EUPHEM

EUPHEM REPORT

Summary of work activities
Michela Sabbatucci
European Public Health Microbiology Training Programme (EUPHEM), 2015 cohort

Background

According to Articles 5 and 9 of ECDC’s founding regulation (EC No 851/2004) ‘the Centre shall, encourage cooperation between expert and reference laboratories, foster the development of sufficient capacity within the community for the diagnosis, detection, identification and characterisation of infectious agents which may threaten public health’ and ‘as appropriate, support and coordinate training programmes in order to assist Member States and the Commission to have sufficient numbers of trained specialists, in particular in epidemiological surveillance and field investigations, and to have a capability to define health measures to control disease outbreaks’. The ECDC Fellowship Training Programme therefore includes two distinct curricular pathways: Intervention Epidemiology Training (EPIET) and Public Health Microbiology Training (EUPHEM). After the two-year training EPIET and EUPHEM graduates are considered experts in applying epidemiological or microbiological methods to provide evidence to guide public health interventions for communicable disease prevention and control. Both paths that provide competency based training and practical experience using the ‘learning by doing’ approach in acknowledged training sites across European Union (EU) and European Economic Area (EEA) Member States.

European preparedness for responding to new infectious disease threats requires a sustainable infrastructure capable of detecting, diagnosing, and controlling infectious disease problems, including the design of control strategies for the prevention and treatment of infections. A broad range of expertise, particularly in the fields of epidemiology and public health microbiology, is necessary to fulfil these requirements. Public health microbiology is required to provide access to experts in all relevant communicable diseases at the regional, national and international level in order to mount rapid responses to emerging health threats, plan appropriate prevention strategies, assess existing prevention disciplines, develop microbiological guidelines, evaluate/produce new diagnostic tools, arbitrate on risks from microbes or their products and provide pertinent information to policy makers from a microbiological perspective.

According to the European Centre for Disease Prevention and Control (ECDC) Advisory Group on Public Health Microbiology (‘national microbiology focal points’), public health microbiology is a cross-cutting area that spans the fields of human, animal, food, water, and environmental microbiology, with a focus on human population health and disease. Its primary function is to improve health in collaboration with other public health disciplines, in particular epidemiology. Public health microbiology laboratories play a central role in detection, monitoring, outbreak response and the provision of scientific evidence to prevent and control infectious diseases. This report summarises the work activities undertaken by Michela Sabbatucci, cohort 2015 of the European Public Health Microbiology Training Programme (EUPHEM) at the National Institute of Health (Istituto Superiore di Sanità, ISS), Rome, Italy.

All EUPHEM activities aim to address different aspects of public health microbiology and underline the various roles of public health laboratory scientists within public health systems.

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Pre-fellowship short biography

Michela completed her PhD training in Medical Microbiology and Immunology at the Tor Vergata University in 2008 while serving the National Institute of Health in Rome, Italy. Her interests focused on identifying endogenous host cellular factors able to restrict the Human Immunodeficiency Virus type 1 (HIV-1) replication. She dissected the molecular mechanisms underlying host innate intracellular viral antagonists highlighting possible target for non-toxic therapeutic intervention. She gained a firm experience in human cell culture methods, molecular and cell biology techniques and flow cytometry. Michela joined the EPIET/EUPHEM programme to broaden her scientific competencies and apply her research laboratory expertise to actively contribute to the promotion of global public health. She believes that an effective response against infectious diseases only come from an integrated interdisciplinary approach. Therefore, she welcomed enthusiastically the exceptional opportunity to work within and contribute to an inspiring high-level international and multidisciplinary European network in the field of infectious diseases.

Fellowship assignment: Public health Microbiology (EUPHEM) path

Methods

This report accompanies a portfolio that demonstrates the competencies acquired during the EUPHEM fellowship by working on various projects, activities and theoretical training modules.

Projects included epidemiological investigations (outbreaks and surveillance); applied public health research; applied public health microbiology and laboratory investigation; biorisk management; quality management; teaching and public health microbiology management; summarising and communicating scientific evidence and activities with a specific microbiological focus.

The outcomes include publications, presentations, posters, reports and teaching materials prepared by the fellow. The portfolio presents a summary of all work activities conducted by the fellow, unless prohibited due to confidentiality regulations.

Results

The objectives of these core competency domains were achieved partly through project or activity work and partly through participation in the training modules. Results are presented in accordance with the EUPHEM core competencies, as set out in the EUPHEM scientific guide1.

1. Epidemiological investigations

1.1. Outbreak investigations

A. A severe community-wide outbreak of invasive Listeria monocytogenes serotype 1/2a with a rare pulsotype associated to processed pork products in Marche region, central Italy, 2015-2016

