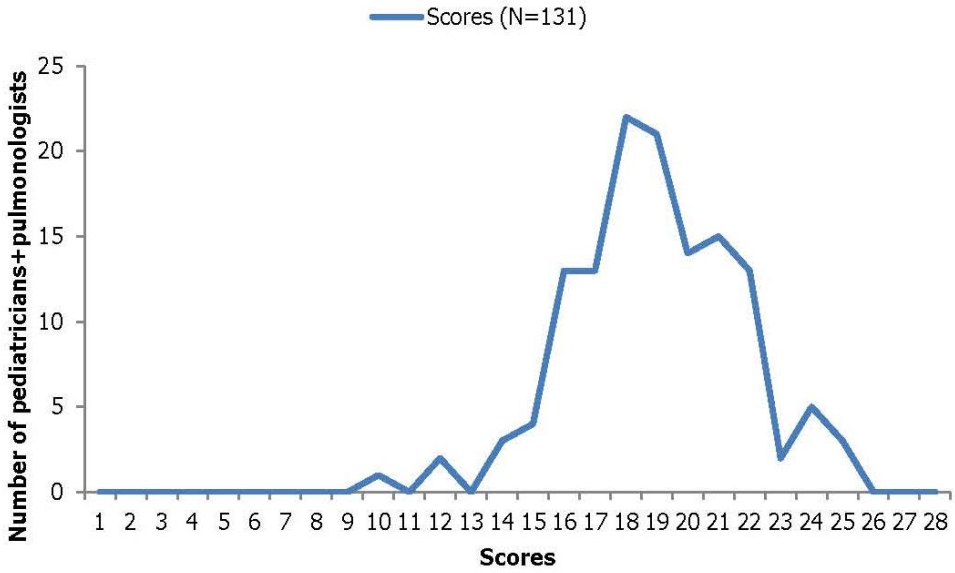
| | | | |
|---|---|---|---|
| vaccination and current infection (one point) | | | |
| 28. Chose correct types of specimens obtained for PCR or culture (gained 2.4-3 points from total 3 points) | 14/66 (20) | 36/139 (26) | 2/36 (5) |
| 21. Ask vaccination history from patients | 69/70 (99) | 131/132 (99) | 28/32 (87) |
| 22. Inform the information of vaccine history to the laboratory | 54/68 (81) | 96/128 (74) | 17/31 (56) |
| **Laboratory confirmation seeking behavior** | | | |
| 12. High frequency of seeking laboratory diagnostics (Frequency ≥75%) | 44/73 (60) | 122/142 (86) | 25/39 (63) |
| 13. The reasons for NOT seeking laboratory diagnostics | | | |
| a. The treatment started immediately as a case of pertussis is clinically suspected; there is no added value for awaiting the laboratory results, which will be too late. | 36/78 (46) | 47/150 (31) | 11/42 (26) |
| b. The sensitivity and specificity of the laboratory diagnostic tests for pertussis are poor | 6/78 (8) | 18/150 (12) | 8/42 (19) |
| c. Laboratory diagnostic test for pertussis is too expensive and funding is not covered by the social insurance companies | 9/78 (12) | 7/150 (5) | 6/42 (14) |
| **Place of practice** | | | |
| a. General Practice ("Ordination") | 73/77 (95) | 66/150 (42) | 19/42 (41) |
| b. General Hospital | 3/77 (4) | 65/150 (45) | 22/42 (57) |
| c. University Hospital | 1/77 (1) | 19/150 (13) | 1/42 (2) |

## Frequency distribution of scores

**Level of knowledge (clinical manifestation+ laboratory diagnostics)**

A total of 131 pediatricians and pulmonologists replied all the questions included in ranking. 61 physicians and pulmonologists who did not complete the questions were excluded. The total 27 scores included question 4, 5, 15, 16, 17, 19, 23, 24 and 28. The distribution of scores gained among the 131 participants was given in Figure 6.

**Figure 6.** Distribution of scores on level of knowledge of pertussis in pediatricians and pulmonologists

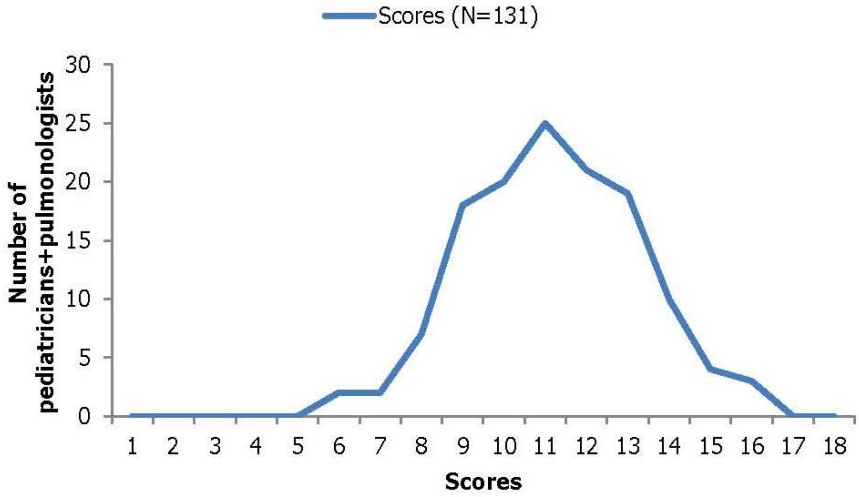



(Average: 17.9, Median: 17.8, Maximum: 24.4, Minimum: 8.6)

**Level of knowledge (laboratory diagnostics)**

A total of 131 pediatricians and pulmonologists replied all the questions included in ranking. 61 physicians and pulmonologists who did not complete the questions were excluded. The total 17 scores included question 15, 16, 17, 19, 23, 24 and 28. The distribution of scores gained among the 131 participants was given in Figure 7.

**Figure 7.** Distribution of scores on level of knowledge on laboratory diagnostics of pertussis in pediatricians and pulmonologists




(Average: 10.1, Median: 10.0, Maximum: 15.4, Minimum: 4.6, SD: 2.14, 75% Percentiles: 11.8)

**Analytical cross-sectional study**

**Table 5.** Prevalence of satisfactory notification practice, high knowledge level and satisfactory laboratory seeking behaviour among the study **paediatricians & pulmonologists** of high-rate provinces and stable-rate provinces

| Attributes | High-rate provinces (N=92) | | Stable-rate provinces (N=100) | | |
|---|---|---|---|---|---|
| | n/N (column%*) | 95%CI | n/N (column%*) | 95%CI | P value |
| **Satisfactory notification practice** | | | | | |
| 1. Aware pertussis is a notifiable disease | 86/89 (96.0) | 88.3-98.8 | 96/100 (95.7) | 89.0-98.4 | 0.82 |
| 2. Aware report to district PH authority | 53/92 (56.6) | 46.0-66.6 | 52/85 (62.1) | 51.1-71.9 | 0.79 |
| 3. Use MoH notification form | 66/87 (76.2) | 65.9-84.1 | 74/95 (76.9) | 67.0-84.5 | 0.75 |
| 4. Use official case definition | 23/88 (26.9) | 18.3-37.6 | 29/96 (29.7) | 21.2-39.8 | 0.54 |
| 5. Notify a clinical suspected case | 7/84 (7.6) | 3.6-15.3 | 8/93 (7.8) | 3.8-15.3 | 0.95 |
| 6. Notify again after receive a lab. confirmation report | 25/91 (27.7) | 19.3-38.1 | 22/76 (29.4) | 19.9-41.1 | 0.75 |
| **Level of knowledge on clinical manifestations** | | | | | |
| 1. High level of knowledge on clinical manifestation (high: 7-9 point, total: 9 points) | 32/92 (34.0) | 24.8-44.5 | 40/100 (42.4) | 32.8-52.6 | 0.46 |
| 2. Differentiate clinical manifestation by age (Yes/No) | 15/89 (17.5) | 10.6-27.4 | 9/99 (9.4) | 4.9-17.3 | 0.11 |
| **High level of knowledge on laboratory diagnostic procedures** (high ≥11.8 point, total: 17 points) | 47/92 (50.3) | 39.9-60.7 | 51/100 (51.5) | 41.5-61.4 | 0.99 |
| **Satisfactory laboratory confirmation seeking behaviour** (seek lab confirmation in ≥75% of all patients) | 70/86 (83.3) | 74.2-89.6 | 77/95 (80.1) | 70.4-87.1 | 1.00 |

| Attributes | Mean (median) | Mean (median) | P value |
|---|---|---|---|
| Knowledge on clinical manifestation (range:0-9 points) | 6.86 (7) | 6.76 (7) | 0.59 |
| Knowledge on laboratory diagnostic procedures (range:0-17 points) | 10.17 (10.2) | 10.12 (9.8) | 0.88 |

*Weighted proportion that allows for sample weights within provinces

Assessing whether knowledge level and laboratory seeking behaviour differ between the pediatricians+pulmonologists who reported a laboratory confirmed cases of pertussis in high notification rate provinces and those in stable notification rate provinces

**Table 6.** Attributes for being a **pediatricians & pulmonologists** who notified a laboratory confirmed case of pertussis (replied Yes for Question31)

| Variables | Confirmed case reporter n/N (%*) | NOT confirmed case reporter n/N (%*) | PR (95%CI) |
|---|---|---|---|
| **High level of knowledge on clinical manifestations** | | | |
| 1. High level of knowledge on clinical manifestation in general (high: 7-9 point, total: 9 points) | 78/107 (73.0) | 29/107 (27.0) | 1.05 (0.85-1.32) |
| 2. Differentiate clinical manifestation by age | 104/147 (70.9) | 43/147 (29.1) | 0.93 (0.70-1.25) |
| **High level of knowledge on laboratory diagnostic procedures** high ≥11.8 point (75% percentile) total: 17 points | 55/74 (73.9) | 19/74 (26.1) | 1.06 (0.87-1.29) |
| **Satisfactory laboratory confirmation seeking behaviour** (seek lab confirmation in ≥75% of all patients) | 99/133 (74.1) | 34/133 (25.9) | 1.2 (0.89-1.63) |
| **Attributes** | **Mean (median)** | **Mean (median)** | **P value** |
| Knowledge on clinical manifestation (range:0-9 points) | 6.88 (7) | 6.74 (7) | 0.51 |
| Knowledge on laboratory diagnostic procedures (range:0-17 points) | 10.30 (10.2) | 9.89 (9.6) | 0.35 |

*Weighted proportion that allows for sample weights within provinces

**Table 7.** Attributes for being a **"pediatrician &pulmonologist"** who notified a laboratory confirmed case and practice in high-rate provinces compare to those who practice in stable-rate provinces.

| Variables | High-rate provinces (N=92 ) | | | | Stable-rate provinces (N=100 ) | | | |
|---|---|---|---|---|---|---|---|---|
| | Sample size | Confirmed case reporter | Notification prevalence % (95%CI) | PR (95%CI) | Sample size | Confirmed case reporter | Notification prevalence % (95%CI) | PR (95%CI) |
| **Knowledge on clinical manifestations** | | | | | | | | |
| Median or low level of knowledge (0-6 point) | 26 | 19 | 72.7 (51.8-86.8) | Ref. | 34 | 23 | 67.2 (49.5-81.1) | Ref. |
| High level of knowledge (7-9 point) | 50 | 35 | 69.6 (54.7-81.2) | 0.96 (0.70-1.31) | 57 | 43 | 75.5 (62.2-85.3) | 1.12 (0.84-1.50) |
| **Differentiate clinical manifestation by age** | | | | | | | | |
| No | 11 | 9 | 78.2 (41.6-94.8) | Ref. | 8 | 6 | 73.5 (35.0-93.5) | Ref. |
| Yes | 64 | 44 | 68.9 (56.0-79.4) | 0.88 (0.59-1.30) | 83 | 60 | 72.2 (61.2-81.0) | 0.98 (0.62-1.55) |
| **Knowledge on laboratory diagnostics** | | | | | | | | |
| Median or low level of knowledge (0 - <11.8 point) | 43 | 26 | 59.3 (43.4-73.5) | Ref. | 50 | 39 | 76.9 (62.5-86.9) | Ref. |
| High level of knowledge (11.8 -17 points) | 33 | 28 | 84.8 (67.2-93.9) | 1.43 (1.06-1.94) | 41 | 27 | 66.5 (50.4-79.5) | 0.86 (0.66-1.14) |
| **Laboratory confirmation seeking behaviour** | | | | | | | | |
| Seek confirmation in <75% of all patients | 14 | 8 | 57.1 (31.1-79.7) | Ref. | 17 | 11 | 64.4 (39.5-83.4) | Ref. |
| Seek confirmation in ≥75% of all patients | 62 | 46 | 73.3 (60.1-83.4) | 1.28 (0.79-2.10) | 71 | 53 | 74.8 (62.9-83.8) | 1.15 (0.79-1.71) |
| **Place of practice** | | | | | | | | |
| General Practice ("Ordination") | 35 | 20 | 55.7 (38.4-71.8) | Ref. | 42 | 28 | 64.8 (48.6-78.2) | Ref. |
| General Hospital | 30 | 24 | 81.5 (63.7-91.7) | 3.50 (1.10-11.1) | 44 | 34 | 77.9 (62.9-87.9) | 1.20 (0.91-1.59) |
| University hospital | 11 | 10 | 87.4 (45.7-98.3) | 5.49 (0.60-50.7) | 5 | 4 | 80.0 (30.0-97.4) | 1.23 (0.75-2.03) |

**Binomial regression**

The binomial regression was to test which attributes are the independent variables to be associated with confirmed–case notification behavior among pediatricians and pulmonologists. We adjusted the effects of the variables that were significant associated with notification behavior in the prior analysis which included place of practice and level of knowledge on laboratory diagnostics.

