EUPHEM

EUPHEM REPORT

Summary of work activities

Anastasia (Nancy) Flountzi
European Public Health Microbiology Training Programme (EUPHEM), 2017 cohort

Background

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.

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 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'.

Moreover, Article 47 of the Lisbon Treaty states that 'Member States shall, within the framework of a joint programme, encourage the exchange of young workers. 'Therefore, ECDC initiated the two-year EUPHEM training programme in 2008. EUPHEM is closely linked to the European Programme for Intervention Epidemiology Training (EPIET). Both EUPHEM and EPIET are considered 'specialist pathways' of the two-year ECDC fellowship programme for applied disease prevention and control.

Stockholm, September 2019

This report summarises the work activities undertaken by Anastasia (Nancy) Flountzi, cohort 2017 of the European Public Health Microbiology Training Programme (EUPHEM) at the National School of Public Health and the Hellenic Center for Disease Control and Prevention, Athens (GR). 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.

Pre-fellowship short biography

The fellow, Anastasia (Nancy) Flountzi, is a Medical Doctor (graduation 2001), specialized as resident in Medical Biopathology – Microbiology/Laboratory Medicine (2009). She attended the Master of Public Health program of the National School of Public Health (Infectious Diseases), in the years 2013-2015, awarded with the grade"Excellent". The PhD award, with grade "Excellent", was awarded to her from the National and Kapodistrian University of Athens, Medical School (2013). Since 2009, she is been working at the National Public Health Organization (E.O.D.Y. – Former Hellenic Centre for Disease Control and Prevention) and particularly at the Central Public Health Laboratory, as Head of the Southern Greece *Legionella* Reference Laboratory. She has been participating as an instructor to the Master Science in Public Health of the National School of Public Health in Greece. She joined the European Legionnaires' Disease Surveillance network (ELDSNet) at ECDC, as a Member, since 2015 and she is the official representative for Greece on Laboratory level (Laboratory focal point). She is also an ESCMID member and member of the study groups ESGLI and ESGPHM.

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 projects or activities (on-job services) 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 guide[1].

1. Epidemiological investigations

1.1. Outbreak investigations

A. Measles outbreak surveillance in Greece, 2017.

Supervisors: Elina Horefti, Andreas F. Mentis

Since May 2017, 326 measles cases were notified to the Hellenic CDC and included 232 laboratory confirmed cases (serological test and/or PCR positive pharyngeal swabs), 76 probable cases meeting the clinical criteria epidemiologically linked with laboratory confirmed cases and 18 possible cases meeting clinical criteria. The highest frequency was observed in Athens and Southern parts of Greece, mostly affecting Roma children of Greek nationality (78% of total cases), whereas the second most affected social group involves Greek adults (8.6%) and, especially, health workers, non or partly vaccinated. This was in concordance with a study published in 2013, by the Hellenic CDC, concerning the vaccination coverage in Greece. MMR vaccination coverage for children of Greek nationality was 99% for the first dose of the vaccine and 86% for the second one, whereas MMR vaccination coverage for Roma children was 48% and 8% for the first and second dose, respectively. In order to contain and, subsequently eliminate the outbreak, it was important to strengthen the laboratory surveillance of the disease by confirming all suspected

[1] European Centre for Disease Prevention and Control. European public health training programme. Stockholm: ECDC; 2019. Available from: http://ecdc.europa.eu/en/publications/Publications/microbiology-public-health-training-programme.pdf

cases and collecting all the available epidemiological information and to reinforce efficient communication among professionals and authorities (local and international). The aim of the project was to identify the possible routes of introduction and transmission of measles virus in Greece. 1023 samples collected from suspected measles cases were received by the reference laboratory. Genotyping and sequencing methodology was implemented in order to identify the sequence variants of the B3 genotype that was detected in all strains. 740 samples were found positive by real-time PCR while 136 isolates which were detected among them were sequenced within the laboratory premises and 16 of them were sequenced at the respective reference laboratory at the Medical School of Thessaloniki, Greece. Two sequence variants were identified, indicating two possible routes of transmission, however, the bioinformatics' analysis, which is still in progress, in collaboration with Dr Dimitris Paraskevis from the Medical School of Athens, reveals three possible transmission routes so far.
The EUPHEM fellow, had the opportunity to be familiarised with laboratory methods used during a measles laboratory outbreak investigation and surveillance and introduced to the utility of advanced laboratory methods for investigating such outbreaks. The fellow participated in the confirmation of the possible/suspected measles cases by conducting the relevant diagnostic tests, in the determination of the circulating measles strains genotypes and their phylogeny (molecular characterization of measles viruses and development of phylogenetic trees), in the assurance of the laboratory results' timely release to the Hellenic CDC, in the reporting the measles confirmed cases in international networks and the Greek authorities and the acquisition of suspected measles cases' epidemiological information from the Hellenic CDC and through the respective measles request examination forms (characterization of the outbreak combining laboratory findings and epidemiological information and assessment of the findings regarding differences among the main transmission groups (Roma and general population). She also acquired experience in writing project proposal, in team working and contributed in the preparation of a scientific abstract. The fellow contributed in the initial draft for the publication at a peer-reviewed scientific journal as a co-author (see 8. Communications/will follow No2).