Supervisors: Dr Luca Busani, Dr Patrizio Pezzotti

From May 2015 through March 2016, an outbreak due to Listeria monocytogenes (L. monocytogenes) serotype 1/2a and pulsotype never isolated before in Europe occurred in Central Italy, involving 24 confirmed clinical cases. Next generation sequencing confirmed the unique outbreak strain. Patients were elderly people (≥70 years) or immunocompromised younger adults affected by chronic diseases or under immunosuppressive therapy. A questionnaire regarding food-consumption habits was distributed to all cases. On January 4th 2016, a L. monocytogenes strain with indistinguishable pulsotype with that isolated from the outbreak cases was detected in a sample of Hog head cheese from a local retail supermarket indicated by one patient. The Hog head cheese was produced by a small plant for meat processing in Marche region, where microbiological investigation highlighted high contamination with the outbreak strain. The contaminate batches of Hog head cheese were withdrawn from the market by February 17, 2016. The plant production was suspended. We observed a sharp decline of clinical cases. Further investigations showed two other plants and two retail shops in Marche region as contaminated by the L. monocytogenes outbreak strain as well. The last outbreak case was reported on March 11, 2016. By participating in the revision of all the official documents for the Ministry of Health and in the operational meetings and videoconferences, as well as in the completion and epidemiological analysis of patient’s database and in the

cooperative multidisciplinary teamwork, the fellow put into practice all the steps of an outbreak investigation, including writing the related reports for the Ministry of Health and the comprehensive scientific manuscript. Besides, the fellow presented the results of these investigations at the Project review Module 2016 and at the European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE) 2016.

**Training modules**

During the EPIET/EUPHEM Introductory Course and the Outbreak Module the fellow was exposed to the methods and logistical aspects of outbreak investigations. The Bioinformatics and Phylogenetic Module provided comprehensive knowledge on constructing and interpretation of phylogenetic trees to support epidemiological tracing of sources of infection. Further, in the Rapid Assessment and Survey Module and in the Multivariate Analysis Module, participants were instructed on how to assess critical events and perform advanced statistical analysis on data from epidemiological studies, including those related to outbreak investigations. Lastly, the Outbreak Communication Guidelines by the World Health Organisation (WHO) provided during the Initial Management in Public Health Microbiology Module instructed on how communicating with authorities, the public and the media in epidemic settings.

**Educational outcome:** Participation in national outbreak control meetings and teleconferences; involvement in outbreak investigation (case definition, food consumption targeted questionnaire design and case-control study, collating and analysing data); collaboration and communication with colleagues from diverse background and regional health protection teams; application of combined microbiological and epidemiological knowledge in outbreak investigation; preparation of an outbreak investigation report and presentation at one international conference.

### 1.2. Surveillance

**A. Salmonella enterica serovar Napoli infection in Italy, 2011-2015: a current and specific Italian public health concern.**

**Supervisors:** Dr Ida Luzzi, Dr Claudia Lucarelli

Human infections by *Salmonella enterica* serovar Napoli (*S. Napoli*) are uncommon in Europe. Instead, since 2000, the proportion of *S. Napoli* clinical cases have been increased in Italy. Its zoonotic reservoir is still unknown, therefore, no public health measure has been taken so far. Since 2004 (access on July 3, 2017), the Rapid Alert System for Food and Feed portal (RASFF) registered eight alerts reporting isolation of *S. Napoli* in six Nordic countries (Denmark, Finland, Ireland, Norway, Slovenia, Sweden). In seven of those alerts, ready to eat vegetables imported from Italy were notified as source of pathogen isolation. This study pointed to identify possible common source(s) of infection with the aim to driving appropriate control measures able at reducing spread further of this serovar.

The fellow analysed statistically 2011-2015 data from two national surveillance systems for human and environmental cases (ENTER-NET) and for animal, food and feed isolates (ENTER-VET), evaluating risk factors associated with *S. Napoli* human infection by multiple logistic regression model (*S. Napoli* isolates versus other serovars). Further, she contributed to characterise genetically 187 *S. Napoli* isolates comparing their genetic similarities by Pulsed-Field Gel Electrophoresis (PFGE) and BioNumerics (version 7.5) among human, environmental, animal and food strains. Most of the reported *S. Napoli* cases were from human and environmental samples, and transmission to human less likely occurred by food of animal origin. The high genetic strain variability of the isolates did not allow the identification of source(s) of infection. Anyway, clustering (80% similarity) was observed by PFGE patterns in the three main geographical areas. The results of this study demonstrating the need for improvement of the two surveillance systems, to increase reporting of cases and molecular characterisation of isolates. The fellow suggested to perform a prospective case-control study possibly indicating specific risk factors driving targeted microbiological investigations. The fellow presented the results of this study at the main European epidemiological conference (ESCAIDE 2016) and submitted the related manuscript to the Emerging Infectious Diseases journal.

**B. Evaluation of the Italian surveillance system of bacteraemia due to carbapenemase-producing Enterobacteriaceae (CPE), 2013-2016**