In high-rate provinces, pediatricians and pulmonologists who practice in a university hospital are 1.55 times more likely to notify a laboratory confirmed case than those who practice in general practices, after adjusting the effects of other variables.

In high-rate provinces, pediatricians and pulmonologists who have high level of knowledge on laboratory diagnostics of pertussis are 1.35 times more likely to notify a laboratory confirmed case than those who have median or low level of knowledge, after adjusting the effects of other variables.

In stable-rate provinces, the variables of interests were not significant.

**Table 8.** Independent attributes for being a confirmed case reporter in high-rate and stable rate provinces from binomial regression analysis

| Variable | High-rate provinces<br>Adjusted PR (95%CI) for confirmed case reporter | Stable-rate provinces<br>Adjusted PR (95%CI) for confirmed case reporter |
|---|---|---|
| **Place of practice** | | |
| General Practice ("Ordination") | Ref. | Ref. |
| General Hospital | 1.32 (0.94-1.87) | 1.18 (0.88-1.57) |
| University Hospital | 1.55 (1.12-2.17) | 1.16 (0.63-2.13) |
| **Level of knowledge on laboratory diagnostics** | | |
| Median or low level of knowledge (0 - <11.8 point) | Ref. | Ref. |
| High level of knowledge ( 11.8 -17 points) | 1.35 (1.02-1.80) | 0.90 (0.67-1.19) |

## Discussion

The survey was originally designed based in a single random sampling method by telephone interviews. However, the response rate was only 6% (21/360). The task force of pertussis project decided to trawl the questionnaire by online survey and convenience samplings from the physicians registered in Austria.

The physicians less frequently (28-34%) considered official case definition when they notified a pertussis case. Few physicians (0-4%) aware of ECDC case definition, which might be due to the official case definition in Austria for pertussis notification was complied with EU case definition, the term "ECDC case definition" might be confused with "EU case definition". Only 10% of the responding physicians had ever reported a possible case of pertussis, as opposed to more than 60% of respondents who had reported a laboratory confirmed case of pertussis. The responding pediatricians had highest proportion (67%) of high level of knowledge on clinical manifestations of pertussis and differentiate the symptoms by age (91%), as compared to GPs (34%) and pulmonologists (40%), who less frequently differentiated the symptoms by age (59% and 69% respectively). Pediatricians had gained significantly higher points of knowledge on pertussis than pulmonologists (18.2 and 16.9, respectively; P=0.01). The frequency of seeking laboratory diagnosis in patients of suspected pertussis infection was highest in pediatricians (86%) and lowest in GPs (60%).

The analytical study identified two independent determinants of notifying a laboratory confirmed case of pertussis among pediatricians and pulmonologists who practice in provinces of high notification rate of pertussis. The pediatricians and pulmonologists who practice in a university hospital and who have high level of knowledge on laboratory diagnostics of pertussis were significantly more likely to notify a laboratory confirmed case of pertussis.

### Limitations

Participation bias would be possible in a nonprobability sampling such as convenience sampling.

Recall bias should be no issue as we ask for current behavior (notification behavior and laboratory confirmation seeking behavior).

Instrument bias should be avoided as much as possible as we use fixed-response questions in the majority of questions.

Interviewer bias will try to be avoided by interviewer training.

It is possible that the notification behavior and the laboratory confirmation seeking behavior among the participants (perhaps also among nonparticipating physicians) will change after participation in the survey. This effect is described as "Question-Behavior Effect" (6, 7). Any influence by "Question-Behavior Effect" should be assessed by further analyses in the annual notification rate of pertussis by province in Austria from 2013 onwards.

In addition, the reporting bias might occur if the physicians prevaricate to avoid the truth of notification frequency during telephone interviews. However, there were only 20 respondents participated through telephone interviews.

The non-respondents of the online self-administered survey cannot be contacted by telephone while no contact information of participants was reachable. However, the head of medical societies will inform their members again to participate in the online survey.

The result of the study might not be representative of the general practitioners, pediatricians and pulmonologists registered in Austria, as the respondents is rather low (22% 53% and 15%, respectively).

## References


1. Cherry JD, Tan T, Wirsing von König C-H, Forsyth KD, Thisyakorn U, Greenberg D, et al. Clinical definitions of pertussis: Summary of a Global Pertussis Initiative roundtable meeting, February 2011. Clin. Infect. Dis. 2012 Jun;54(12):1756–64.

2. Publications - bordetella-pertussis-guidance-protocol-serological-diagnosis.pdf... [Internet]. [cited 2013 Apr 2]. Available from: http://www.ecdc.europa.eu/en/publications/Publications/Forms/ECDC_DispForm.aspx?ID=982

3. Celentano LP, Massari M, Paramatti D, Salmaso S, Tozzi AE. Resurgence of pertussis in Europe. Pediatr. Infect. Dis. J. 2005 Sep;24(9):761–5.

4. Guiso N, Wirsing von König C-H, Forsyth K, Tan T, Plotkin SA. The Global Pertussis Initiative: Report from a Round Table Meeting to discuss the epidemiology and detection of pertussis, Paris, France, 11–12 January 2010. Vaccine. 2011 Feb;29:1115–21.

5. Reichenheim ME, Coutinho ES. Measures and models for causal inference in cross-sectional studies: arguments for the appropriateness of the prevalence odds ratio and related logistic regression. BMC Medical Research Methodology. 2010;10(1):66.

6. Levav J, Fitzsimons GJ. When Questions Change Behavior: The Role of Ease of Representation. Psychological Science. 2006 Mar 1;17(3):207–13.

7. Zwane AP, Zinman J, Van Dusen E, Pariente W, Null C, Miguel E, et al. Being surveyed can change later behavior and related parameter estimates. Proc. Natl. Acad. Sci. U.S.A. 2011 Feb 1;108(5):1821–6.

8. Pertussis [Internet]. [cited 2011 Oct 18]. Available from: http://ecdc.europa.eu/en/healthtopics/pertussis/Pages/index.aspx

# Appendix

## List of case definition

**Table 10.** EU Case definition by EU Commission Decision of 28 April, 2008 (8)

| **Case definition** | |
|---|---|
| Clinical criteria | Any person with a cough lasting at least two weeks and at least one of the following three:<br>paroxysms of coughing, inspiratory "whooping",<br>Post-tussive vomiting or Any person diagnosed as pertussis by a physician or Apnoeic episodes in infants |
| Laboratory criteria | At least one of the following three:<br>Isolation of *Bordetella pertussis* from a clinical specimen<br>Detection of *Bordetella pertussis* nucleic acid in a clinical specimen<br>*Bordetella pertussis* specific antibody response<br>Serology results need to be interpreted according to the vaccination status |
| Epidemiological criteria | An epidemiological link by human to human transmission<br>Additional information<br>Incubation period 6-20 days, most often 10 days |
| **Case classification** | |
| Possible case | Any person meeting the clinical criteria |
| Probable case | Any person meeting the clinical criteria and with an epidemiological link |
| Confirmed case | Any person meeting the clinical and the laboratory criteria |

**Table 11.** The distribution of the 31 questions in the four categories of interests and the characteristics of answers

| Question no. and contents | No. of options | Tape of answers | Optional / Required question |
|---|---|---|---|
| **Notification behavior (8 required questions)** | | | |
| 1. Do you regard pertussis as a notifiable disease? | 2 | Binary (Y/N) | R |
| 2. If yes, to whom should you notify a pertussis case | 2 | Binary | R |
| 3. Do you use the standardized notification form for notifying a case of any notifiable disease provided by Federal Ministry of Health? | 2 | Binary | R |
| 8. Do you use an officially recommended case definition? | 2 | Binary | R |
| 9. Do you know the ECDC (European Centre for Disease Prevention and Control) case definition of pertussis? | 2 | Binary | R |
| 10.If yes, do you notify a pertussis case based on the ECDC case definition criteria? | 2 | Binary | R |
| 11. Do you already notify a clinically suspected case (= clinical criteria fulfilled, laboratory criteria not yet fulfilled)? | 2 | Binary | R |
| 31. Do you notify a clinical suspected case again after having received a laboratory confirmation? | 2 | Binary | R |
| **Level of knowledge on clinical manifestation of pertussis (2 required questions )** | | | |
| 4. Which clinical signs and symptoms are compatible with a case of pertussis (multiple choice) | 9 | Multiple choices High:7-9 | R |
| 5. Do you differentiate the clinical signs and symptoms by age (for example age-groups defined as 0-3m; 4m-9y; >10y)? | 2 | Binary | R |
| 6. Cough is a major symptom of B. pertussis infection. The characteristics of clinical manifestation and duration of symptoms rely on age. Which statement is true? | 3 | Single choice | O |
| 6.1. Which clinical picture is compatible with pertussis in children aged ≤ 3 months? (Single choice) | | | |
| 6.2. Which symptoms in children between 4 months - 9 years should be considered for whooping cough? (Single choice) | 3 | Single choice | O |
| 6.3. Which symptoms in children aged ≥ 10 years and adults should be considered for whooping cough? (Multiple choice) | 3 | Single choice | O |
| 7. To meet the clinical case definition, ≥ 1 symptoms should persist accompanying with cough. | 10 | Multiple choices High:8-10 | O |
| 7.1. Which symptoms are in accordance with the clinical case definition in young children ≤ 3 months? | | | |
| 7.2. Which symptoms are in accordance with the clinical case definition in children between 4 months - 9 years? | 10 | Multiple choices High:8-10 | O |
| 7.3. Which symptoms are in accordance with the clinical case definition in children between children aged ≥ 10 years and adults? | 10 | Multiple choices High:8-10 | O |
| 14. Which duration of cough is regarded as the threshold between early stage and late stage of disease? | 3 | Single choice | O |
| **Level of knowledge on laboratory diagnosis (8 required questions )** | | | |
| 15. Which diagnostic test(s) is your first choice for laboratory confirmation in young children ≤ 3 months old with clinically suspected *B. pertussis* infection? (general) | 3 (3 points) | Multiple choices | R |
| 16. Which diagnostic test(s) is your first choice for | 3 | Multiple | R |

| | | | |
|---|---|---|---|
| laboratory confirmation in children > 3 months old, adolescents and adults with clinically suspected B. pertussis infection while cough lasted < 3 weeks? (general) | (3 points) | choices | |
| 17. Which diagnostic test(s) is your first choice for laboratory confirmation in children > 3 months old, adolescents and adults with clinically suspected B. pertussis infection while cough lasted ≥ 3 weeks? (general) | 3 (3 points) | Multiple choices | R |
| 19. Which immunoglobulin as the measurement(s) is (are) regarded of high diagnostic reliability (=highest sensitivity and highest specificity) for the serological confirmation of pertussis? (serology) | 3 (3 points) | Multiple choices | R |
| 23. How long should IgG-titer not be used to diagnosis pertussis because of cross-reaction in patients <1 year after pertussis vaccine formulation? (serology) | 3 (3 points) | Single choice | R |
| 24. Do you regard the level of IgG-titer to be reliable for discriminating between recent vaccination and current infection? (serology) | 2 (3 points) | Binary (Y/N) | R |
| 26. In the acute or convalescent cases, do you use follow-up serum specimens (taken at least three weeks apart) to confirm the suspected B. pertussis infection? (serology) | 2 (3 points) | Binary (Y/N) | R |
| 28. Which specimen do you regard as eligible for PCR or culture testing? (general ) | 5 (3 points) | Multiple choices | R |
| 21. Do you ask for pertussis vaccination history from your patients? (general) | 2 | Binary (Y/N) | O |
| 22. If Yes, Do you inform the information to the laboratory for submitting specimens? (general) | 2 | Binary (Y/N) | O |
| 25. Do you regard the level of IgG-titer to be reliable for distinguishing between previous infection and current infection? (serology) | 2 | Binary (Y/N) | O |
| 30. How do you perform a nasopharyngeal swab? | Open quesions | | O |
| **Laboratory confirmation seeking behaviour (2 required questions)** | | | |
| 12. How often do you seek laboratory diagnostics for a patient clinically suspected with B. pertussis infection? | 5 | Single choice (Satisfactory: ≥75%) | R |
| 13. Please give the reasons for NOT seeking laboratory diagnostics for a patient suspected with B. pertussis infection | 4 | Multiple choices | R |

## Questionnaire

The questionnaire for clinical physicians about notification, clinical manifestation and laboratory diagnostic methods of pertussis, Austria, 2013

**Pertussis-Fragebogen für klinisch tätige Ärztinnen und Ärzte**

**Interview Nr:** □ □ □

**Fachgebiet:** □ Allgemeinmedizin □ Kinderheilkunde □ Lungenheilkunde

**Lokalisation der ärztlichen Tätigkeit (hauptsächlich):**

□ Ordination/Praxis □ Krankenhaus der Normalversorgung □ Universitätsklinik

**Bundesland:**

□ Wien □ Burgenland □ Oberösterreich □ Niederösterreich □ Steiermark □ Salzburg □ Kärnten □ Tirol □ Vorarlberg

PLZ: □ □ □ □ Stadt/ Ortschaft: _____

Einzugsgebiet des Krankenhauses bzw. der Ordination:

**1.** Ist Keuchhusten eine meldepflichtige Krankheit?

□Ja □Nein

**2.** Falls ja, an wen ist ein Fall von Pertussis zu melden?

□ zuständige Bezirksverwaltungsbehörde
□ zuständige Landessanitätsdirektion
□ Bundesministerium für Gesundheit

**3.** Benützen Sie zur Meldung eines Falles von Pertussis das *Melde(Anzeige-) formular für meldepflichtige Krankheit*, welches vom Bundesministerium für Gesundheit vorgegeben ist?