B. Outbreak investigation on a cluster of gastroenteritis cases during a school excursion to Athens from Larissa-Thessaly in Greece, in December 2018.

Supervisors: Kassiani Mellou, Theologia Sideroglou

On the 04/12/2018, the Food and Water-borne Diseases Unit of the Department of Epidemiological Surveillance and Intervention of the Hellenic Center for Disease Control and Prevention (H.C.D.C.P.), was informed through press reports of a cluster of gastroenteritis cases, exhibiting no blood in feces, among students of a Larissa (Thessaly region) high school and their teachers, who traveled to Athens on a school trip. Communications with the school principal revealed that 62 students and 5 teachers had traveled. The excursion started on the 1/12/2018 and two stops were held during the trip. All travelers stayed at a hotel in the center of Athens where they had dinner on the 1st of December and breakfast and lunch on the 2nd day. On the 2nd of December, several students and teachers presented with symptoms of gastroenteritis. Nine of the students were hospitalized at "Agia Sofia" Children's Hospital " with mainly diarrhoea as a main clicical symptom, The retrospective cohort study that was conducted indicated the consumption of chocolate log during the dinner at 19:30 on 01/12/2018 as the only marginally positive correlation found, among a food item and the acquisition of gastroenteritis. This hypothesis was consistent with the shape of the epidemic curve which was compatible with a point common source outbreak. The clinical picture of the cases was compatible with that of viral gastroenteritis however laboratory confirmation of the causative agent was not possible. Thus, important information that could strengthen the epidemiological investigation results was missing. Overall, this gastroenteritis outbreak could have been attributed to the consumption of a specific food item during the dinner at the hotel. However, the conclusion should be carefully taken under consideration due to the absence of environmental investigation findings and the limitations of epidemiological and laboratory investigations conducted. The fellow participated in different stages of the outbreak investigation: (a) creating a database by the use of EpiData, entering the structured questionnaire, in fformulating a case definition, in data entry of the results, in the performance of descriptive and analytic statistical analyses with the use of Stata software. In addition, the fellow was actively involved in the formulation of conclusions and public health recommendations and she wrote the final outbreak report in Greek and in English (see section 8, report No5).

C. Training modules

During the EPIET/EUPHEM fellowship and in the context of the introductory course, the basic of the outbreak investigation and the analytical tool that can be used to assess the ten steps of an outbreak investigation, have been provided. In particular, during the "introductory course" the 10 steps of an investigation were presented by several lectures and case studies, as well as the logic and the statistical approach to each step, while the "Outbreak investigation" module provided participants with the essential skills and competencies in practical aspects of data entry and management, questionnaire and training in performing analytical studies for an outbreak investigation, including descriptive, cohort/case control studies and stratified analyses using Stata. The software packages such as

EpiData, STATA and Microsoft excel were discussed and presented. In the module "Multivariable analysis", participants were provided with the statistical principles to build up the optimal model, such as linear, logistic, Poisson and Cox regression in Stata, showing them simultaneously, the usefulness of this methodology in order to apply them in outbreak investigations and the importance of identifying the relevant variables in order to check for confounding and effect modification factors. Moreover, in "Rapid assessment and survey" module it was made possible to explore tools for structuring questionnaires and mapping, which was important for field investigation. The training modules instructed participants how to make recommendations, best communicate the results, and write outbreak reports and scientific manuscripts.

Educational outcome: The fellow participated in α multidisciplinary outbreak control team and had hands-on involvement in outbreak investigation; case definition, case finding, data analysis; generating and testing appropriate hypotheses; efficiently communicating results to multidisciplinary team; and developing recommendations. The fellow comprehended the need for integrated microbiological and epidemiological knowledge in outbreak investigation; the importance of a cooperative teamwork among laboratories, local and central authorities and the advantages of international collaboration. The fellow prepared the outbreak report in two languages.