**Supervisors:** Dr Annalisa Pantosti, Dr Patrizio Pezzotti

ECDC data indicates that in 2015, four countries (Greece, Italy, Turkey and Malta) reported an endemic situation for carbapenemase-producing Enterobacteriaceae (CPE) among 38 EU countries. Carbapenemases are β-lactamase enzymes able to inactivate the β-lactam antibiotics, including carbapenems, which are among the few effective antimicrobials available for the treatment of multidrug-resistant bacterial infections. The resistance to carbapenems in Italy is much higher than the mean values reported in Europe. Besides, bacterial genes responsible for antibiotic resistance can quickly spread within and between healthcare and community settings and diverse bacterial species, and cause high mortality infections, representing a rising international threat. An active surveillance identifying patients at high risk for CPE and timeliness case notification are key to counteract the spread of this threat. Therefore, in 2013 the Italian Ministry of Health instituted a national surveillance for bacteraemia due to *K. pneumoniae* and *E. coli*. To provide an overall picture on the quality, acceptability, representativeness and timeliness of this new national surveillance system, and to describe cases and trends of infections, the fellow analysed data notified in the period 2013-2016 statistically. A case was defined as a patient with one or more blood cultures positive for *K. pneumoniae*.
or *E. coli* with one or both these characteristics: non sensibility to meropenem and/or imipenem and/or carbapenemases production tested by genotypic and/or phenotypic confirmation test. The fellow identified geographical area, health settings and patients at high-risk for bacteraemia due to *K. pneumoniae* and *E. coli*, indicating current limits of the surveillance system and recommending improvements needed. She presented the results of this study at the Ministry of Health and at national (XLV conference of the Associazione Microbiologi Clinici Italiani - AMCLI, and the 49th conference of the Società Italiana di Igiene - SITI) and international (the 27th European Congress of Clinical Microbiology and Infectious Diseases - ECCMID) scientific conferences and contributed to writing the related national report published in ISTISAN and the scientific manuscript to be published in an international peer-reviewed journal.

**Training modules**
The fellow familiarised with the development, evaluation and data analysis of surveillance systems during the EPIET/EUPHEM Introductory Course. The Multivariate Analysis Module further instructed the fellow with advanced statistical methods for data analysis. The Bioinformatics and Phylogenetic Module provided comprehensive knowledge on phylogenetic trees for the analysis of molecular relatedness of pathogens’ isolates.

**Educational outcome:** performed laboratory and computer-based genetic characterisation of *Salmonella* isolates; got knowledge of national surveillance system; application of combined microbiological and epidemiological knowledge; surveillance data management and analysis; evaluation of surveillance system; given recommendations to implement a new surveillance system; presented the results of these studies at four international conferences; written two related manuscripts and one national report.

### 2. Applied public health microbiology research

**A. Experimental studies on susceptibility of Aedes albopictus and Culex pipiens to Zika Virus infection**

Supervisors: Dr Giulietta Venturi, Dr Claudia Fortuna

Clinical presentation of Zika fever is nonspecific and most of the patients remain asymptomatic. International concern was raised when ZIKV virus (ZIKV) infection was associated with a 20-fold increase of Guillain-Barre syndrome incidence during the Zika epidemic occurred in French Polynesia in 2013. Besides, the association between Zika and microcephaly or other birth defects has lead the World Health Organisation (WHO) to declare the ZIKV epidemic as a global public health emergency on February, 1st 2016. ZIKV is transmitted usually by the bite of infected mosquitoes, even if other routes of transmission to humans have been already proved. *Aedes aegypti* is considered as the main vector. In Europe, particularly in Italy, *Aedes albopictus* and *Culex pipiens* are extremely widespread and no information was available about their competence (ability to become infected and transmit the virus) representing a potential risk for ZIKV autochthonous outbreaks.

The aim of this project was to evaluate the vector competence of Italian *Ae. albopictus* and *Cx. pipiens* mosquitoes by experimental infection with ZIKV to assess (I) the risk of autochthon transmission following imported cases (by evaluating the presence of viral RNA in body, legs plus winds and saliva of the vectors) and for *Ae. albopictus* only (II) the capacity of vectors’ vertical transmission (by evaluating offspring infection).

The fellow had the opportunity to collaborate with the entomologists during mosquitoes’ infection with ZIKV working in BSL-3 facility. She performed RNA extraction from mosquitoes and quantitative reverse transcription PCR. Nine time points (from 3 to 28 days) post infection were evaluated. The offspring was also examined for virus presence in *Ae. Albopictus* keeping *Aedes aegypti* samples as positive control. *Ae. albopictus* was susceptible to ZIKV infection and it was able to disseminate and transmit ZIKV, even if with a lower competence than that of an *Ae. aegypti* colony tested in parallel. Instead, Viral RNA was detected in the body of *Cx. pipiens* up to three days post-infection, but not at later time points, indicating that *Cx. pipiens* was not susceptible to ZIKV infection.

Evaluating the concrete risk of ZIKV infection in Italy could allow a timely detection of illness to anticipate, control and avoid ZIKV outbreaks. The results of this study on vector competence and degree of vertical ZIKV transmission by these two mosquitoes’ populations were presented at the scientific conference International Zika Summit 2016. One article was published in the national epidemiology portal EpiCentro managed by ISS for public health and two manuscripts were published in the international scientific journal Eurosurveillance.

**B. Comparison between trends of Chlamydia trachomatis (Ct) genital infection in Sentinel Surveillance Systems and trends in hospital admissions for pelvic inflammatory disease (PID) due to Ct genital infection in women, Italy, 2005-2014**

Supervisors: Dr Barbara Suligoi, Dr Maria Cristina Salfa, Dr Vincenza Regine

Genital Chlamydia is the most commonly reported sexually transmitted infection (STI) across Europe and it is caused by the *Chlamydia trachomatis* (Ct) bacterium. Ct can also be transmitted from mother to child during pregnancy and childbirth. Ct infection is asymptomatic in approximately 70% of cases and it often goes untreated. This could cause
in women severe complications (sequelae) as pelvic inflammatory disease (PID), tubal factor infertility (TFI) and ectopic pregnancy (EP), causing considerable distress to the affected women and cost implications for health services. In Italy Ct infection is not subjected to mandatory notification, and no studies are available so far on the severity of Ct female genital infection. However, cases are reported voluntarily to two lab-based sentinel surveillance systems (SSS). The fellow compared epidemiological data regarding Ct positive women attending the microbiological and clinical laboratories participating in the surveillance systems with those of hospitalised women with diagnosis of PID and/or Ct infection to estimate the proportion of hospitalised PID attributable to genital Ct infection, performing descriptive statistical analysis.