□Ja □Nein

**4.** Welche klinischen Zeichen und Beschwerden sind vereinbar mit Keuchhusten?

□ (1) Hochfieberhafte Bronchitis

□ (2) Hustenanfälle mit hustenbedingten, unkontrollierbaren und anhaltenden Exspirationen, gefolgt von einem ausgeprägten inspiratorischen Jauchzen oder Keuchen (=inspiratory whoop)

□ (3) Durch massive Hustenanfälle ausgelößtes Erbrechen

□ (4) Paroxysmaler Husten mit einer Dauer von ≥14 Tagen

□ (5) Paroxysmaler produktiver Husten mit einer Dauer von ≥7 Tagen

□ (6) Paroxysmaler, nichtproduktiver Husten mit einer Dauer von ≥7 Tagen

□ (7) Paroxysmaler Husten nicht notwendigerweise mit typischer Keuchhusten-charakteristik, ohne Apnoeepisoden, ohne Erbrechen und ohne Zunahme der Beschwerden in der Nacht

□ (8) Hustenbedingte Petechien im Gesicht oder subkonjunktivale Einblutungen

□ (9) Hustenbedingte Apnoeepisoden

□ (10) Andere klinische Zeichen und Beschwerden, bitte benennen _____.

**5.** Beurteilen Sie klinische Zeichen und Symptome bei V.a. Pertussis altersgruppen-spezifisch, für Altersgruppen ≤ 3 Monate, zwischen 4 Monaten und 9 Jahren, >10Jahre?

□ Ja □Nein

**6.** Husten ist ein zentrales Symptom von Pertussis. Bei V.a. Keuchhusten wird die Hustencharakteristik und -dauer altersabhängig bewertet. Welche Aussage ist zutreffend?

**6.1.** Bei Kindern **≤ 3 Monaten** sollte Pertussis erwogen werden...

□ ... **nur** bei paroxysmalem Husten ≥ 1 Wochen
□ ... **nur** bei paroxysmalem Husten ≥ 2 Wochen
□ ... Husten jeglicher Dauer und Form (paroxysmal/oder non-paroxysmal) bei fehlender Besserung

**6.2.** Bei Kindern zwischen **4 Monate - 9 Jahre** sollte Pertussis erwogen werden...

□ bei produktivem Husten ≥ 2 Wochen mit Temperatur ≥ 39°C.
□ bei nicht-produktivem, paroxysmalem Husten ≥ 1 Woche
□ Husten jeglicher Dauer und Form

**6.3.** Bei Kindern **≥ 10 Jahren, Jugendlichen und Erwachsenen** sollte Pertussis erwogen werden:

□ bei nicht-produktivem, paroxysmalem Husten >= 1 Woche
□ bei nicht-produktivem, paroxysmalem Husten >= 2 Woche
□ Husten jeglicher Dauer und Form

**7.** Neben dem Husten zeigt sich Pertussis in aller Regel mit einer ebenfalls altersabhängigen Begleitsymptomatik. Zur Erfüllung der klinischen Falldefinition müssen neben der Hustensymptomatik zusätzlich ≥ 1 Begleitsymptom bestehen.

**7.1.** Bei Kindern **≤ 3 Monate** sind im Sinne der klinischen Falldefinition folgende Symptome oder Umstände relevant:

□ (1) inspiratorischer "whoop" (der Hustenanfall ist assoziiert mit hustenbedingten, unkontrollierbaren und anhaltenden Exspirationen, an die sich ein ausgeprägtes inspiratorisches Jauchzen oder Keuchen)
□ (2) Nächtliche Aggravierung des Beschwerdebildes
□ (3) Apnoe
□ (4) Posttussives Erbrechen
□ (5) Zyanose
□ (6) Schweißausbrüche zwischen den Hustattacken
□ (7) Krampfanfälle
□ (8) Pneumonie
□ (9) non-produktiver Schnupfen
□ (10) naher Kontakt zu einer Person (zumeist Familien-/Haushaltmitglied) mit prolongiertem Husten

**7.2.** Bei Kindern zwischen **4 Monate - 9 Jahre** sind im Sinne der klinischen Falldefinition folgende Symptome oder Umstände relevant:

□ (1) inspiratorischer "whoop" (der Hustenanfall ist assoziiert mit hustenbedingten, unkontrollierbaren und anhaltenden Exspirationen, an die sich ein ausgeprägtes inspiratorisches Jauchzen oder Keuchen)
□ (2) Nächtliche Aggravierung des Beschwerdebildes
□ (3) Apnoe
□ (4) Posttussives Erbrechen
□ (5) Zyanose
□ (6) Schweißausbrüche zwischen den Hustattacken
□ (7) Krampfanfälle
□ (8) Pneumonie
□ (9) non-produktiver Schnupfen
□ (10) ohne sonstige Begleitsymptome
□ (11) Naher Kontakt zu einer Person (zumeist Familien-/Haushaltmitglied) mit prolongiertem Husten

**7.3.** Bei Kindern **≥ 10 Jahren und Erwachsenen** sind im Sinne der klinischen Falldefinition folgende Symptome oder Umstände relevant:

□ (1) inspiratorischer "whoop" (der Hustenanfall ist assoziiert mit hustenbedingten, unkontrollierbaren und anhaltenden Exspirationen, an die sich ein ausgeprägtes inspiratorisches Jauchzen oder Keuchen)
□ (2) Nächtliche Aggravierung des Beschwerdebildes
□ (3) Apnoe
□ (4) Posttussives Erbrechen
□ (5) Zyanose
□ (6) Schweißausbrüche zwischen den Hustattacken
□ (7) Krampfanfälle
□ (8) Pneumonie
□ (9) non-produktiver Schnupfen
□ (10) ohne sonstige Begleitsymptome
□ (11) naher Kontakt zu einer Person (zumeist Familien-/Haushaltmitglied) mit prolongiertem Huste

**8.** Benutzen Sie im klinischen Alltag offizielle Falldefinitionen?
□ Ja □Nein

**8.a** Wenn ja, von welcher Institution/ Organisation?

□ CDC
□ Robert Koch Institut
□ EU/ECDC
□ WHO
□ andere, bitte benennen Sie diese_____

**9.** Kennen Sie die Falldefinition des ECDC (Europäisches Zentrum für die Prävention und die Kontrolle von Krankheiten)?

□ Ja □ Nein
Wenn ja, nennen Sie die Definitionskriterien
_____

**10.** Wenn ja, haben Sie bisher die ECDC Falldefinition als Basis für die offizielle behördliche Meldung verwendet?

□ Ja □ Nein

**11.** Melden Sie bereits den klinischen Pertussis-Verdacht (klinische Kriterien erfüllt, Laborkriterien noch nicht erfüllt)?

□Ja □Nein

**12.** Wie oft veranlassen Sie beim klinischen Verdacht auf ein Pertussis eine Labordiagnostik?

□ In jedem Fall
□ In ca. 75% aller Fälle
□ In ca. 50% aller Fälle
□ In ca. 25% aller Fälle
□ In < 25% aller Fälle

**13.** Was sind Ihre Gründe, warum Sie bei Verdacht auf Pertussis **KEINE** Labordiagnostik veranlassen?

□ Beim klinischen Verdacht wird sofort mit einer Therapie begonnen und die Ergebnisse der Labordiagnostik treffen meist zu spät ein
□ Die Sensitivität und Spezifität der Labordiagnostik ist unzureichend
□ Die notwendige Labordiagnostik ist zu teuer und wird im ambulanten Bereich nicht von den Krankenkassen übernommen
□ Andere Gründe, bitte benennen_____

**14.** Bei Pertussis wird zwischen einer frühen Phase und einer späten Phase der Krankheit unterschieden. Wann beginnt die Spätphase?

□ nach 3 Wochen Hustensymptomatik
□ nach 6 Wochen Hustensymptomatik
□ nach 9 Wochen Hustensymptomatik

**15.** Welche diagnostischen Tests sind bei Kindern ≤ 3 Monate zur Bestätigung des klinischen Verdachts geeignet?

□ Serologie
□ PCR
□ Kultur

**16.** Welche diagnostischen Tests sind bei Kindern > 3 Monate, Jugendlichen und Erwachsenen mit einer Hustendauer von < 3 Wochen zur Bestätigung des klinischen Verdachts geeignet?

□ Serologie
□ PCR
□ Kultur

**17.** Welche diagnostischen Tests sind bei Kindern > 3 Monate, Jugendlichen und Erwachsenen mit einer Hustendauer von ≥ 3 Wochen zur Bestätigung des klinischen Verdachts geeignet?

□ Serologie
□ PCR
□ Kultur

**18.** In welcher Situation sind serologische Untersuchungen in der Regel nicht sinnvoll?

□ Im ersten Jahr nach einer Pertussis-Impfung
□ Bei Kindern ≤ 3 Monate
□ Bei allen gegen Pertussis geimpften Personen

**19.** Die Bestimmung von welchen Immunglobulinen wird zur Bestätigung einer Pertussis-Infektion als diagnostisch sinnvoll (ausreichende Sensitivität und Spezifität) erachtet?

□ IgG-anti-PT
□ IgA-anti-PT
□ IgM-anti-PT

**20.** Erhalten Sie von Ihrem Labor nur qualitative (positiv / negativ) oder auch quantitative (Angabe einer Titerhöhe) Ergebnisse?

□ Nur qualitative Ergebnisse (positiv oder negativ)
□ Nur quantitative Ergebnisse (Titer-Angabe)
□ Qualitative und quantitative Ergebnisse

**21.** Fragen Sie Ihre Patienten auch nach stattgehabten Pertussis-Impfungen?

□Ja □Nein

**22.** Falls ja, geben Sie diese Information an das untersuchende Labor weiter?

□Ja □Nein

**23.** In welchem Abstand zu einer Pertussis-Impfung sollte der IgG-Titer aufgrund von möglicher Kreuzreaktionen mit größer Zurückhaltung interpretiert werden?

□ Innerhalb des ersten Jahres nach einer Pertussis-Impfung
□ Innerhalb der ersten 2 Jahre nach einer Pertussis-Impfung
□ Innerhalb der ersten 5 Jahre nach einer Pertussis-Impfung

**24.** Halten Sie die Höhe des IgG-Titers als zuverlässig für die Unterscheidung zwischen einer stattgehabten Impfung und frühere Infektion?

□Ja □Nein

**25.** Halten Sie die Höhe des IgG-Titers als zuverlässig für die Unterscheidung zwischen einer aktuellen und früheren Infektion?

□Ja □Nein

**26.** Lassen Sie bei Patienten ein Serumpaar (im Abstand von > 3 Wochen) zur Bestätigung einer frischen Infektion mit Bordetella pertussis untersuchen?