1.2. Surveillance

A. Epidemiology of Invasive Meningococcal Disease (IMD) in Greece during 2006-2016.

Supervisors: Georgina Tzanakaki, Theano Georgakopoulou

Invasive Meningococcal Disease (IMD), is an acute, severe and potentially life-threatening disease characterized by meningitis, sepsis or, less commonly, pneumonia, arthritis, pericarditis and abdominal disorders with an overall case fatality rate (CFR) of 10%. Greece has introduced MenC in 2005 and replaced it by MenACWY in 2011. The aim of the project was to describe the epidemiological and microbiological characteristics of IMD in Greece during 2006-2016. Surveillance of IMD is mandatory in Greece and IMD cases are notified to the National Public Health Organization (NPHO) by physicians nationwide as well as the Greek Public Health directorates. Data collected included demographic and epidemiological characteristics, vaccination status for some of the cases, clinical manifestations, potential antibiotic treatment prior to CSF collection and disease outcome. Laboratory testing was performed by the Hellenic National Meningitis Reference Laboratory (HNMRL, National School of Public Health). Isolates and biological fluids (CSF, blood) received by the HNMRL were obtained as part of the routine activity and analyzed anonymously. A total of 796 IMD cases were notified, of those, 720 (91%) were confirmed. Overall, a decline on the annual incidence of confirmed cases was observed; ranging from 0.91 (2006) to 0.47 (2016) /100,000. A similar trend was observed in most age groups especially in children 0-4 years (7.7 to 2.9/100,000), with the exception of an increase in the incidence rate in adults >20 years (0.21 to 0.32/100,000). The overall case fatality rate was 6.5% (52/796); annual range 2%-13%. Among 658 strains which were typed by sero/genogroup, 80% were identified as MenB (annual range 65-92%); however, a decline was observed in MenB incidence from 5.3 (2006) to 2.7 (2016), among infants and toddlers, while MenW (1%), MenY (2%) and MenA (1%) remained low. The EUPHEM fellow, received the database, performed data clearance, the data analysis, by the use of STATA and Excel and interpreted the extracted results. Data obtained were communicated as a publication in a peer reviewed Journal and as a poster presentation in ESCAIDE order to inform clinicians and public health authorities. The EUPHEM fellow prepared the poster presentation and drafted the manuscript (see section 8., publications No1, presentations No1)

B. Seasonal influenza surveillance in southern Greece – Season 2018–2019.

Supervisors: Athanasios Kossyvakis, Andreas F. Mentis

Influenza activity in Southern Greece started in week 51/2018 and remained at low levels until week 52/2018. Since then, epidemiological and laboratory data indicated accelerating epidemics of seasonal influenza. During week 5, influenza intensity is considered as medium with widespread circulation across the country. Influenza B virus accounted for the vast majority of detected viruses in Southern Greece and it was associated with a considerable number of ICU and fatal cases. The greatest proportion of ICU cases were adults above 50 years of age with only 9% of them concerning vaccinated patients while fatal cases included only unvaccinated individuals. Genetic characterization of influenza B viruses revealed circulation of B/Yamagata lineage. A(H1N1) pdm09 subtype accounted for the 80.6% of influenza type A detections while only a small number of A(H3N2) influenza viruses (6 in total) have been detected up to week 6.
In total, 806 respiratory specimens (mainly nasopharyngeal swabs and BAL) were tested at the NIRLSG. The vast majority of specimens (83.7%) were collected from patients consulting hospital GPs and hospitalized or intensive care unit patients and the remaining 16.3% from sentinel sources. Ninety-five specimens (11.8%) of the 806 tested till week 6, were found positive by rRT-PCR for influenza virus. Positive cases were mainly resulted from non-sentinel

patients (73.7%) (Figures 3 and 4) and included 64 samples positive for influenza B (45 from non-sentinel and 19 from sentinel samples) and 31 positive for influenza A viruses. From type A viruses, A(H1N1) pdm09 subtype accounted for the 25 out of 31 type A positive cases (19 from non-sentinel and 6 from sentinel samples). Only a small number of A(H3N2) influenza viruses (6 in total) have been detected since week 6, all from non-sentinel patients (Table 1). Interestingly, the greatest proportion of influenza positive cases occurred in children within the age group of 6-18 and in adults within the 36-65 age group. From week 40/2017 to week 1/2018, only up to 5,7% of specimens received were tested positive by PCR for influenza virus (with the exception of week 51 where positivity rate was 11.5), whereas during weeks 2/2018 and 6/2018 the positivity rate gradually reached 27.7%. The fellow became acquainted with influenza surveillance systems at national and international level, as she recognized the importance of the influenza surveillance data delivery on a weekly basis to the Greek health authorities. The EUPHEM fellow contributed to the national and international influenza surveillance data system, by submitting epidemiological and typing data to The European Surveillance System (TESSy), and sequences to the Global Initiative on Sharing All Influenza (GISAID) database. The fellow was involved and contributed as a co-author to the official report on the country's seasonal influenza surveillance for the 2018–2019 influenza season (see 8. Reports 4), which was uploaded to the World Health Organization (WHO)'s Global Influenza Surveillance and Response System (GISRS) platform as part of the annual WHO Consultation of Influenza Virus Vaccines Composition for the Northern Hemisphere 2019–2020. The fellow also prepared, submitted an abstract for a scientific Conference and also prepared and delivered the oral presentation (see 8. Conference presentations No4).

C. Training modules

The EPIET/EUPHEM introductory course exposed participants to the main concepts of surveillance, providing the basis of surveillance systems' different approaches, including all logical and analytical tools in use to develop, validate and evaluate the attributes of a surveillance system. During the rapid assessment and survey methods module, sampling methodology was presented, as well as suitable sampling methods adapted to study populations and ways to contribute to complex emergency situations multidisciplinary response and application of epidemiological skills for diseases surveillance purposes. The Vaccinology module taught participants the main aspects of vaccine-preventable diseases surveillance, including vaccine coverage and efficacy.