Using STATA software, the fellow calculated that among the women hospitalised in Italy between 2005 and 2014, 0.77% (283,279 out of 36,856,038 admissions) were PID cases and that 253 were also diagnosed with Ct. The median age of PID cases was 32 years and their median hospitalisation stay was 5 days. The number of Ct diagnoses reported in the same period in the SSS increased from 76 to 127 women (median age 25y; IR 2.9 per 100,000 in 2005 and IR 4.8 per 100,000 in 2014). Conversely, in the NHIF, the number of PID cases decreased (32,012, IR 1.5 per 1,000 in 2005; 25,081, IR 1.1 per 1,000 in 2014) as well as that of Ct-associated PID cases (53 during 2005-2006; 41 during 2013-2014). The fellow proposed specific recommendations, i.e. operating opportunistic screenings and/or national screening programmes for Ct in young women to detect and treat infected asymptomatic women or with unrecognized symptoms. These public health interventions could reduce both the transmission of infection and its progressing to upper reproductive tract damage, causing sequelae. Besides, the usefulness of the two Italian STI Sentinel Surveillance Systems in translating results to public health programmes was assessed. The fellow proposed the results of this study at the Project review Module 2017 and wrote the related manuscript to be published in an international peer-reviewed journal.

Training modules
The EPIET/EUPHEM Introductory Course provided the fellow with useful instructions on developing research study protocols and writing scientific abstracts and manuscripts with an epidemiology focus. Helpful knowledge on time and human relationships’ management, interpersonal communication and oral communications was provided at the Initial Management in Public Health Microbiology Module. Further, the Multivariate Analysis Module abled the fellow to manage and analyse data from surveillance systems statistically, including descriptive and stratified analysis, different multivariate techniques, linear, logistic, Poisson and Cox regressions.

Educational outcome: applied relevant laboratory methods and sampling preparation techniques; collaborated with professionals from diverse background; exercised realistic timelines; identified limits of surveillance; got knowledge and managed data from sentinel surveillance systems and from hospital medical records; got knowledge of ICD-9-CM codes for the classification of hospitalised cases; performed descriptive and multivariate analysis; communicated the scientific findings.

3. Applied public health microbiology and laboratory investigations

Supervisors: Dr Annalisa Pantosti, Dr Maria Del Grosso, Dr Marina Camilli

A. Whole Genome Sequencing (WGS) of multidrug resistant Streptococcus pneumoniae isolates belonging to serotype 24F, a frequent non-vaccine serotype isolated from Italian patients, 1997-2016

Streptococcus pneumoniae is a human pathogen causing upper and lower respiratory tract infections (otitis, sinusitis, and pneumonia) and invasive diseases (i.e. meningitis and sepsis) mostly in children and the elderly worldwide. So far, 96 pneumococcal serotypes have been described. In Italy, since 2000 the 7-valent pneumococcal conjugative vaccine (PCV7), composed of 7 major serotypes, has been available for paediatric immunization. In 2010, it was replaced by the 13-valent vaccine. The use of PCVs has resulted effective in reducing the overall incidence of invasive pneumococcal disease (IPD) caused by the vaccine serotypes (VS). Anyway, as an effect of the “replacement phenomenon”, an increase in the incidence of IPD caused by non-vaccine serotypes (NVS), has been observed indeed. In particular, in Italy in the last years, an increment in the proportion of some NVS (i.e. 12F, 24F, 22F) was described in children 0-4 years old. Among these, serotype 24F is of particular concern due to its association with antibiotic resistance. The fellow set up Whole Genome Sequencing (WGS) as a tool to characterise multi drug-resistant (MDR) serotype 24F pneumococcal clones circulating in Italy over a long-time period comprising the pre- and post- vaccine era among the pneumococcal isolates (N=3,103) collected at ISS from 1997 to 2016 from Italian adults and children. Sequence types and antibiotic resistance genes were identified by using a Galaxy platform available at ISS, so far optimised for the analysis of Escherichia coli only, which was implemented for analysis of S. pneumoniae genomes. The fellow cultivated in vitro MDR strains of S. pneumoniae serotype 24F, identified the genes responsible for antimicrobial resistance and got familiar with phylogenetic trees to study strains’ clonal evolution. She contributed to set up WGS (Illumina MiSeq strategy) and to implement the genomic framework currently available at ISS for S. pneumoniae genomic analysis. This tool will serve as long-term resource for the future nationwide routine typing
and surveillance of *S. pneumoniae* invasive infections. The scientific results of this project will be completed in the next future.