□Ja □Nein

**27.** Zu welchem Labor schicken Sie Ihre Serum-Proben?

---

**28.** Welche Proben sind für die Durchführung einer Pertussis-PCR oder –Kultur sinnvoll?

□ (1) Rachenabstrich (oraler Zugang)
□ (2) Nasen-Rachen-Abstrich (nasaler Zugang)
□ (3) Sputum
□ (4) Nasensekret (nasopharyngeales Aspirat)
□ (5) EDTA Blut

**29.** Zu welchem Labor schicken Sie Ihre Proben?

Für die Kultur _____
Für die PCR_____

**30.** Wie führen Sie einen Nasen-Rachen-Abstrich (nasaler Zugang)

---

**31.** Melden Sie einen durch das Labor bestätigten Pertussis-Fall erneut an die Behörde?

□Ja □Nein

**32.** Verordnen Sie symptomatischen Patienten mit labordiagnostisch bestätigter Pertussis…

□ … in jedem Fall ein Antibiotikum unabhängig von der Dauer der Erkrankung
□ … ein Antibiotikum nur innerhalb der ersten 3-4 Krankheitswochen
□ … ein Antibiotikum nur innerhalb der ersten 3-4 Krankheitswochen, in wenigen Ausnahmen auch noch später

Vielen Dank für Ihre Zusammenarbeit!

9. 教學案例—奧地利沙門氏菌群聚事件

# Lebensmittelbedingte Ausbruchsabklärungen Workshop

AGES Spargelfeld,Vienna, Austria, 11 September 2013

# A Gastroenteritis outbreak,

# Austria

(Exercise: 3.5 hours)

This case study is based on an investigation that was performed by:
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## Learning Objectives

After completing the case study, participants should be able to:

- Describe the steps of an outbreak investigation
- Generate and interpret an epidemic curve
- Calculate and interpret attack rates and risk ratios
- List the necessary environmental and laboratory investigations
- Make recommendations for the implementation of control measures

**Introduction**

On July 27, 2011, Austrian Agency for Health and Food Safety (AGES) received a mandate from Federal Ministry of Health to investigate an outbreak. The signal has been detected by the Austrian Reference Centre for *Salmonella* on July 18, 2011 with the specimens from a cluster of six patients showed indistinguishable PFGE patterns of Salmonella Typhimurium DT3 isolates, among those four of the notified cases had attended a party in Vienna on July 13.

It was decided to further investigate the outbreak to determine its extent and to identify the source of infection and the likely reservoir(s) of the outbreak strain in order to control the outbreak and prevent possible future outbreaks.

**Step 1- Confirm outbreak and diagnosis**

**Step2- Form outbreak control team**

**Question 1: What next steps would you take in investigating the outbreak?**

(15 mins)

*Form communication team*

*The ten steps of an outbreak investigation:*

- *Confirm outbreak and diagnosis: contact the laboratories*
- ***Form outbreak control team**: the outbreak control team may consist of district or provincial medical officers, epidemiologists, microbiologists, environmental health officers, clinicians, food inspectors, engineers, veterinarians...some of them would be team coordinators*
- *Define a case: Case definition: standard set of criteria (time, place, person and clinical/biological criteria) for deciding if a person should be classified as suffering from the disease under investigation*
- *Identify cases and obtain information*
- *Describe data by time, place person: When did they become ill? Where do they live? Who are the cases?*
- *Develop hypothesis*
- *Test hypothesis: analytical studies*
- *Additional studies*
- *Communicate results: outbreak report , publication*
- *Implement control measures: prophylaxis, exclusion and isolation, public warning, hygienic measures…*

*Investigate etiological agent, mode of transmission, vehicle of transmission, source of contamination, population at risk and exposure causing illness*

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*Investigate etiological agent, mode of transmission, vehicle of transmission, source of contamination, population at risk and exposure causing illness*

In late July 2011, the outbreak investigation team has built and an outbreak control meeting was arranged. The outbreak investigation team consisted of the district and provincial medical officers, epidemiologists, microbiologists, environmental health officers and veterinarians. To measure disease occurrence we need to first count patients with a specific disease, which means to define the disease.

## Step 3- Define a case

**Question 2: How would you define a case?** (10 mins)

***A typical case definition would include:***

1. *Clinical criteria and laboratory findings to characterise the disease,*
2. *A clear time period within which we count cases,*
3. *A precise identification (personal characteristics) of the population from which we count cases and its location.*

*Therefore: the disease, the time, the place and the person.*

***The case definition include***

- *Possible:*
- *Probable: Gastroenteritis in an attendee of the party on July 13 with disease* onset between July 14 and 21 *(At some occasions you can't generate a case definition with a specific time frame at the moment, so a sensitive case definition would be used ).*
- *Confirmed: A probable case with a stool sample positive for S. Typhimurium DT3*

**The definition of gastroenteritis in a probable case: At least two of the following clinical manifestations: Nausea, vomiting, abdominal pain, cramps, fever and diarrhoea.*

## Step 4- Identify cases and obtain information

**Question 3: How would you carry out further case finding? What other information would you like to obtain?** (15 mins)

***Trawling a questionnaire***

*Active case-finding was performed by the public health authorities by interviewing known cases on their knowledge of other attendees who suffered from gastroenteritis.*
*For each case, information on demographic information (i.e. age, sex) date of disease onset, symptoms (diarrhoea, vomiting, fever, nausea, stomach ache and cramps) and on laboratory testing of stool specimen were collected.*

***Exposures and known risk factors***

*We conducted trawling interviews with the first ten case-patients on exposure to food and on physical or household contact to gastroenteritis cases within the **three** days (incubation period: 12-72 hours) preceding disease onset in order to generate hypotheses about the potential source(s) of infection.*

***Organize information: Generate case line list***

*Names, Date of Birth, Address, Date of symptom onset, Signs and symptoms, Date of notification, Date of diagnosis, Treating physicians, Hospital stay, Epidemic linkage, Laboratory results…*

After actively finding cases from the attendees of the party, a total of 25 cases met the outbreak case definition, including twelve confirmed cases.

Table 1. List of case-patients among the attendees in a party, Vienna, July 13, 2011

| Case ID | Gender | Age | Province | Dateof Onset | Time of Onset | Laboratory confirmation |
|---|---|---|---|---|---|---|
| **1** | F | 27 | Wie | 15.07.2011 | 07:00 | N |
| **2** | M | 28 | Wie | 14.07.2011 | 20:00 | Y |
| **3** | M | 70 | Wie | 14.07.2011 | 12:00 | Y |
| **4** | F | 25 | Wie | 15.07.2011 | 07:00 | N |
| **5** | F | 75 | Wie | 14.07.2011 | 21:00 | Y |
| **6** | M | 41 | Wie | 15.07.2011 | 08:00 | Y |
| **7** | F | 71 | Wie | 14.07.2011 | 20:00 | N |
| **8** | F | 69 | Wie | 14.07.2011 | 18:00 | N |
| **9** | F | 52 | Wie | 16.07.2011 | NA | N |
| **10** | M | 51 | Wie | 17.07.2011 | NA | N |
| **11** | M | 82 | Wie | 15.07.2011 | 18:00 | Y |
| **12** | F | 63 | NÖ | 14.07.2011 | 19:30 | N |
| **13** | M | 72 | NÖ | 14.07.2011 | 19:30 | N |
| **14** | M | 68 | Wie | 15.07.2011 | 07:00 | Y |
| **15** | F | 13 | Wie | 14.07.2011 | 15:00 | Y |
| **16** | F | 35 | Wie | 16.07.2011 | NA | N |
| **17** | F | 70 | NÖ | 14.07.2011 | 18:00 | N |
| **18** | M | 71 | NÖ | 14.07.2011 | 12:00 | N |
| **19** | F | 75 | Wie | 14.07.2011 | 16:00 | Y |
| **20** | M | 25 | Wie | 14.07.2011 | 12:00 | N |
| **21** | M | 71 | Wie | 15.07.2011 | 01:30 | N |
| **22** | F | 38 | Wie | 14.07.2011 | 12:00 | Y |
| **23** | M | 35 | Wie | 14.07.2011 | 11:00 | Y |
| **24** | M | 6 | Wie | 14.07.2011 | 12:00 | Y |
| **25** | M | 87 | Wie | 14.07.2011 | 18:00 | Y |

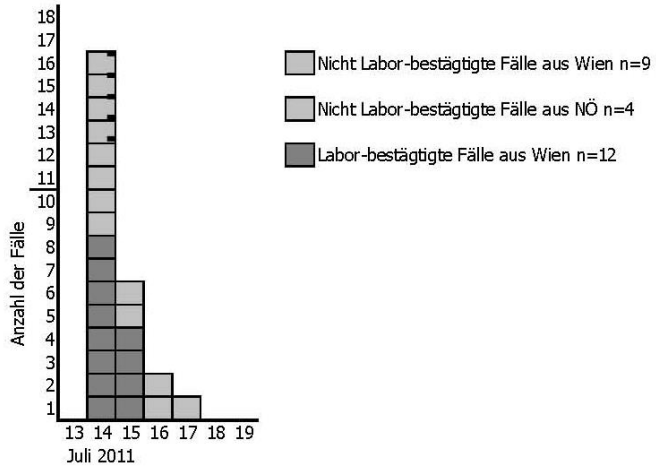
The outbreak can be visually described with a chart showing the number of persons who were diagnosed each time unit. This chart is called an epidemic curve or epi curve.

**Step 5- Descriptive study- Describe data by time, place and person**

**Question 4: Please generate an epidemic curve and interpret the data.** (20 mins, then coffee break)

**Answer:**

**Ausbruchsfälle *Salmonella* Typhimurium DT3, Österreich, Juli 2011 nach Bundesland und Erkrankungsbeginn; N=25**




*The epidemic curve helps to develop hypotheses: incubation period, etiological agent, type of source, type of transmission, time of exposure.*

*Time and place:*
*The shape of the epidemic curve suggested a common point source of infection. The outbreak lasted from July 14th to July 17th and peaked with 16 cases on July 14th, indicating a point source active on July 13th, which corresponds to the date of the party.*

*Person:*
*The median age was 63 years (min: 6, max: 87) with a male-to-female ratio of 1.1:1 (males n=13).*

**Step 6- Develop hypothesis**

**Question 5: Do you have any hypothesis at this stage based on the information available?** (10 mins)

***Who is at risk of becoming ill?***

***What is the disease?***

***What is the source and the vehicle?***

***What is the mode of transmission?***

*The hypothesis was that exposure of the attendees to the infectious agent took place on 13 July, the date of the party held. The contaminated food or water that the attendees consumed might be:*

*Food items served for the party: meat, eggs, fruits, salad…,*

*Ingredients of the food items,*

*Water contamination, OR*

*Common animal contact*

**Step 7- Test hypothesis: analytical studies**

**Question 6: What kind of studies would you like to use in order to test the hypotheses? Why?** (15 mins)

*Analytical studies:*

*Cohort studies*

*-attack rate exposed group*

*-attack rate unexposed group*

*Case-control studies*

*-proportion of cases exposed*

*-proportion of control exposed*

**Advantages and disadvantages of cohort and case control studies** *(source : FEM wiki)*

| | Cohort studies | Case control studies |
|---|---|---|
| **Suited for rare diseases** | *No* | *Yes, since starting with a set of cases* |
| **Suited for rare exposures** | *Yes, since starting with exposure status* | *No* |
| **Allows for studying several exposures** | *Difficult but examples exists (Framingham study)* | *Yes* |
| **Allows for studying several outcomes** | *Yes* | *No* |
| **Disease status easy to ascertain** | *Sometimes difficult* | *Easier since starting point of the study* |
| **Exposure status easier to ascertain** | *Yes, since starting point of the study. Except for retrospective cohorts* | *Sometimes difficult. Information biases.* |
| **Allows computation of risk and rates** | *Yes* | *No* |
| **Allows computation of effect** | *Computation of risk ratio and rate ratio* | *Estimation of risk ratio, rate ratio from odds ratio* |
| **Allows studying natural history of disease** | *Yes. Easier to show that cause precedes effect.* | *More difficult. Temporality between cause and effect difficult to establish* |
| **Based on existing data sources** | *Difficult* | *Yes, but access to information sometimes difficult* |
| **Easiness to find a reference group** | *Usually not difficult to identify an unexposed population* | *No. Major potential biases when selecting a control group* |
| **Sample size** | *Large* | *Small* |
| **Cost** | *Elevated except if retrospective cohorts* | *Smaller* |
| **Time required** | *Long, sometimes very long except if retrospective cohorts* | *Shorter* |
| **Follow up** | *Difficult, loss to follow up* | *No follow up* |
| **Logistics** | *Heavy. Many staff, large data sets. Long duration* | *Easier* |
| **Concept** | *Easy to understand* | *Difficult to understand particularly if case cohort or density case control study* |
| **Ethical issues** | *Major if studying risk factors. Interruption of study if exposure shown to be harmful. Need for intermediate analysis.* | *None since outcome already happened.* |

The hypothesis was that exposure of the attendees to the infectious agent took place on 13 July, the date of the party held. It was decided to further look at the role of the food attendees consumed that day. A ***retrospective cohort study*** among all the 39 attendees of the party was carried out in July 2011 by telephone interviews using a standardized questionnaire. Data on exposure to different food items (i.e. suckling pig, potato salad, pickled cabbage, Yogurt-raspberry cake…) was collected.