Educational outcome:
The EUPHEM fellow experienced the learning by doing on several aspects of surveillance, such as the need to integrate microbiological and epidemiological data in disease surveillance, the analysis of combined syndromic and laboratory surveillance data, the laboratory-based surveillance, the operation of microbiological support for surveillance systems, and the participation in disease-specific networks at national and European level. During the projects, different tools have been used, such as STATA and Microsoft excel, while the fellow was engaged in interacting with different authorities in order to formulate specific public health recommendations, such as a continued surveillance for monitoring emerging clones to assess epidemiological trends and plan vaccine policies. She prepared an abstract for a scientific Conference; she participated in a report delivery for the WHO and drafted a manuscript for a scientific journal.

2. Applied public health microbiology research

A. Investigation of *Klebsiella pneumoniae* clinical isolates since 2016 for the putative presence of the plasmid-mediated *mcr*-1 gene for colistin resistance.

Supervisors: Panagiota Giakkoupi, Kyriaki Tryfinopoulou

In November 2015, the European Centre for Disease Prevention and Control (ECDC) reported the highest endemic situation of Enterobacteriaceae producing carbapenemases from three countries, i.e. Greece, Italy and Turkey (Munoz-Price LS., et al., 2013). Colistin resistance in *K. pneumoniae* has been reported globally, including regions of Europe, North America, South America, Asia and South Africa (Ah YM. et al., 2014). In particular, regarding the plasmid-mediated colistin resistance: Liu et al., in November 2015, described the emergence of colistin resistance in community-acquired *E. coli* from China from animal and human sources for the first time and attributed it to a plasmid-mediated *mcr-1* gene (Liu YY et al., 2016). A new plasmid (pHNSHP45) was successfully transferred between *E. coli* strains as well as to *K. pneumoniae* and *P. aeruginosa* strains, being quite stable, indicating that selection pressure by colistin was not necessary for its maintenance (Liu YY. Et al., 2016. The extent to which the *mcr-1* gene has spread in community acquired *E. coli* is still unknown.

The aim of the study was to investigate the potential presence of the plasmid-mediated *mcr*-1 gene for colistin-resistance, in *Klebsiella pneumoniae* multiresistant clinical isolates, in Greece, from 2016 onwards and in case of detection of the particular gene, the further molecular epidemiological investigation on its possible distribution and dissemination. Three hundred two *Klebsiella pneumoniae* clinical isolates, part of the collection of the Health Care Associated Infections & Antimicrobial Resistance Reference Laboratory in the Central Public Health Laboratory were subjected to polymerase chain reaction with primers specific for the gene mcr-1 as an initial screening regarding the presence of the plasmid-mediated colistin-resistance. The strains were isolated from Greek health care settings in

Athens and other Greek cities from 2016 onwards; and the carbapenem resistant ones had been already characterized for the respective resistance mechanisms in the reference laboratory; 93 KPC, 60 NDM, 24 VIM, 25 OXA-48, 8 ESBL, and 10 with various β-lactamases' combinations (2 KPC/VIM, 1 KPC/OXA-48, 1 NDM/VIM, 2 NDM/OXA-48, 1 VIM/OXA-48, 2 OXA-48/CTX-M1 and 1 MBL/ESBL). All 302 multiresistant *K. pneumoniae* isolates were screened and were found negative regarding the presence of the mcr-1 gene. Despite the extensive, continuous use of colistin as a last line antimicrobial agent against KPC-KP infections, the *mcr*-1 gene hasn't been transferred among the *Klebsiella pneumoniae* isolates tested throughout our collection. The isolates' diversity, with regards to time (3-year period) and geographical distribution could be a strong indication of a non *mcr*-1 gene plasmid mediated transfer. Colistin resistance among the isolates, seem to be a consequence of chromosomal mutations. The EUPHEM fellow was involved in all stages of the PHM research project, discussing the public health issue with the supervisors, revising literature, gathering, categorizing and evaluating the data, creating a data file and analysing the data in order to present the results. The fellow prepared the research protocol, performed the experiment, prepared and presented the results to an international conference (see section 8. Conference presentations No2).

B. Training modules

The EPIET/EUPHEM introductory course familiarized fellows with the development and presentation of research study protocols. The MLCPH module focused on other laboratory aspects of research, such as stress management, time management and team working and effective communication of the laboratory results. Guidance on how to present the research outcome have been introduced during the introductory course, the outbreak investigation and the multivariable analysis modules.

Educational outcome: The fellow conducted and/or was involved in all stages of a research project in public health microbiology, such as the public health problem identification, revising literature, study design, delivering the research protocol, applying relevant laboratory methods, identifying the use and limitation of diagnostic and their interpretation in surveillance and molecular epidemiology studies. The fellow prepared and presented the results at a prestigious international scientific conference (see 8. Conference presentations No2).

3. Applied public health microbiology and laboratory investigations

A. Detection of West Nile Virus (WNV) in mosquito pools collected during the 2018 transmission period from the East Macedonia-Thrace (NUTS 3) region in Greece.