### B. Mycology training at Policlinico A. Gemelli, December 2016, Rome, Italy

**Supervisor:** Prof Maurizio Sanguinetti

The fellow benefited from a 4-day Mycology training at the Institute of Microbiology, Cattolica del Sacro Cuore University, in Rome. She gained two collaborations regarding statistical analysis of research data from two research teams. The results of these studies will be published in one scientific manuscript. Michela wrote a report on the activities performed at the Mycology laboratory.

**Training modules**

The Bioinformatics and Phylogenetic Module provided to the fellow comprehensive knowledge on constructing and interpretation of phylogenetic trees to support epidemiological tracing of sources of infection. The Biorisk and Quality Management Module provided further knowledge on sample management and biorisk assessment and mitigation.

**Educational outcome:** performed lab methods with *S. pneumoniae* isolates (i.e. *in vitro* culture, antibiotic susceptibility testing, DNA extraction); understood principles of multiple alignment; constructed and interpreted simple multiple alignment; created and queried the local basic local alignment search tool BLAST database; performed phylogenetic analyses techniques; written a manuscript to communicate findings.

### 4. Biorisk management

**A. Experimental studies on susceptibility of two Italian mosquito species to Zika Virus infection**

As part of the project (described above), the fellow worked under Biosafety level 3 conditions participating in *in vivo* mosquito’s infection with ZIKV and handling infected samples.

The fellow had previous extensive experience in biorisk/biosafety assessment and mitigation procedures and personal protective equipment having worked in diverse BSL3 facilities continuously since 2001 on HIV-related projects.

**B. Whole Genome Sequencing (WGS) of multidrug resistant Streptococcus pneumoniae isolates belonging to serotype 24F, a frequent non-vaccine serotype isolated from Italian patients, 1997-2016**

The fellow got practical experience in handling invasive strains of multi-drug resistant *S. pneumoniae* isolates following biorisk and biosafety procedures and appropriate decontamination strategies.

**C. Visit to the BSL-4 facility at the Public Health Agency of Sweden, Solna, February 4, 2016**

All the fellows of Cohort 2015 had the privilege to visit the BSL-4 facility at the Public Health Agency of Sweden during the Biorisk and Quality Module held in Solna in 2016. This high-containment facility is the only one in the Nordic countries and one of few in Europe. Michela wrote a report describing that visit.

**Training modules**

The Biorisk and Quality Management Module provided knowledge on biosafety and biosecurity assessment and mitigation in Biomedical Laboratories allowing the fellow to assess biosafety procedures on BSL3 facility for Tuberculosis management at the host site. Specific training for international shipping of infectious substances according to international regulations for transport of dangerous goods as defined by ICAO (International Civil Aviation Organization) was also received. WHO recommendations on Biosafety and Biosecurity Management in Laboratories were also given, as well as the CEN document CWA 15793 CEN Workshop Agreement entitled "Laboratory Biorisk Management" was explained and provided.

The fellow had the opportunity to visit the BSL4 laboratories at the Swedish Agency for Public Health (SAPH) and to write a detailed report of this experience.

**Educational outcome:** applied the principles and practices of biosafety according to those outlined by WHO, EU and national directives; experienced different personal protection equipment (PPE) systems; understood the principles and practices regarding decontamination processes associated with infection control and equipment decontamination; understood processes associated with BSL3 laboratories: communicated findings by one abstract, one online article and two peer-reviewed manuscripts.
5. Quality management


Supervisor: Dr Patrizia Rossi, Dr Gianluca Marucci

The fellow had the opportunity to assist as external observer at the three-day joined audits for Proficiency Testing (PT) for the parasite *T. spiralis* and general requirements for the competence of the organisers of inter-laboratory circuits (regulations ISO/IEC 17025 and UNI CEI EN ISO/IEC 17043:2010, respectively) during two joined audits by Accredia (the Italian accreditation body) at the International Trichinella Reference Centre (ITRC) at the host site. The ITRC is the official reference laboratory for both the International Commission on Trichinellosis (since 1988) and the World Organization for Animal Health (since 1992). PT on the digestion method to detect *Trichinella larvae* in meat intended for human consumption is mandatory for laboratories performing official controls according to the EC Regulation 2075/2005. Achieving accreditation to be able to performing PT on this method aimed to assure the maximum level of food safety to European consumers, leading the National Reference Laboratories (NRL) to a very high standard of technical competence in Europe. Michela followed the inspectors through the control procedures and achieved knowledge on the details to be regulated to get quality accreditation for one *T. spiralis* diagnostic method. The evaluation aimed to establish documents, registers and traceability of information, preventative actions and staff curricula, method validation and instruments maintenance, complains/appeals ever occurred by the participating labs, purchasing and processing of the samples (fish meatballs containing *T. spiralis larvae*), their packing, labelling and shipping to the participant labs in the PT in Italy and Europe. This activity highlighted the importance of data traceability and corrective actions of systematic errors in laboratory quality management.