For the cohort study, a more specific case definition was used restricting the time frame. A probable case was defined as gastroenteritis (at least having two of the symptoms listed on the questionnaire) in a person attending the party in Vienna on July 13 with disease onset between July 14 and 21, 2013. A confirmed case was defined as a probable case with a stool sample positive for S. Typhimurium DT3.

All 39 attendees of the party completed the questionnaire and were included in the food-specific cohort analyses. Table 2 listed the food items and beverages consumed for the party.

**Question 7: Please calculate and fill the blank regarding attack rates (AR) and risk ratios (RR) associated with each of the food items and water samples. Interpret the results.** (20 mins)

Table 2: Salmonella Typhimurium DT3 outbreak in Austria, July 2011; Results of the food-specific cohort analyses; Food unexposed defined as participants having not consumed or having consumed a small portion of the food item under study

| **Food items** | **Food exposed** | | | **Food unexposed** | | | | |
|---|---|---|---|---|---|---|---|---|
| | ill | total | AR% | ill | total | AR% | RR | 95% C.I. |
| **Sucklingpig/dumpling filling** | 24 | 37 | | 1 | 2 | | | 0.3-5.3 |
| **Potato salad** | 21 | 29 | | 4 | 10 | | | 0.8-4.0 |
| **Pickled cabbage** | 22 | 34 | | 3 | 5 | | | 0.5-2.3 |
| **Chocolate cake** | 7 | 11 | | 18 | 28 | | | 0.6-1.7 |
| **Yogurt-raspberry cake** | 17 | 24 | 70.8 | 8 | 15 | 53.3 | 1.3 | 0.8-2.3 |
| **Lemon cake** | 11 | 19 | 57.9 | 14 | 20 | 70.0 | 0.8 | 0.5-1.3 |
| **Egg-liqueur cake** | 12 | 16 | 75.0 | 13 | 23 | 56.5 | 1.3 | 0.8-2.1 |
| **Tap water** | 9 | 13 | 69.2 | 16 | 26 | 61.5 | 1.1 | 0.7-1.8 |
| **Mineral water** | 11 | 16 | 68.8 | 14 | 23 | 60.9 | 1.1 | 0.7-1.8 |
| **Beer** | 11 | 15 | 73.3 | 14 | 24 | 58.3 | 1.3 | 0.8-2.0 |
| **Wine** | 8 | 14 | 57.1 | 17 | 25 | 68.0 | 0.8 | 0.5-1.4 |
| **Champagne** | 9 | 12 | 75.0 | 16 | 27 | 59.3 | 1.3 | 0.8-2.0 |

**Step 8- Additional studies**

**Question 8: What other additional investigation would you like to conduct in order to verify your hypothesis?** (15 mins)

- *Microbiological investigation of food samples*

*Food leftovers were tested for Salmonella as described elsewhere.*

- *Molecular typing*

*Stool samples from 13 cases were available for testing for enteric pathogens, including Salmonella, Shigella, Yersinia, Campylobacter and enterohaemorrhagic E. coli. Human and non-human isolates were serotyped according to the Kauffmann-White scheme , phage typed and genotyped by the use of variable number of tandem repeats (VNTR)-analysis and by pulsed-field gel electrophoresis (PFGE) using the restriction enzyme XbaI.*

- *Veterinarian investigation*
- *Environmental investigation*
- *Trace back investigation (when you have the preliminary result of possible contaminated food items )*

*Egg producers identified as epidemiologically outbreak-related by trace-back analyses were sampled in accordance with the sampling strategy specified by the Austrian 15-week regulatory monitoring program (Bundesministerin für Gesundheit, Familie und Jugend, 2007), including one sample of 150 g dust and two paired boot swabs per flock.*

*Sampling of the pig farm was performed according to the European baseline survey on Salmonella positivity in breeding pig holdings (Bundesministerium für Soziale Sicherheit und Generationen, 2001) and included paired boot swabs, pooled faeces samples, dust samples and feed samples. The samples from the egg-producing and pig-producing holdings were tested for Salmonella.*

Twelve (92%) out of 13 outbreak case-patients who provided stool specimens were positive for S. Typhimurium DT3. Samples of the potato salad, the pickled cabbage salad and the roast suckling pig were all negative for *Salmonella* spp.

The pig farm that provided the suckling pig was operated by the caterer, who works mainly as a pig farmer. Three pooled faeces samples, two paired boot swabs and one dust sample out of the 21 environmental samples collected at the farm on August 1 tested positive for S. Typhimurium DT3. In addition, two of the three flocks in one laying-hen holding from whom the caterer purchased the eggs as ingredients of the suckling pig dumpling also tested positive for S. Typhimurium DT3. All the human isolates, the six environmental samples from the pig farm and egg samples from the laying-hen holding shared indistinguishable PFGE and VNTR profiles.

In late August 2011, another outbreak was investigated involving a total of 13 cases in 25 visitors of a wine tavern in Lower Austria. Stool specimens obtained from three of the eight laboratory confirmed cases tested positive for S. Typhimurium DT3 accompanying indistinguishable VNTR and PFGE patterns from the human, laying hen holding and egg isolates obtained during the investigation of the previous DT3 outbreak in July.

**Step 9-Communicate results: outbreak report, publication**

**Question 9: Based on all the findings, what conclusions would you like to draw and communicate to the public?** (15-20 mins)

*Please look at the summary described at the last page*

## Step 10- Implement control measures

**Question 10: What kind of specific control measures were required to be implemented during and after the outbreak?** (15-20 mins)

***Interrupt transmission and control the source of the pathogen***

*The eggs originated from the laying hen holding (laying hen holding A) involved in the DT3 outbreak in July before a marketing ban was imposed on August 16th as part of the control measures for the preceding DT3 outbreak. The DT3 positive flock was culled on August 31.*

***General control measures***

*Cross-contamination of foods should be avoided. Uncooked meats should be kept separate from produce, cooked foods, and ready-to-eat foods. Hands, cutting boards, counters, knives, and other utensils should be washed thoroughly after touching uncooked foods. Hand should be washed before handling food, and between handling different food items.*

*Better education of food industry workers in basic food safety and restaurant inspection procedures may prevent cross-contamination and other food handling errors that can lead to outbreaks. Wider use of pasteurized egg in restaurants, hospitals, and nursing homes is an important prevention measure.*

*Education people that contact with live poultry and their environment can be a source of human Salmonella infections. Live poultry can be carrying Salmonella bacteria but appear healthy and clean and show no signs of illness. People should wash their hands after contact with animal feces.*

**Question 11: What can be learned from this outbreak to prevent possible future outbreaks?** (15-20 mins)

*The cooperation and communication between the experts in an outbreak investigation team including experts from human medicine, veterinary medicine and food safety officers are important.*

*What can you do to prevent future outbreaks as a PH officer, a medical officer, a food inspector or a veterinarian?*

**Summary**

This was the first documented foodborne outbreak of S. Typhimurium DT3 in Austria. Following a party on July 13 2011, 25 of 39 attendees fell sick with gastroenteritis. Food-specific cohort analyses of food items served at the party identified potato salad as the possible outbreak source, even though at weak levels of statistical significance limited by smaller cohort size. Accepting this significance level led to the hypothesis that potato salad was contaminated with the outbreak strain during preparation through contact with the suckling pig or eggs used for the pig filling. The suckling pig, the egg-containing dumpling filling and the potato salad were indeed all prepared in close vicinity in the caterer's kitchen. According to the observations of the food inspector, the potato salad was not processed as required by the Austrian guidelines on hygiene in commercial kitchens, which stipulates that the pH value of potato salad must be ≤4.5.

This hypothesis was supported by the microbiological findings associated with the outbreak. The caterer also operated the pig farm that supplied the suckling pig. The S. Typhimurium DT3 isolates from the pig farm, two flocks of the laying hen holdings and the outbreak cases were indistinguishable from one another.

The eggs originated from the laying hen holding involved in the outbreak were imposed on August 16 as part of the control measures. After the incident of the second outbreak, the DT3 positive flock was culled on August 31. As of May 2012, no more human cases of S. Typhimurium DT3 were detected at the National Reference Centre for *Salmonella*.

The two Austrian foodborne outbreaks (the party outbreak and the tavern outbreak) linked to a single laying hen holding contaminated with identical S. Typhimurium DT3 strains within a short time interval were confined to two neighbouring Austrian provinces. The outbreak investigation identified eggs as the likely vehicle for S. Typhimurium. Educational materials warning food caterers and customers and advising them on how to reduce the risk for *Salmonella* infection from live poultry should be distributed with all live poultry and eggs purchases.

**Reference**

A.Voss, E. Simons, C. Micula, c. Kornschober, R. Ableitner, J. Stirling, B. Gleiss, S. Karner-Zuser, L. Hrivniakova, S. Kasper, F. Allerberger and D. Schmid. A foodborne outbreak due to Salmonella Typhimurium DT3 seemingly linked to more than one reservoir, Austria July 2011. Wiener Tierärztliche Monatsschrift 2012 99: 30-37.

10. 歐洲及奧地利百日咳流行病學近況口頭報告投影片

## Possible factors contributed to pertussis re-emergence

- Waning immunity after administration of DTaP or natural infection
- Enhanced surveillance
- Increased awareness among physicians
- Greater access to laboratory diagnostics (e.g. PCR )
- Limited discrimination between the different *Bordetella* species
- Pathogen adaptation: e.g. Pertactin-negative variants, PtxP3 strain
- Macrolide resistant *B. pertussis* strains
- Room for improvement
  - Age-stratified clinical definition for notification
  - Laboratory diagnostics SOP
  - Immunization schedules
    - Primary vaccination, boosters and vaccination during pregnancy (e.g. UK, USA)
  - New vaccines



EPIET

## Investigation of increased pertussis incidence in Austrian provinces, 2005-2012

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Department of Infectious Disease Epidemiology
Austrian Agency for Health and Food Safety (AGES)
14 May 2013

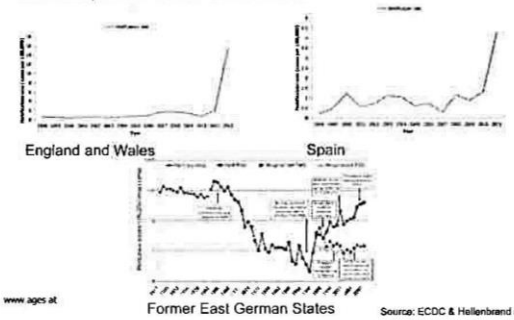


## Previous studies in Austria



## Pertussis in Europe

- Increase in several EU countries, particularly among older children, adolescents and adults

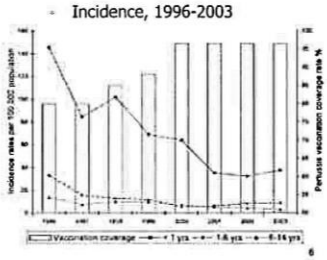



Source: ECDC & Hellenbrand et al, 2009



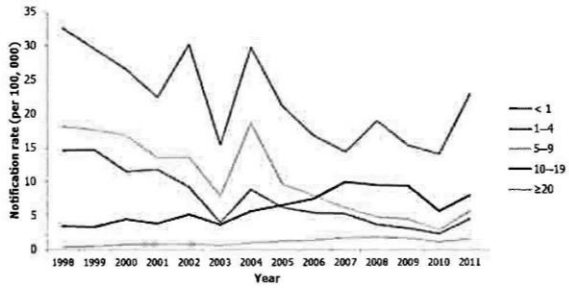
## Pertussis studies in Austria-1

- Rendi-Wagner et al, 2006
  - Hospital-based active surveillance of pertussis in hospitalised children, 1996-2003
  - Estimates of **incidence** and **VE** of whole-cell and acellular vaccine
- Vaccine effectiveness (after 3rd dose):
  - Whole-cell (1996-1997): 79%
  - Both types (1998): 86%
  - Acellular (2000-2003): 92%
- Incidence, 1996-2003

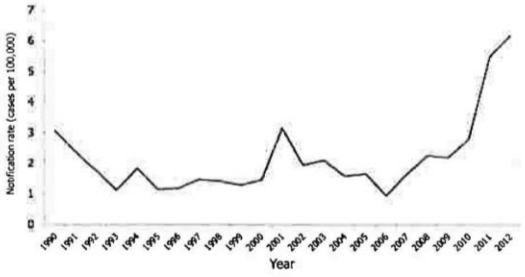




## Pertussis notification rate by age group, 12 EU countries, 1998-2011



## Annual incidence of pertussis, Austria, 1990-2012





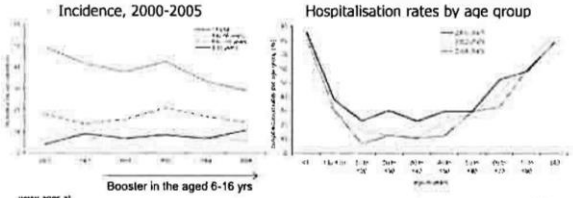

## Pertussis studies in Austria-2

- Rendi-Wagner et al, 2007
  - Impact of pertussis booster in adolescents and adults, Austria, 2000-2005