Supervisors: Eleni Patsoula, Nikolaos Tegos

In the summer of 2010, the second largest WNV infection outbreak in Europe, after the outbreak of 1996 in Romania (Tsai TF et al., 1998), occurred in Greece, with a total of 262 clinical human cases and 35 deaths. The majority of cases were observed in proximity to the four rivers forming a large Delta, a major Mediterranean wetland close to Thessaloniki in Central Macedonia (ECDC, http://www.ecdc.europa.eu/en/healthtopics/west_nile_fever/West-Nile-fever-maps/Pages/2011-table.aspx). During 2010-2014 and 2017 (June - October), cases of West Nile virus infection were reported in humans and in various regions of Greece, with virus circulation being recorded in almost all regions studied. After the 2010 WNV infection outbreak, a continuous and systematic entomological surveillance programme was implemented for the first time in the Greece, as during the years before only sporadic entomological studies were performed, from some institutes and organizations, without central data collection and analysis. Since 2010, the Hellenic Center for Disease Control and Prevention (HCDCP) started collaboration with international and national authorities, aiming to set up standards for a future national strategic plan (Patsoula et al. 2016). The aim of the study was to investigate the presence of WNV in mosquito pools collected between April and October, for 2 years (2017 and 2018), from the Prefecture of East Macedonia-Thrace (Regional Unions/R.U. of Drama and Xanthi) where, particularly in Xanthi R.U., WNV human cases were recorded in 2018, as an early warning system for WNV circulation in the entomological surveillance program. Mosquito samples were collected by CO_2 traps in representative sites of Xanthi and Drama Regional Units (R.U.) in Northern Greece -69 and 15 respectively, during 2017-2018 (April-October). Samples were sent to the National School of Public Health (NSPH) for morphological identification and *Culex pipiens* mosquitoes were grouped in 84 pools of 1-200 adults. RNA extraction was performed and samples were analyzed by Real-Time PCR for WNV lineages 1 and 2, moreover, positive samples were subjected to conventional PCR and purification for sequencing targeting the WNV E-region. Eleven among 84 mosquito pools were positive for WNV presence. Positive pools were isolated from Xanthi R.U. (five from traps in July 2017- four in May, July, September and October 2018) and Drama R.U. (two from traps in August 2018). Two WNV disease cases were recorded in Xanthi R.U. (September/October 2018). Conventional PCR and sequencing were implemented and results are pending (sequencing only). Although no human cases were diagnosed in 2017, WNV was detected in mosquito pools. The virus re-emerged in 2018 and results concur with epidemiological data, as WNV circulation in the area has been noted in dates preceding human cases' detection. This highlights the importance of a stable early warning system, regarding mosquito monitoring and WNV circulation in areas/countries with high endemicity rates, reinforcing a crucial type of integrated surveillance (human/bird/insects/horse). The EUPHEM fellow familiarized with the various laboratory protocols for the detection of WNV RNA by real-time PCR and their applications accordingly, the biological

and morphological characteristics of the mosquito population in the area, the importance of their geographical and temporal distribution in relation to human cases, the understanding of the early detection system function as a part of an integrated surveillance, including not only the vector and human surveillance but also the intermediate hosts' one. The fellow prepared the scientific abstract, the work has been accepted as a poster which will be presented in the upcoming ESCAIDE conference (November 2019) (see section 8, conference presentation No- 3). Furthermore, a manuscript for a peer-reviewed scientific journal is under preparation (see 8. Communication/will follow No2).

B. Training modules:

The EPIET/EUPHEM introductory course familiarized participants with the main concepts of surveillance, including how to develop, validate, evaluate and operate a surveillance system. The rapid assessment and survey methods module provided fellows with knowledge on how to contribute to the multidisciplinary response to complex emergencies and apply their epidemiological skills to serve diseases surveillance. The management, leadership and communication in public health module, and the outbreak investigation module broached many concepts necessary for successful completion of projects, such as understanding and applying the role and responsibilities of effective management within a Public Health environment relating to a variety of situations and circumstances, communicating efficiently and writing scientific articles. Through all modules mentioned above, the fellow has deepened her public health microbiology knowledge in terms of laboratory investigations, including becoming familiar with parasitology, managing time, formulating recommendations and collaborate with different experts and disciplines. The biorisk and quality management module provided understanding of biorisk and quality control management, which are important in any laboratory investigation.

Educational outcome: The EUPHEM fellow learned by doing several crucial aspects of surveillance, such as the need to integrate microbiological and epidemiological data in disease surveillance, the analysis of combined syndromic and laboratory surveillance data, the laboratory-based surveillance, the operation of microbiological support for surveillance systems, entomological surveillance and participation in disease-specific networks at national and European level. Also, she has deepened her knowledge in public health microbiology applying concepts of parasitology and entomology and environmental microbiology to the public health disciplines, identifying the use and limitation of diagnostic and typing methods and their interpretation in patient diagnosis, surveillance and epidemiological studies in the community. She also acquired experience in team working, prepared a scientific presentation at a conference and in preparing a scientific article.