B. External Quality Assessment (EQA) for Trichinella spiralis

Supervisor: Dr Patrizia Rossi, Dr Gianluca Marucci

The fellow achieved practice knowledge on the technical requirements for performing Proficiency Testing (PT) for qualitative detection of the parasite *T. spiralis* at the International Trichinella Reference Centre (ITRC) at the host site. In order to assuring high quality meat for human consumption in Europe, a PT on the accredited digestion method to detect *Trichinella larvae* is mandatory for laboratories performing official controls in Europe according to the EC Regulation 2075/2005. The ITRC organises PT for the National Reference Laboratories (NRL) of the Member States and for public/private laboratories performing official controls in European countries, in order to assess their competence and improve laboratory performance in detecting *T. spiralis* larvae in meat. Good performance in PTs provides evidence of reliable test results. PT carried out by the ITRC allowed most of the participating NRL to organise PT in their own country according to the same schemes, making diagnostic capacity for *T. spiralis* comparable at European level. The ITRC manages PT on *T. spiralis* for about 30 NRLs once a year (March-April), and for about 10-15 public/private laboratories about bimonthly. The fellow became familiar with all the steps of a PT, since contacting the participating labs and pre-test activities, through obtaining *T. spiralis larvae* and making the infected and control meat samples to be sent and tested by the participants, to analyse participants’ results and send them the lab-specific and global report of the current PT.

Training modules

The Biorisk and Quality Management Module provided overview of concepts of the Total Quality Management in diagnostic and public health laboratories. Concepts of accreditation and certification, addressing the process of auditing (either internal or external) according to the requirements of the norms ISO 15189 and ISO 17025 were given to the fellow.

Educational outcome: described the efficacy of quality assurance; applied the concepts of EQA; followed all the steps of EQA; followed an accreditation audit; understood and applied local and European accreditation procedures; understood the principles and practices of quality assurance according to those outlined by international and EU directives; written a report of the activity.

6. Teaching and pedagogy

A. Epi4Lab Course: applied epidemiology for the microbiologist

The fellow planned, organised and contributed to a two-morning pilot course on infectious disease epidemiology for junior training fellows and staff professionals working in microbiologic laboratories and performing research, surveillance, and/or European or national reference activities at the host site. The course had the primary objectives to training the participants to communicate properly laboratory and surveillance data through adequate graphical presentation and accurate descriptive statistics, according to ECDC standards. Secondary aims were getting the participants aware on the role of microbiological investigations in surveillance activities, national/European reference laboratories, and in case of epidemic. The ten steps of an outbreak investigation were also presented and explained.
by true examples. Collaboration and sharing of diverse competences among different professionals working at the Dept. Infectious were favoured. Lectures to provide theoretical and practical background on epidemiology and on the role of microbiological labs in public health were given with the support of an interdisciplinary team (one biologist, one statistician, one medical infectivologist and an EPIT alumni infectious disease epidemiologist). Pre and post course questionnaires related to various topics and aspects of the course gave the fellow indications that the course was highly appreciated from the participants who requested to further develop the course to be proposed yearly for specific staff training at ISS. The fellow wrote a comprehensive report on the various aspects of the course.

B. Teaching on antibiotics and antimicrobial resistance

The fellow was involved in a national project mandated by the Ministry of Health providing short job experience to high school adolescents. The ISS participated to this project favouring students’ exposure to diverse laboratory activities with the aim to improve their knowledge in some scientific matters (e.g. biological, chemical, vet, biochemical fields) and to better realise specific scientific professions by direct experience. The fellow had the opportunity to present to the students information related to antibiotics, antimicrobial resistance and its functional mechanisms with the aim to raise awareness of the risks associated with misuse and abuse of antibiotics and to encourage their responsible use to limit the phenomenon of antibiotic resistance. After the presentation, a quiz testing the students’ understanding on the topics discussed showed their comprehension of the matter and acquired knowledge as well as their enthusiasm and positive feedback.

C. Contribution to the website “Portal of Knowledge” on Tuberculosis

The fellow contributed in writing the section on Tuberculosis in the online “Portal of Knowledge” managed by the host site. This web Portal is under construction (https://wp-produzione.iss.it/conoscenza/?cat=6) and will disseminate scientific knowledge for the citizens in order to protect and promote public health.

Training modules

During the Introductory Course the fellow had the opportunity to present and communicate to peers, and to receive training on interactive teaching and learning methods such as problem based learning (PBL), case studies, cooperative learning, and brainstorming. Besides, at ESCAIDE 2016 and ECCMID 2017 the fellow had great occasions to transfer knowledge and receive feedbacks from several health professionals in international settings. The Project Review Modules 2016 and 2017 were useful chances to prepare, deliver and moderate lectures to multidisciplinary audience as well.

Educational outcome: Identified training needs at ISS; defined learning objectives; planned, organised and moderated a scientific course; identified teaching and assessment methodologies; prepared presentations and given lectures; trained a range of health-care professionals; assessed own performance through feedbacks by participants; re-evaluated delivery and content; prepared one scientific report.

7. Public health microbiology management

Public health microbiology management was a practice training throughout the fellowship in all the developed projects and activities. Especially during the listeriosis outbreak investigations, the fellow experienced time and laboratory management, team working and communication among the diverse professionals involved (epidemiologists, vets, statisticians, microbiologists, laboratory technicians, public health officers) and with regional and national health authorities, team roles and team evolution, ethical and integrity considerations, while developing conflict resolution skills. She participated in videoconferences with professionals involved in the listeriosis outbreak investigations. The fellow was also involved in the revision of assigned abstracts for ESCAIDE 2015, 2016 and 2017.