Result

- Based on the laboratory-based pertussis notification report

Incidence, 2000-2005 | Hospitalisation rates by age group

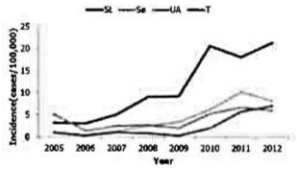


Booster in the aged 6-16 yrs

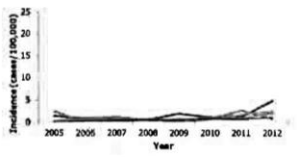


## Incidence of pertussis by province, 2005-2012

High incidence provinces:
Styria,
Salzburg,
Upper Austria
Tyrol




Low incidence provinces:
Vorarlberg,
Burgenland,
Lower Austria,
Carinthia
Vienna

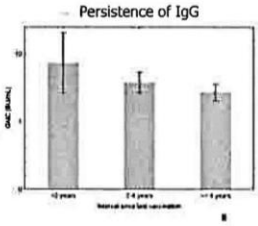





## Pertussis studies in Austria-3

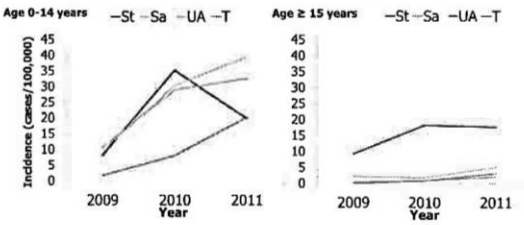
- Paulke-Korinek M et al, 2011
  - Persistence of antibodies in the aged 4-8 years after DTaP-HBV-IPV/Hib (≥3 doses) and/ or MMR vaccinations (≥ 1 dose), Sep 2007-Aug 2008
  - Pertussis vaccine schedules in 2000-2005: 3m, 4m, 5m, 2yrs
- Results (N=322)
  - Seroprotection: Detection of anti-Ptx and anti-FHA IgG ≥10BU/ml
  - Seroprotection rate on pertussis:
  - 4 doses: 41.8%
  - 3 doses: 23.5%

Persistence of IgG





## Pertussis incidence by age group of high incidence provinces, 2009-2011




**High incidence in both age groups in Styria**



## Surveillance data description

## Objectives

To assess

- notification behavior for pertussis,
- knowledge on clinical manifestation and laboratory diagnostic methods for pertussis, and
- attitude towards seeking laboratory confirmation for suspected pertussis cases

among general practitioners, pediatricians and pulmonologists in Austria, 2013



## Geographical location of high incidence provinces, Austria




## Cross-sectional study

- To measure and analyze whether there are differences regarding the following factors between physicians of high and low incidence provinces
  - Quality of notification behavior
  - Level of knowledge on clinical manifestations
  - Level of knowledge on laboratory diagnostic procedures
  - Frequency of seeking laboratory confirmation in a clinically suspected case



## Conclusion of baseline survey

- Significant increase of incidence
  - Styria, Salzburg, Upper Austria and Salzburg
- Stable incidence in the other five provinces
- Possible reasons:
  - Notification behavior of physicians
  - Misclassification of cases regarding clinical criteria
  - Different laboratory diagnostic methods
  - Different vaccine coverage



## Method

- The source population
  - General practitioners, pulmonologists, and pediatricians registered with the Austrian Chamber of Medical Doctors
- The study sample
  - Random sample stratified by province
  - Representative sample => 360 physicians
- Online 32-question questionnaires will be delivered
  - Non-respondents will be contacted by phone



**KAP survey:**
Knowledge, attitude and practices on pertussis among physicians in Austria, 2013

## ECDC protocols for RT-PCR and serological diagnosis





## Method-analysis/Dummy table

| Exposure factors | High incidence provinces n (%) | Low incidence provinces n (%) | aOR | 95% CI | P-value |
|---|---|---|---|---|---|
| **Notification practice** | | | | | |
| High/Moderate satisfactory | | | | | |
| Unsatisfactory | | | | | |
| **Knowledge on clinical manifestations** | | | | | |
| High/ Median level | | | | | |
| Low level | | | | | |
| **Knowledge on laboratory diagnostic procedures** | | | | | |
| High/ Median level | | | | | |
| Low level | | | | | |
| **Attitude concerning laboratory confirmation** | | | | | |
| Satisfactory | | | | | |
| Unsatisfactory | | | | | |

## Thank you for your attention

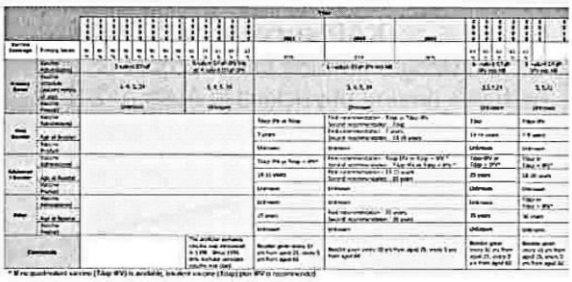


## Limitations

- Question-Behavior Effect
  - No influence on the observed data during 2005-2012
  - Assess the annual incidence by province from 2013-
- Reporting bias
- Selection bias
  - If non-responder rate > 20%



## Vaccine schedules and coverage in Austria, 1990-2012





## Recommendations for future work

- Monitor outbreaks
  - Vaccine effectiveness study
- Estimate vaccine coverage in the provinces
  - Primary vaccines
  - Boosters
- Conduct seroprevalence survey
- Standardize diagnostic procedures
  - E.g. ECDC protocol
- Revise pertussis vaccine strategies
  - Mathematical modelling

# 11. 人類感染 H10N8 禽流感病毒風險評估報告發表文章



## 人類感染 H10N8 禽流感病毒風險評估報告

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衛生福利部疾病管制署疫情中心

**摘要**

中國大陸於近期發布三例人類感染 H10N8 禽流感病毒個案，為全球唯一發布人類感染該亞型禽流感之地區。由於兩岸旅客往返頻繁，且不乏有走私禽鳥事件發生，亟需評估該疫情於我國發生之風險及造成之衝擊。本文參考國際間風險評估架構，依評估項目如病毒特性、實驗動物感染情形、病毒生態學及流行病學資料、國內易感族群及群體免疫力與疫苗等資訊，以評估 H10N8 禽流感疫情對我國之衝擊。評估結果顯示，就現有資訊及科學證據推斷該病毒傳播效率不高，發生境外移入病例並造成國內流行之可能性極低，因此影響國人健康的可能性低。若國內發生 H10N8 禽流感個案，受限該病毒尚不具人傳人之能力，因此僅限於零星散發個案，將不致造成社區傳播之風險；加以我國實施加強監測、禁止陳列、展示及販售活禽政策及抗病毒藥劑整備等防治作為下，綜合研判目前中國大陸 H10N8 禽流感疫情，造成我國衝擊之可能性亦極低。建議維持現有監視及通報定義以及對民眾衛教宣導內容，並加強相關研究及監測資訊蒐集；另建議國內農政單位持續進行溼地監測及加強走私禽鳥查緝工作，以降低國人風險。

**關鍵字：**H10N8 禽流感、風險評估、新興傳染病

### 前言

A 型流感病毒各種亞型普遍存在禽鳥間，有些亞型於禽類爲無症狀或輕症感染，惟該等病毒對人類造成衝擊不一，因此早期發現新型禽流感人類病例並及時因應爲降低疫病傳播的不二法門。全球曾有包括如 H7N7、H9N2、H7N2、H7N3、H10N7 等亞型禽流感零星人類報告病例，症狀以結膜炎或一般類流感症狀爲主，個案經治療後均已康復。我國亦曾於 102 年發布全球首例人類感染 H6N1 禽流感病例，肺炎經治療已康復。造成重症肺炎、呼吸道感染且致死率高之亞型爲 H5N1 禽流感，以及自 102 年 3 月迄今已造成逾 300 人感染之 H7N9 禽流感疫情[1]。新型禽流感個案於發生初期，由於該亞型對於動物及人類流行病學等相關資訊較不完整，需持續追蹤及瞭解病毒人傳人之能力、疾病嚴重性及病毒抗藥性等相關資訊，以評估對全球疫情流行風險之可能性及衝擊及調整相關防治整備及因應措施。

根據中國大陸官方網站於 102 年 12 月 17 日發布全球首例人類感染 H10N8 禽流感病毒死亡個案，個案爲江西省南昌市一名 73 歲婦女，有高血壓、糖尿病和重症肌無力等慢性病史，且曾進行胸腺摘除術及具免疫功能低下情形，其於 11 月 27 日發病，11 月 30 日入院治療後於 12 月 6 日死亡，臨床診斷爲嚴重肺炎。個案有活禽市場接觸史，其家人和密切接觸者並無病徵和其他異常情況。約一個月後，中國大陸再發布全球第 2 例 H10N8 病例，個案亦居住於江西省南昌市，55 歲婦女，於 103 年 1 月 8 日發病，

1月15日入院治療，臨床診斷爲重症肺炎，目前病情穩定，個案曾於1月4日至當地某活禽市場，其家庭成員等密切接觸者均未出現症狀。第3例H10N8病例則爲居住於江西省南昌市一名75歲男性，其於103年2月4日入院治療後於2月8日死亡，臨床診斷亦爲重症肺炎。截自103年3月4日，中國大陸共發布3例H10N8人類感染病例[2-3]。

爲因應中國大陸陸續傳出人類感染H10N8禽流感疫情，本文分析目前H10N8禽流感疫情概況及相關資料，評估疫情對國人健康影響風險及造成可能衝擊，以提供國內防治政策及整備工作之參考依據。

## 材料與方法

本文傳染病風險評估方式係參考國際公共衛生機構如世界衛生組織、美國疾病預防及控制中心(CDC)及歐洲疾病預防及控制中心(ECDC)等傳染病風險評估或風險模擬架構，蒐集風險評估要項所需之H10N8禽流感疫情資訊與相關研究，包括病毒特性(病毒變異性與人類呼吸道細胞受體結合力及抗藥性)、實驗動物感染情形、國內外動物生態學及流行病學、國內外人類流行病學、國內易感族群及群體免疫力與疫苗等資訊，並依上述評估項目之科學證據，評估H10N8禽流感疫情造成我國發生境外移入病例之可能性以及對國內疫情造成之衝擊。

## 結果

### 一、病毒特性及實驗動物感染情形

中國大陸於2007年曾在湖南省洞庭湖濕地區域，於環境中檢體分離出H10N8禽流感病毒，經遺傳學親緣分析結果顯示，該病毒株具多源組合性，係由不同病毒亞型之多基因片段重組而成，其中內部基因可能來自H5及H7亞型病毒，H10N8禽流感病毒於禽類屬低病原性病毒，但該病毒在小鼠肺臟細胞可複製良好，且經適應培養後複製效率更佳，經適應培養的病毒甚至可於小鼠肺臟外的其他器官分離到，並擴及腦部。其毒性於兩次繼代後增強，可造成小鼠死亡。將不同繼代之病毒株基因定序分析後發現，其分離的病毒株在肺臟細胞適應培養過程中有多胺基酸序列突變的情形，該病毒株命名 A/environment/Dongting Lake/Hunan/3-9/07 (H10N8) [4]。

非H5及H7之低病原性禽流感病毒在文獻中曾有數次重組而變異爲高病毒株的紀錄[5]。另有研究指出，2012年1月份曾於廣東省活禽市場的鴨隻分離到H10N8禽流感病毒，由基因親源演化分析判定該病毒血清凝集素基因來自歐亞種系(Eurasian lineage)，神經胺酸酶基因來自北美種系（North American lineage）。其病毒株命名爲 A/Duck/Guangdong/E1/2012 (H10N8)[6] 。

近期研究分析全球首例中國大陸H10N8禽流感個案上呼道分離病毒之基因序列資料顯示，該病毒之血清凝集素蛋白源自湖南鴨隻之 H10N3 禽流感病毒(A/duck/Hunan/S11205/2012)，神經胺酸酶蛋白則源自南韓綠頭鴨之 H10N8 禽流感病毒 (A/mallard/Korea/1041/2010)，其他6段病毒內部基因則皆源自 H9N2 禽流感病毒重組而成，且基因親源演化分析顯示該病毒屬新型 H10N8 禽流感病毒，已與