4. Biorisk management

A. Assessment on Procedural Biorisk (Biosafety and Biosecurity) Management (TB diagnostic services)

Supervisors: Dimitrios Papaventsis, Simona Karabela

Management of safety risks is essential practice to all laboratories that work with biological agents, in order to protect the working personnel and the human and animal community in the surrounding areas. According to the World Health Organization (WHO) Tuberculosis Laboratory Biosafety manual, decisions on which are the most appropriate biosafety/biosecurity measures for a specific tuberculosis (TB) laboratory should be undertaken using an approach based on risk assessment that considers all the different types of procedures performed (Procedural Risk Assessment/WHO Tuberculosis Laboratory Biosafety Manual, 2012). During this project, procedural biosafety and biosecurity risk assessments were conducted using the BioRAM tool (Sandia National Laboratories, USA) at the National Reference Laboratory for Mycobacteria (NRLM), Athens, Greece, on November and December 2018. The EUPHEM fellow performed the biorisk assessments along with the Biosafety Officer and the Quality Manager of the lab. The BioRAM software was used for the biosafety risk assessments in three different TB laboratory procedures; a) direct molecular testing with XpertMTB/Rif, b) clinical specimen handling for acid fast smear microscopy and inoculation to Löwenstein–Jensen medium (LJ) for solid culture, and c) manipulation of *M. tuberculosis* cultures for phenotypic Drug Susceptibility Testing (first and second-line anti-TB drugs). The NRLM_GR is a high risk level TB laboratory (TB-containment laboratory), performing tests that cover the entire Mycobacteriology diagnostics and research range. All the implemented biorisk mitigation measures in the NRLM_GR, a BSL-2 laboratory with BSL-3 practices, have been taken into account through the biorisk assessment process. The relative biosafety risks as assessed with BioRAM software for the three different procedures have been judged as acceptable. However, improvement is needed, as well as the need for financial support for the construction of a BSL-3 laboratory, necessary for the ideal safety of the laboratory personnel providing high-quality TB diagnostics for the entire country. During this project, the fellow was familiarized with the most recent biorisk management guidelines and procedures concerning a TB clinical laboratory and the factors that drive the risk governance in these settings. She also got acquainted with the biosafety and biosecurity risk assessment processes., the methodology, the models and the

implementation of the BioRam software tool. Finally, she was engaged in the evaluation and recommendation processes and prepared a report for these purposes (see 8. Reports No2).

B. Biorisk management audit/Internal Audit at the National Meningitis Reference Laboratory

Supervisors: Konstantinos Kesanopoulos, Georgina Tzanakaki

Biorisk management/Internal audit at the National Meningitis Reference Laboratory was performed following a post-module homework assignment, after the biorisk and quality management module at ECDC, Sweden, in 2018. The fellow had the opportunity to become familiarized with a laboratory biorisk management evaluation using an evaluation tool provided by the Head of EUPHEM. The fellow conducted the audit in the National Meningitis Reference Laboratory, which is accredited according to ISO:15189. The quality manager responded to all the questions regarding the accommodation and environmental conditions, the biorisk management policy, the internal controls in use, the biosafety and biosecurity guidelines and procedures, the practices, the transport practices, several critical steps during the pre-, analytical and post-analytical process, and procedures in place for biorisk management improvement. In addition, a thorough evaluation of the existing documentation in the laboratory was conducted. The biorisk management system of the laboratory was evaluated as efficient and satisfactory, reaching the score of 98%. Biosafety documentation reached the 91% score. The audit inspected process management, quality control indicators, and documentation. The referral laboratory completed its technical documentation records and kept records of nonconformities. The EUPHEM fellow completed the audit assignment by interviewing laboratory personnel, going through protocols, methods, descriptions and workflows in the laboratory (see Section 8. Report No9).

C. Training modules:

The Biorisk and Quality management module provided training on techniques for Biorisk assessment and mitigation, including WHO recommendations on laboratory Biorisk management. The module was dedicated to the international regulations for the transportation of dangerous goods and WHO certification was acquired on completion. A visit to the biosafety level-4 laboratory at the Swedish Agency for Public Health as part of this module illustrated all aspects of biosafety management learned during the module. Post module assignments contributed to consolidation of acquired knowledge.

Educational outcome: The EUPHEM fellow deepened her knowledge on biorisk management, and the requirements necessary to control risks associated with the handling, storage and disposal of biological agents and toxins in laboratories and facilities. She had the opportunity to conduct biorisk assessments in the laboratory during her projects and as simulation exercise. The fellow performed an internal audit as a simulation exercise highlighting challenges and importance of biorisk practices assurance and detection of place for improvement, and gained insight into how standards are maintained. She also practiced safe laboratory procedures, decontamination and experienced different personal protective equipment when working on practical parts of her projects.

5. Quality management

A. INSTAND eV External quality assurance (EQA) scheme, 2017 for Mycobacteria Detection, Identification and Antimicrobial susceptibility testing and Internal NRLM Laboratory Audit.