Training modules

The five-day module Initial Management in Public Health Microbiology gave the participants rational and emotional understanding of Initial Management within the Public Health environment, allowing them to develop management and leadership skills. The fellows gained a thorough understanding of requirements to motivate and manage individuals and teams successfully, practiced combined techniques to manage different situations and identified microbiological threats and countries’ preparedness at European level to the health of the public.

Educational outcome: identified elements of stress management; applied principles of scientific communication to peers, stakeholders and media/public; become an effective team member, adopting the role needed to contribute constructively to the accomplishment of tasks by the group; promoted team building to accomplish public health microbiology programme objectives; used rapid assessment in the early phase of crisis due to infection diseases; got knowledge of planning outbreak responses at national and international level.
8. Communication

Publications

10. Whole Genome Sequencing of multidrug resistant *Streptococcus pneumoniae* isolates 24F, a frequent non-vaccine serotype isolated from Italian patients, 1997-2016. (In preparation).

Other publications


Reports


Conference presentations

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Other oral presentations


2. Prevent HIV acquisition and transmission in Italy. Introductory Course, Spetses. 9 October, 2015.

3. What I did and what I will do. Presentation of the fellow and the EUPHEM fellowship to Dept. Infectious Diseases at Istituto Superiore di Sanità, Rome, Italy. 27 October 2015.


8. Laboratory preparedness for (re)emerging pathogens/diseases, Italy. Presented to the Director of ECDC during the Initial Management in Public Health Microbiology Module, Stockholm, Sweden. 11 February 2016.


Training modules

Many modules gave support to this section. The Introductory Course provided clear instructions on scientific abstract and manuscript writing, and on oral presentation tips. The ECDC online course Scientific Abstract Writing Course 1st Edition (course ID 41) provided specific knowledge on writing and reviewing scientific abstracts with a field epidemiology focus. The Initial Management in Public Health Microbiology Module further gave insights on interpersonal communication strategies and with the public, the media and health authorities in the field of public health. The Project Review Modules 2016 and 2017 represented a great opportunity to receive detailed feedback from peers on content and form of oral presentations.

Educational outcome: submitted abstracts to the national scientific conferences SITI and AMCLI and to the European scientific conferences ESCAIDE 2016, ESCAIDE 2017 and ECCMID 2017; prepared scientific reports and papers; made an oral scientific presentation at ESCAIDE 2016; trained to be involved in the preparation of a press release.

9. EPIET/EUPHEM modules attended

1. EPIET/EUPHEM Introductory Course, Anargyrios and Korgialenios School of Spetses (AKSS), Spetses, Greece, 28 September – 16 October 2015.

2. Outbreak Investigation (OBI), Robert-Koch Institute, Berlin, Germany, 7-11 December 2015.

6. Project Review module (PRM), Instituto de Higiene e Medicina Tropical, Universidade NOVA de Lisboa, Lisbon, Portugal, 22-26 August 2016.

10. Other training

   1. Reviewer for ESCAIDE 2015, 2016 and 2017
   2. Online course: Basic security in the field II, WHO, 9 June 2016
   3. Online course: Advanced security in the field, WHO, 9 June 2016
   6. Online course: certified EpiCore member, 8 June 2016.
   9. Scientific event: Food safety and food security. ISS, Rome, Italy, 5.11.2015
   10. Workshop: Characteristics of people living with HIV in Italy. ISS, Rome, Italy, 24.11.2015
   16. Scientific seminar: Tuberculosis - why do I have to take so many pills? Prof. E.J. Rubin (Harvard School of Public Health, UK), Policlinico Umberto I, Rome, Italy, 06.06.2016
   21. Conference: Hepatitis E virus (HEV) and Substances of Human Origin (SoHO) security. ISS, Rome, Italy, 04.04.2017
   22. Conference: Antimicrobial resistance in Italy: current problems and future commitments. ISS, Rome, Italy, 05.05.2017

Discussion

Coordinator’s conclusions

One of the main goals of the EUPHEM programme is to expose the fellows to different public health experiences and activities, thus enabling them to work across various disciplines. This portfolio includes laboratory and epidemiological...
projects covering bacterial, viral, parasitic and fungal pathogens across a variety of disease programmes, such as vector-borne diseases, sexually-transmitted diseases, food and waterborne diseases, respiratory tract infections, vaccine-preventable disease and antimicrobial resistance. The projects here described are in line with the 'learning by doing' approach of the EUPHEM programme and fulfilled the core competency domains described for professionals in their mid-career and beyond. During the two-year fellowship, the fellow, supervisors and training site have demonstrated the capability of addressing communicable disease threats in a structured joint approach between public health microbiology and epidemiology such as the use of whole genome to investigate multidrug resistant Streptococcus pneumoniae or outbreak and surveillance investigations ranged from local outbreaks to the analysis of national database. The projects have been nicely selected to cover not only important international and national public health topics such as Zika infection or drug resistant Enterobacteriaceae but also a very broad panel of microorganisms and involved different professional groups, such as physicians, laboratory technicians, epidemiologists, statisticians, government officials, public health officers and logisticians, strengthening the fellow's ability to work in a multidisciplinary team and to adapt to different environments and contexts. Michela has been active in contributing to training of others during her fellowship with the development of new training materials as well as direct training and facilitation activities which highlights the contribution that fellows can make to capacity building beyond the programme.