2007 年及 2012 年分別於洞庭湖及廣東檢出之 H10N8 禽流感病毒屬不同的次分支(subclade)。就病毒特性分析病毒與宿主細胞受體結合能力、人體感受性及抗藥性，該新型 H10N8 禽流感病毒株在血清凝集素蛋白第 226 位點胺基酸未發生突變，顯示該病毒仍以結合禽類細胞受體爲主，較 H7N9 禽流感病毒已於該位點由麩醯胺酸(Glutamine) 突變爲白胺酸(Leucine)的情形不同，因此該病毒與哺乳動物上呼吸道細胞結合能力較差；另在神經胺酸酶未有變異，因此對於神經胺酸酶抑制劑類抗病毒藥劑如克流感及瑞樂沙等，仍具敏感性；在聚合酶蛋白(PB2) 第 627 位點胺基酸已有由麩胺酸(glutamic acid) 突變爲離胺酸(lysine)的現象，此與增加哺乳動物毒性有關，尚需密切監測病毒流行與演化情形[2]。

## 二、國際生態學及流行病學資料

H10N8 禽流感病毒過去曾於中國大陸廣東省活禽市場與湖南省洞庭湖濕地，以及日本、南韓、美國、加拿大、義大利及瑞典的候鳥或家禽發現(表一及圖一)[7－12]。近期多種亞型禽流感病毒仍持續在中國大陸南方循環及演化，常見亞型包括 H3、H5、H6 及 H9[13]，中國大陸南方的活禽市場被認爲是家禽將禽流感病毒傳播至人類的重要途徑之一[14,15]。中國大陸於 2011 年冬季至 2012 年春季，曾主動監測湖南省洞庭湖區域周遭養鴨場之禽流感病毒盛行情形，經採集鴨隻及環境檢體，檢出禽流感病毒亞型包括 H3、H4、H5、H6、H9、H10、H11、H12，其中鴨隻檢體檢出陽性率爲 3.5%[16]。經分析該地區除爲飼養鴨隻的主要地區外，亦爲野生水禽及來自西伯利亞及大陸北方遷徙度冬之候鳥棲息地，因此洞庭湖區域爲禽流感病毒重組及循環的溫床，病毒株的基因重組情形頻繁。

另有關人類感染其他 H10 亞型禽流感疫情，首次發生於 2004 年埃及伊斯梅利亞省(Ismaillia)，當時出現 2 例均 1 歲孩童感染 H10N7 低病原性禽流感病毒，出現發燒及咳嗽症狀後復原，其中 1 名個案之父親爲販禽商人，經常往返伊斯梅利亞省及杜姆亞特省(Damietta)間，其中杜姆亞特省在 2004 年 4 月期間，曾自市場販賣的 5 隻野鴨檢體檢出同亞型病毒，惟後續採集 75 件個案接觸者及 13 件市場其他候鳥檢體皆爲陰性[17]。另一事件則發生於 2010 年澳大利亞新南威爾斯省，7 名屠宰場工人感染 H10N7 禽流感病毒，產生之結膜炎疫情，其中 2 名工人有鼻炎及 1 名喉嚨痛之症狀，其檢體檢出 H10 亞型禽流感病毒基因，惟無法培養分離病毒，經基因親源演化分析顯示，其血清凝集素蛋白基因來自北美種系。後於 2012 年研究證實，H10N7 禽流感病毒約自 2007-2008 年間傳入澳大利亞野生水禽族群，並已在澳國境內與其他病毒種系重組演化[16]。

**表一、全球 H10N8 禽流感病毒分離紀錄**

| 國家/地區 | 分離時間 (西元年) | 檢體來源 |
|---|---|---|
| **義大利** | 1965、1992-1998 | 鵪鶉，白冠雞 |
| **美國** | 1979、2004-2006、2008 | 野生水鳥 |
| **加拿大** | 1998 | 綠頭鴨 |
| **瑞典** | 2003 | 綠頭鴨 |
| **臺灣** | 2005 | 鴨 |
| **日本北海道** | 2006 | 野生水鳥 |
| **中國大陸湖南省洞庭湖區** | 2007 | 環境及水 |
| **中國大陸廣東省** | 2012 | 鴨 |
| **南韓** | 2012 | 綠頭鴨 |


**圖一、全球 H10N8 禽流感病毒檢出地理分布**

## 三、國內生態學及流行病學資料

我國農業委員會家畜衛生試驗所曾於 2005 年監測 4,506 件野鳥樣本，共分離 49 株病毒株，其中該年 1-4 月於臺北野鴨排遺 5 件檢體中檢出 H10N8 禽流感病毒，2011-2014 年，我國境內候鳥禽流感病毒帶病毒監測結果則未於候鳥檢體檢出(表二)。

我國自 1999 年起，以流感併發症爲法定傳染病監測項目，並針對社區類流感病患及不明原因肺炎住院病患採檢送驗，經由系統性監測國內流感病毒活動情形及臨床實際狀況，每年檢驗之檢體件數約 1 至 2 萬件，至今累計超過 25 萬件，共計分離約 86,000 株流感病毒，未曾自人體檢體中檢出 H10N8 禽流感病毒。

**表二、我國 2011-2014 年禽流感病毒候鳥帶毒監測結果**

| 年份 | 檢測件數 | 陽性件數 | 陽性率 | 檢出亞型（件數） |
|---|---|---|---|---|
| **2011** | 3935 | 27 | 0.7% | H3N6(3)、H3N8(1)、H4N6(7)、H5N2(4)、H7N3(1)、H7N6(2)、H7N9(6)、H10N7(3) |
| **2012** | 4428 | 18 | 0.4% | H1N1(1)、H1N3(1)、H4N6(1)、H7N1(13)、H10N7(2) |
| **2013** | 7858 | 21 | 0.3% | H5N3(4)、H6N1(2)、H7N3(1)、H7N7(2)、H10N7(10)、H12N5(2) |
| **2014~** | 1183 | 3 | 0.3% | H1N3(1)、H4N6(2) |

資料來源:行政院農業委員會

## 四、風險評估結果

就現有資訊評估，由於中國大陸目前公布之 3 例病例均屬散發個案，且無人傳人之證據，推測國內出現境外移入新型 H10N8 禽流感個案可能性低；中國大陸曾有動物感染 H10N8 禽流感監測資料，我國野鳥監測亦曾發現 H10N8 禽流感病毒紀錄，推測 H10N8 禽流感仍可能經由大陸貿易及走私禽鳥傳入我國或於國內環境中具暴露病毒之風險；惟就基因親源演化分析，中國大陸病例所感染之新型 H10N8 禽流感，與野鳥分離之病毒不同，研判國內發生新型 H10N8 禽流感人類病例風險可能性極低。國內未曾出現人類感染 H10N8 禽流感或新型 H10N8 禽流感病例及動物等疫情，推測國人應不具該等病毒之免疫力，推斷國人應無保護力，

所幸新型 H10N8 禽流感病毒之傳播力及對哺乳動物受體結合力尚差，甚較近期持續出現人類感染病例之 H7N9 禽流感病毒不佳情況下，若國內發生 H10N8 禽流感疫情，推測僅可能有散發個案，造成社區傳播之可能性極低。但目前 H10N8 禽流感病毒之保毒動物、動物傳播及人類感染途徑皆不明，僅有病毒對哺乳動物細胞適應性之動物實驗資料，因此仍須持續監測及更新資訊及相關研究。

目前人類 H10N8 禽流感病例雖爲重症或死亡，且由實驗室資料顯示 H10N8 禽流感病毒對於小鼠有強毒性，惟新型 H10N8 禽流感病毒之傳播力及對哺乳動物受體結合力尚不及 H7N9 禽流感病毒，加上經病毒序列分析神經胺酸酶未變異，對神經胺酸酶類抗病毒藥劑如克流感及瑞樂沙仍未出現抗藥性，充足之抗病毒藥劑整備將可降低疫情之衝擊。另我國自 102 年 5 月 17 日實施傳統市場禁宰活禽政策等各項防治因應作爲，整體而言，現階段中國大陸 H10N8 禽流感疫情對我國造成之衝擊極低[18]，惟對於該病毒毒性及對人類侵襲之嚴重度尚須持續收集資料觀察。綜合評估 H10N8 流感對我國感染機率及衝擊之風險皆低(表三)。

**表三、H10N8 禽流感對國內風險評估表**

| 感染機率<br>評估項目 | 證據 | 結果 | 風險<br>等級 |
|---|---|---|---|
| **境外移入的可能性** | - 中國大陸至今公布 3 例散發個案<br>- 個案感染爲 2013 年新病毒株，與先前大陸檢出 H10N8 禽類禽流感，屬不同病毒株<br>- 近期未有 H10N8 禽類禽流感相關監測資料 | - 個案數少，且未人傳人，境外移入風險極低<br>- H10N8 禽類禽流感經由大陸貿易及走私禽鳥頻繁下仍具境外移入風險 | **低** |
| **國內流行的可能性** | | | **低** |
| 1.由動物傳人感染機率 | - H10N8 禽類禽流感屬低病原性禽流感病毒<br>- 2005 年臺北 5 件鴨科排遺檢體檢出 H10N8 禽類禽流感病毒，2011-2014 年候鳥監測未發現相關病毒 | 國內雖曾檢出 H10N8 禽類禽流感病毒但與新型 H10N8 禽流感病毒不同，保毒動物、動物 傳播及人類感染途徑目前皆不明 | |
| 2.易感族群與群體免疫力 | - 公布個案數少，中國大陸境內是否有輕症或無症狀感染情形不明<br>- 國內法傳、類流感及住院不明原因肺炎監測未曾檢出 H10N8 流感 | 推測國人無群體免疫力 | |
| 3.疾病傳播力 | - 家人及密切接觸者均未出現症狀<br>- 新 H10N8 禽流感病毒株與哺乳動物細胞受體結合力差，惟具哺乳動物細胞適應性 | 病毒於人體細胞結合力差，推斷人傳人之風險低於 H7N9 禽流感病毒 | |

| 衝擊<br>評估項目 | 證據 | 結果 | 風險<br>等級 |
|---|---|---|---|
| **疾病嚴重性** | - 目前兩例個案症狀皆爲重症，對小鼠毒性強<br>- 是否有輕症或無症狀感染情形不明 | 病毒毒性及疾病嚴重性仍待觀察 | **不明** |
| **治療與控制**<br>1.疫苗使用 | 無 | | **低** |
| 2.抗病毒藥劑 | - 神經胺酸酶胺基酸位點未突變<br>- M2 蛋白胺基酸位點已突變(Ser31Asn) | - 對國內儲備之神經胺酸酶抑制劑無抗藥性。<br>- 對 Adamantanes 具抗藥性 | |
| 3.防治政策 | 加強監測、禁止陳列、展示及販售活禽政策及抗病毒藥劑整備等防治作爲 | 執行國內各項整備應變政策將可降低國內衝擊 | |

## 結論

依據世界衛生組織 2013 年 12 月 20 日公布之評估報告顯示，H10N8 禽流感個案應屬散發病例，推測與中國大陸加強流感監測有關；雖然該病毒於當地禽鳥間盛行率不明，但若病毒持續於當地循環，預期仍將有零星人類病例出現[19]。目前新型 H10N8 禽流感病例之接觸者均無臨床症狀，且無證據顯示病毒具人傳人之跡象，病毒傳播效率亦不高，推測對公眾健康構成風險的機會低，惟仍需持續密切監視疫情再評估風險[20]。

本文囿於 H10N8 禽流感病毒及流行病學等相關資訊有限，風險評估結果有其限制性；依現有 H10N8 禽流感病毒之證據顯示，該病毒傳播風險低於 H7N9 禽流感病毒，推估中國大陸 H10N8 禽流感疫情，目前對我國未構成立即性的風險，國內疫情等級亦無提升之必要性，惟 H10N8 禽流感病毒對國人感染率及後續疫情發展，仍需持續觀察以評估對我國的衝擊。

以人類感染 H10N7 禽流感病毒病例經驗來看，H10 亞型禽流感病毒之毒性及致死率不高，且多屬輕症；惟感染 H10N8 禽流感病毒之三例個案均屬重症或死亡，在該病毒傳播途徑、病毒毒力與致病性等均未明之情形下，建議維持現有監視及通報定義以及對民眾衛教宣導內容，另加強相關研究及監測資訊蒐集，另建議國內農政單位應持續進行溼地監測及加強走私禽鳥查緝工作，以降低國人風險。

## 誌謝

感謝農委會提供近年候鳥監測禽流感病毒資料，及疾病管制署研究檢驗中心劉銘燦博士協助提供病毒分析資料、疾病管制署疫情中心監測政策及系統發展科同仁提供疫情相關資訊，一併致謝。

## 參考文獻

1. To KKW, Tsang AKL, Chan JFW, et al. Emergence in China of human disease due to avian influenza A(H10N8) – Cause for concern? J Infect 2014. Available at: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2814%2960111-2/fulltext
2. Chen H, Yuan H, Gao R, et al. Clinical and epidemiological characteristics of a fatal case of avian influenza A H10N8 virus infection: a descriptive study. The Lancet. 2014. Available at http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(14)60111-2/abstract
3. Health and family planning commission of Jiangxi province. Available at: http://www.jxwst.gov.cn/
4. Zhang H, Xu B, Chen Q, et al. Characterization of an H10N8 influenza virus isolated from Dongting lake wetland. Virol J 2011;8:42.
5. Alexander DJ. An overview of the epidemiology of avian influenza. Vaccine 2007 26;25(30):5637 – 44.
6. Jiao P, Cao L, Yuan R, et al. Complete genome sequence of an H10N8 avian influenza virus isolated from a live bird market in Southern China. J Virol 2012;86(14):7716.