Supervisor: Dimitrios Papaventsis

The Greek National Reference Laboratory for Mycobacteria (NMRL_GR) in “Sotiria” Chest Diseases Hospital, Athens-Greece, is an accredited laboratory following international standards and ISO guidelines and with regards to External Quality Assessment (EQA) schemes in particular, the ISO standard EN ISO 15189:2012 standard, which specifies the requirements for quality and competence in medical laboratories. External Quality Assessment (EQA) is considered essential to ensure accurate diagnosis of TB and drug-resistant TB. The implementation through organising regular EQA rounds and identification of training needs is one of the key activities of both the European TB reference laboratory network (ERLTB-Net) and the NMRL_GR (in the context of EN ISO 15189:2012 accreditation). A single EQA round on TB laboratory diagnostic methods (except genotyping and Whole Genome Sequencing), co-ordinated by the German NRL for Mycobacteria, and the PHE, in collaboration with INSTAND e.V., was conducted in Year 4 of the ERLTB-Net. EQA results were analyzed and certificates were issued to the laboratories achieving at least an 80% score. Within the project, EQA for smear microscopy, primary culture, species identification, and molecular and phenotypic drug susceptibility testing (DST) provided in 2017 by the German National Reference Laboratory (NRL) for Mycobacteria in collaboration with INSTAND e.V., were demonstrated, NMRL_GR procedures

and results were discussed and a short-report was also produced. NMRL_GR demonstrated an excellent performance suggesting that the laboratory follows the good laboratory practice principles and adheres to existing international standards. In all modules, performance was above 80% and a certificate was issued. During the project, the fellow got acquainted with standardized ISO protocols for quality assurance accreditation and certification of National Reference Centres and WHO-Collaborating Centres, and in particular with the EN ISO 15189:2012 standard. She obtained an overview of the quality management system in use in NMRL_GR, following the current norms and regulations. The rational and the approach of external quality, accreditation, assessment and audit were discussed, and the fellow participated in the analysing, evaluating and reporting of the results steps of the ECDC/ERLTB-Net 2017 EQA Scheme. Finally, the fellow provided recommendations for improvement and she prepared the EQA report (see 8. Reports No1).

B. Quality management audit/Internal Audit at the National Meningitis Reference Laboratory

Supervisors: Konstantinos Kesanopoulos, Georgina Tzanakaki

Quality management/Internal audit at the National Meningitis Reference Laboratory was performed following a post-module homework assignment, after the biorisk and quality management module at ECDC, Sweden, in 2018. The fellow had the opportunity to become familiarized with a laboratory quality management evaluation using an evaluation tool provided by the Head of EUPHEM. The fellow conducted the audit in the National Meningitis Reference Laboratory, which is a laboratory accredited according to ISO:15189. The quality manager responded to all the questions regarding the accommodation and environmental conditions, the quality management policy, the internal controls in use, the participation of the laboratory to an External Quality Assessment program, several critical steps during the pre-, analytical and post-analytical process, and procedures in place for quality improvement. In addition, a thorough evaluation of the existing documentation in the laboratory was conducted. The quality assurance system of the laboratory was evaluated as efficient and satisfactory, up to 98%. The audit inspected process management, quality control indicators, and documentation. The referral laboratory completed their technical documentation records and kept records of nonconformities. The EUPHEM fellow completed the audit assignment by interviewing laboratory personnel, going through protocols, methods, descriptions and workflows in the laboratory (see 8. Reports No9).

C. Training modules:

In the Biorisk and Quality management module the fellows were familiarized with all aspects of laboratory quality management, including EQA and accreditation procedures.

Educational outcome:
The EUPHEM fellow became acquainted, throughout her various projects, with the quality management in different laboratories, learned about accreditation processes and required laboratory standards. As a simulation exercise τηε φελλος analyzed the results and wrote a technical report, performed an internal audit highlighting challenges and importance of good practices assurance and detection of targets to be developed, and gained insight into how standards are maintained.

6. Teaching and pedagogy

A. Problem based learning exercise (3nd week of the IC in Spetses). Presentation of the PBL assignment in groups by the EUPHEM fellows, titled "Carbapenem resistance in Enterobacteriaceae; Resistance mechanisms of CRE Enterobacteriaceae".

During the introductory course in Spetses, Greece, the Head of EUPHEM, presented a lecture on the Problem-based learning method to the EUPHEM fellows and subsequently, she gave us the assignment to present a topic implementing the particular method. The fellows were divided in groups and presented the topic which was also divided into subjects. The presentation took place and the audience were the Head of EUPHEM, the coordinators and the fellows. PBL is a teaching method in which learners are introduced to a subject through the exposure to problem/s, which was/were presented to them (Scenario). The next steps were: the clarification of the facts of the case, the definition of what the problem/s is/are, the brainstorming with ideas based on prior knowledge, the identification of what they do not know (learning issues, new problems), the identification of what they need to learn (learning objectives) and the specification of an action plan to work on the problem/s. The aim of this teaching activity was to introduce the fellows to the Problem based-learning method, presenting another, more "learning-by-doing" approach to the problem or a topic and simultaneously, introduce them to the carbapenem resistant Enterobacteriaceae and their resistance mechanisms. The exercise took place in two stages: stage 1-brain storming

and stage 2-final presentations and discussion, which were held in separate sessions and days. During the second stage, fruitful discussions took place after each presentation and the fellows realized that, with all this actively gained knowledge, they were finally in position to discuss and find the solution to the problem.