All projects had a clear educational outcome, with results communicated in scientific journals and at conferences and the activities were complimented by nine training modules providing theoretical knowledge. Michela has been active in contributing to cascade her acquired knowledge within her training site developing and organizing a new course on Applied epidemiology for microbiologists. The contributions made by this EUPHEM fellow indicates the importance of developing and maintaining a critical mass of highly skilled field public health microbiologists within Member States to contribute towards national preparedness as well as being available for responses in the interest of the EU. The EUPHEM Coordinator Team concludes that the fellow has succeeded in performing all her tasks to a very high standard and has conducted herself in a highly professional and effective manner throughout. We wish the fellow every success in her future career as a public health microbiologist.

**Supervisor’s conclusions**

Michela Sabbatucci was the second EUPHEM fellow at the ISS training site. She joined the Department Infectious Diseases for the purpose of the fellowship after being a staff scientist at the National AIDS Center and then at the Department of Haematology, Oncology and Molecular Medicine. Since Michela's previous exposure to infectious diseases and microbiology was limited to HIV/AIDS she was highly motivated to enlarge her knowledge, skills and competencies to embrace the field of Public Health Microbiology. Michela was hard-working and tenacious, with an ability to organize her time. She would not shrink from a task or duty and out of curiosity would undertake extra work. During the two-year fellowship Michela has grown professionally and personally. She faced several challenges, especially when involved in a multi-disciplinary outbreak investigation including different Institutions. In this situation Michela showed good “political” skills of coordination and negotiation. Michela was instrumental to the preparation and presentation of the first report of the National surveillance of CPE bacteraemia that was very appreciated by the Italian national and local health authorities and represented a benchmark for the surveillance and control of CPE infections in Italy. Michela has also organized the first edition of a mini-course of epidemiology for microbiologists involving EPIET and EUPHEM fellows and alumni. The initiative has been highly appreciated and hopefully will become a yearly appointment of our Department. Hosting the EUPHEM fellowship has greatly benefitted our Department and our Institution, strengthening the collaboration between the Microbiology and the Epidemiology Units. In addition the program has promoted multidisciplinary and cooperation at all levels to adequately respond to the present public health challenges at the national and global level.

**Personal conclusions of fellow**

I have always appreciated international multicultural environments, group and multidisciplinary work and practical applied learning. Therefore, since my first knowledge of the ECDC training programmes I felt attracted by and wished to be able to seize this exceptional training opportunity. Being part and contributing to such a high-level and multidisciplinary European network of professionals as the EUPHEM programme builds has been a very great enriching personal and professional experience for me. I have appreciated and got inspired by the excellent ECDC staff I came in close contact with, their high-level expertise and professionalism and sincere devotion to teaching. Following through the modules, projects and activities to accomplish the EUPHEM requirements has been an unforgettable fantastic experience which broaden my scientific knowledge and competences, allowing me to develop new skills and attitudes harmoniously although quickly. I have gained valuable experience in multidisciplinary team working to the health of the public, within and beyond the laboratory setting to which I was used to previously. Broaden my microbiological knowledge and developing while applying new competences in the field of infectious diseases was a privilege, a pleasure and gave me a deep satisfaction and sense of usefulness. I had the unique opportunity to be involved in a wide variety of infectious disease groups and competences’ development, from epidemiology, surveillance, outbreak investigation, quality procedures and teaching that I was quite unfamiliar before,
to research, laboratory investigation, biorisk management and communication that I have dealt with concretely with a new perspective on public health. This fellowship also has allowed me to put in practice and further develop my ability to easily adapt to different people and situations. I wish to continue to contributing to these high-impact public health microbiology and epidemiology fields.

**Acknowledgements of fellow**

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I am also grateful to all my projects’ supervisors as listed in each project above, for having shared their high-quality expertise with me, with continued availability. I also would like to thank all co-authors who were precious human and professional resources from whom I had the opportunity to learn in several settings and on many topics. I am also sincerely grateful to the staff people with whom I have had the pleasure to work with at Istituto Superiore di Sanità (Department Infectious Diseases; Department Food safety, Nutrition and Veterinary Public Health; National Center for Epidemiology, Surveillance and Health Promotion; Centro Operativo AIDS). I would also like to acknowledge the opportunities provided by external Italian collaborators from Istituto Zooprofilattico Sperimentale delle Venezie, Istituto Zooprofilattico Sperimentale dell’Umbria e delle Marche (Ancona, Fermo and Perugia operational offices), Agenzia Regionale Sanitaria Marche, and Istituto Zooprofilattico Sperimentale dell’Abruzzo e del Molise ’G. Caporale’. I greatly thank my peers from cohort 2015 for their friendship, exceptional reciprocal support and amazing team spirit together with previous and following members. In particular, I wish to thank Claudia Lucarelli, previous EUPHEM fellow at my host site, who kindly supported me during these two years. I would like to thank the fellowship programme office also, for its continued administrative support and guidance through the fellowship. A special thank goes to all the teachers I met in the ECDC modules as they provided the fellows with passion and effective method lectures to widen our knowledge.

Last but not least, I wish to thank my family gratefully as allowed me to attending all the EUPHEM modules and meetings taking care of my beloved little daughter during my absences harmoniously.