7. Manzoor R, Sakoda Y, Mweene A, et al. Phylogenic analysis of the M genes of influenza viruses isolated from free-flying water birds from their Northern Territory to Hokkaido, Japan. Virus Genes 2008 Oct;37(2):144 - 52.
8. Kim H-R, Lee Y-J, Oem J-K, et al. Characterization of H10 subtype avian influenza viruses isolated from wild birds in South Korea. Vet Microbiol 2012;161(1-2):222 - 8.
9. De Marco MA, Campitelli L, Foni E, et al. Influenza surveillance in birds in Italian wetlands (1992-1998): is there a host restricted circulation of influenza viruses in sympatric ducks and coots? Vet Microbiol 2004;98(3-4):197 - 208.
10. Pasick J, Pedersen J, Hernandez MS. Avian influenza in North America, 2009-2011. Avian Dis 2012;56(4 Suppl):845 - 8.
11. Senne DA. Avian influenza in the Western Hemisphere including the Pacific Islands and Australia. Avian Dis 2003;47(3 Suppl):798 - 805.
12. Schlingemann J, Leijon M, Yacoub A, et al. Novel means of viral antigen identification: Improved detection of avian influenza viruses by proximity ligation. J Virol Methods 2010;163(1):116 - 22.
13. Pepin KM, Wang J, Webb CT, et al. Multiannual patterns of influenza A transmission in Chinese live bird market systems. Influenza Other Respir Viruses. 2013;7(1):97 - 107.
14. Arzey GG, Kirkland PD, Arzey KE, et al. Influenza virus A (H10N7) in chickens and poultry abattoir workers, Australia. Emerg Infect Dis 2012;18(5):814 - 6.
15. Vijaykrishna D, Deng Y-M, Su YCF, et al. The recent establishment of North American H10 lineage influenza viruses in Australian wild waterfowl and the evolution of Australian avian influenza viruses. J Virol 2013;87(18):10182 - 9.
16. Deng G, Tan D, Shi J, et al. Complex Reassortment of Multiple Subtypes of Avian Influenza Viruses in Domestic Ducks at the Dongting Lake Region of China. J Virol 2013;87 (17):9452 - 62.
17. Pan American Health Organization. Avian influenza virus A (H10N7) circulating among humans in Egypt. Available at: http://new.paho.org/hq/dmdocuments/2010/Avian_ Influenza_Egypt_070503.pdf
18. Yu H, Wu JT, Cowling BJ, et al. Effect of closure of live poultry markets on poultry-to-person transmission of avian influenza A H7N9 virus: an ecological study. The Lancet. Available at: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(13) 61904-2/abstract
19. World Health Organization. Influenza at the human-animal interface. Summary and assessment as of 20 December 2013. Available at: http://www.who.int/influenza/ human_animal_interface/Influenza_Summary_IRA_HA_interface_20December13.pdf?ua=1
20. World Health Organization. Avian influenza A(H10N8). Available at: http:// www.wpro.who.int/china/mediacentre/factsheets/h10n8/en/

12. 人類感染 H7N9 流感病毒風險評估報告發表文章

Journal of the Formosan Medical Association (2014) 113, 397–399

Available online at www.sciencedirect.com

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PERSPECTIVES

# Risk assessment of human infection with avian influenza A (H7N9) virus in Taiwan

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Received 29 January 2014; accepted 7 February 2014

The first peak of human cases of influenza A (H7N9) virus infection from February to May followed by two cases in July 2013 and August 2013, accounting for 135 cases along with 47 deaths. A second ascent of cases started in October 2013 and surged to 102 cases including 11 deaths, which have been reported in four provinces of China (Jiangsu, Zhejiang, Fujian, and Guangdong), Hong Kong, and one travel-related case from Taiwan, as of January 24, 2014. Furthermore, compared to the past year's peak, the age distribution in the second wave of cases does not tend to skew toward the elderly. To formulate appropriate prevention and control strategies for public health, the Taiwan Centers for Disease Control (Taiwan CDC) assessed the risk associated with emergence of H7N9 virus and provided guidance for health care workers and the public. Information on characteristics of the H7N9 virus, attributes of the human population at risk, and epidemiology of the virus were systematically assessed. An internal expert meeting was held at Taiwan CDC to evaluate the assessment report.

## Viral characteristics

The avian influenza A (H7N9) virus is a novel reassortant with six internal genes pertaining to the Eurasian avian influenza H9N2 lineage. Gene segments of hemagglutinin (HA) and neuraminidase (NA) came from Eurasian avian influenza lineage.[1] Current studies demonstrated increased binding properties of human H7N9 isolates to $\alpha$-2,6 sialic acid, attributed to substitutions Q226L. However, the major $\alpha$-2,3 linkage to terminal galactose limits the ability of human-to-human transmission.[2] To assess human adaptation of the H7N9 virus, we compared the human isolates from August 2013 onward with prototype A/Anhui/1/2013 (Table 1).[3] The substitution Q226L of HA in the six isolates but lacking G228S mutations indicated an absence of affinity for human receptors. In addition, the polymerase 2 protein (PB2) E627K substitution identified in Taiwan, Guangdong, and Hong Kong isolates contributed to high polymerase activity possibly associated with human adaptation. Nevertheless, the other important signatures, D701Q in the PB2, N66S in the PB1-F2, and D92E in the NS1 were not detected in the recent H7N9 isolates. All the isolates were sensitive to neuraminidase inhibitor (NI) but resistant to amantadine attributed to substitution S31N of M2.[4] Currently, NI remains the recommended antiviral treatment. The human-to-human transmissibility of current H7N9 virus remains limited; however, because of the continually changing nature of influenza viruses, monitoring of the genetic variations of H7N9 virus is ongoing.

## Avian and environmental surveillance

China's Ministry of Agriculture detected a higher positive rate of H7N9 virus among birds and in the environments

Conflicts of interest: We certify that we have no affiliations with or involvement in any organization or entity with any financial interest or nonfinancial interest in the subject matter or materials discussed in this manuscript.

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http://dx.doi.org/10.1016/j.jfma.2014.02.001

**Table 1** Molecular analysis of the H7N9 viruses isolated from August 2013 to January 2014.

| Name of viruses | Collection date | HA | | NA | PB2 | | | | PB1-F2 | M2 | NS1 | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | (yy/mm/dd) | 226 | 228 | 292 | 559 | 570 | 627 | 701 | 66 | 31 | 27 | 67 | 80 | 92 | 111 | 114 | 152 |
| A/Anhui/1/2013 | 2013/03/20 | L | G | R | N | M | K | D | N | N | M | R | S | D | I | S | E |
| A/Guangdong/1/2013 | 2013/08/10 | L | G | R | T | I | K | D | N | N | L | R | T | D | V | S | D |
| A/Zhejiang/DTID-ZJU10/2013 | 2013/10/14 | L | G | R | T | M | E | D | N | N | M | R | S | D | I | S | E |
| A/Zhejiang/22/2013 | 2013/10/14 | L | G | R | T | M | E | D | N | N | M | R | S | D | I | S | E |
| A/Hong Kong/5942/2013 | 2013/11/30 | L | G | R | T | I | K | D | N | N | L | R | T | D | V | S | D |
| A/Taiwan/3/2013 | 2013/12/27 | L | G | R | T | I | K | D | N | N | M | Q | S | D | I | P | E |
| A/Hong Kong/734/2014 | 2014/01/07 | L | G | R | T | I | K | D | N | N | L | R | T | D | V | S | D |
| Signature substitution | | Q226L | G228S | R292K | | | E627K | D701Q | N66S | S31N | | | | D92E | | | |

H7N9 = avian influenza A; HA = hemagglutinin; NA = neuraminidase; PB2 = polymerase 2 protein.

from Guangdong, Zhejiang, and Fujian provinces in December 2013 and January 2014, when compared to the survey in the first half of the year 2013.[5] Targeted testing of poultry and the environment in live poultry markets identified more positive results in areas with human cases of H7N9 infection. In Taiwan, the Council of Agriculture has conducted surveillance on wild birds and domestic poultry since 1998. In 2009 and 2011, there have been seven H7N9 virus-positive samples among migratory birds in Tainan and Yilan, respectively, which belonged to different phylogenetic lineages of H7N9 virus in China.[6] No newly emerged H7N9 virus in the poultry or environment of Taiwan has been detected during routine serologic and viral surveys. As H7N9 infection in humans appears to be associated with exposure to live poultry markets or contaminated environments, the possibility of acquiring the disease through wild birds or domestic poultry in Taiwan remains low.

### Morbidity and mortality

The H7N9 outbreak in mainland China has a major effect on public health in Taiwan, particularly because of the severity and case fatality rate of H7N9 infections in humans. All avian influenza A (H7N9) vaccines in development are still in the clinical trial stage. Therefore, no vaccines are currently available for H7N9 prevention. Because of the increasing number of passengers traveling between Taiwan and mainland China, the assessment indicates that additional imported human cases during the Chinese New Year should be expected. Although more imported cases in Taiwan over the coming weeks are projected, the current evidence does not support community or sustained human-to-human transmission of H7N9.[7] Therefore, public health impact and the probability of a spread of the virus at a community level currently remain low.

## Conclusion

In summary, a higher likelihood at the moment is imported cases who have acquired the infection in mainland China. The risk of disease widely spreading in Taiwan via humans in the near future is considered low. Currently, information on the animal reservoir of the viruses and the mode of transmission between animals and humans remains limited. We recommended that any suspected case of H7N9 infection, listed as a Category V Notifiable Infectious Disease, should be reported immediately to Taiwan CDC.[8] Additionally, we reminded physicians to reinforce inquiries about patients' travel and contact history in order to facilitate the diagnosis of H7N9 infection and notify health authorities immediately regarding any suspected cases to assist implementation of subsequent measures that can prevent further transmission of the disease. Continued vigilance is essential to monitor variation of H7N9 and other influenza viruses and regularly update estimates of the risks associated with this virus.

## Acknowledgments

The authors would like to thank Dr Ho-Sheng Wu and Dr Ming-Tsan Liu at the Research and Diagnostic Center of Taiwan CDC for providing the table and comments on the chapter of viral characteristics.

## References

1. Chen GW, Lai MC, Wu SC, Chang SC, Huang LM, Shih SR. Is avian influenza A (H7N9) virus staggering its way to humans? *J Formos Med Assoc* 2013;112:312–8.
2. Dortmans JCFM, Dekkers J, Ambepitiya Wickramasinghe IN, Verheije MH, Rottier PJM, van Kuppeveld FJM, et al. Adaptation of novel H7N9 influenza A virus to human receptors. *Sci Rep* 2013;3:3058.
3. Mok CK, Chang SC, Chen GW, Lo YL, Chen SJ, Wu HS, et al. Pyrosequencing reveals an oseltamivir-resistant marker in the quasispecies of avian influenza A (H7N9) virus. *J Microbiol Immunol Infect* [Epub ahead of print], http://dx.doi.org/10.1016/j.jmii.2013.09.010; 2013.
4. Wu Y, Bi Y, Vavricka CJ, Sun X, Zhang Y, Gao F, et al. Characterization of two distinct neuraminidases from avian-origin human-infecting H7N9 influenza viruses. *Cell Res* 2013;23:1347–55.
5. Veterinary Bureau. Ministry of Agriculture of the People's Republic of China. Report of national animal surveillance on H7N9 [accessed 23.01.14], http://www.moa.gov.cn/sjzz/syj/dwyqdt/; 2014.

6. Olson SH, Gilbert M, Cheng MC, Mazet JAK, Joly DO. Historical prevalence and distribution of avian influenza virus A(H7N9) among wild birds. *Emerg Infect Dis* 2013;**19**:2031—3.
7. World Health Organization. *Monthly risk assessment summary*. World Health Organization http://www.who.int/influenza/human_animal_interface/HAI_Risk_Assessment/en/index.html. [accessed 23.01.14].
8. Wu HS, Chuang JH, Chang FY. Taiwan faces challenges on the emerging avian influenza A (H7N9) virus in China. *J Formos Med Assoc* 2013;**112**:299—301.