B. Preparation and delivery of lectures at the School for disinfection professionals of the Department of Microbiology / Greek National School of Public Health, on behalf of the Greek Ministry of Health.

The EUPHEM fellow is an instructor at the School for disinfection professionals of the Department of Microbiology / Greek National School of Public Health, on behalf of the Greek Ministry of Health, since 2011.

1) Preparation and delivery of a 1-hour lecture on "The potable water disinfection"
2) Preparation and delivery of a 1-hour lecture on "The swimming pool water disinfection"
3) Preparation and delivery of a 1-hour lecture on "*Legionella*".

C. Lecture and practical on *Legionella* bacteria and Legionnaires` Disease, in the context of the Master Science Programme in Public Health at the National School of Public Health in Athens/ Public health Laboratory module

The EUPHEM fellow is the Head of the Southern Greece Legionella Reference Laboratory and member of the European Legionnaires' Disease Surveillance Network (ELDSNet), which belongs to ECDC. As an expert on this field, the fellow is preparing and delivering lectures and supervise practical sessions each year for the MSc students of the National School of Public Health on Athens.

1) Preparation and delivery of a 1-hour lecture on "*Legionella* and Legionnaires" Disease (LD)". The training included the testing of environmental and clinical specimens for *Legionella* spp. and molecular typing of *Legionella* spp. isolates. Summarizing, the topics were: Legionella bacteria, morphology, species identification, modes of transmission, natural reservoirs, LD (diagnosis, transmission, epidemiology, and treatment), environmental and clinical samples (detection, identification, typing of *Legionella* spp.), epidemiological investigations, sampling instructions, corrective actions.

2) Practical session of 1 ½ hours on samples receipt, data entry, handling, transport, guidelines and ISO methodology introduction of environmental and clinical samples, pre-treatment, treatment, results evaluation and final report.

D. Facilitation of a case-study to MSc (PH) students at National School of Public Health (NSPH)

The European Society for Clinical Virology (ESCV) organized the 21st ESCV Annual Meeting in Athens. A pre-conference workshop on "Update on West Nile virus infection" was organised by the ESCV, the Hellenic Centre for Disease Control & Prevention in collaboration with the Hellenic National School of Public Health. The workshop took place on Saturday 22nd of September 2018 from 10am until 5pm at the Hellenic National School of Public Health in Athens and consisted of an introductory part and the West Nile outbreak case study. The duration of the case study was 3.5 hours and it was facilitated by EPIET- EUPHEM supervisors: Angeliki Lambrou, Kassiani Mellou, Kyriaki Tryfinopoulou, current fellows: Elisavet Mouratidou, Anastasia Flountzi and EPIET/EUPHEM alumni: Heli Harvala and Maria Tseroni. The 27 participants were divided in three groups of 8-10 people and each group had two facilitators. The overall goal of this case study was to illustrate the steps of a cross-sectional study to estimate prevalence. The aim was at the end of this case study, participants to be able to: outline the main steps used for the design of a cross-sectional epidemiological study, explain the principles of sampling, select a sampling approach suitable for the study objectives, calculate sample size, calculate sampling weights, estimate prevalence, interpret the results of a cross-sectional survey.

E. Translation in Greek and facilitation of a case-study: "HIV surveillance in Spain" to MSc (PH) students at National School of Public Health (NSPH)

The National School of Public Health offers postgraduate education and training to a wide variety of graduates through the following postgraduate programs (PG): PG in Health Services Management, PG in Public Health, PG in Applied Public Health.

The HIV surveillance in Spain case study was translated in Greek and presented by the fellow, following the structure and content of the same case study which was presented in Spetses island in Greece, on September 2017, during the introductory course of the EPIET and EUPHEM training programs of the ECDC. The duration of the case study was 3.5 hours and it was facilitated by the EPIET- EUPHEM Cohort 2017 fellows: Dr Anastasia Flountzi and Miss

Elisavet Mouratidou. The overall goal of this case study was to illustrate the characteristics of different surveillance systems, their implications and the difference between incidence and prevalence. The aim was at the end of this case study, participants to be able to describe the characteristics of a surveillance system and explain the implications of these, differentiate the difference between incidence and prevalence in disease surveillance, and assess how they are used to inform public health action, interpret surveillance information, propose public health recommendations on the basis of surveillance information, and critically evaluate the comparison of reported data from across Europe. The case study was delivered twice in presence of the scientific supervisor and head of the HIV Reference Laboratory at the NSPH, Dr Marika Kotsianopoulou, who was supervising:

1. During the Master's Program in Public Health of the NSPH, in the context of the Public Health Laboratory module (5 participants)
2. During the Master's Program in Public Health of NSPH , in the context of the "Sexually Transmitted Diseases" class (8 participants)

The above mentioned case-study was translated in Greek and delivered by the fellow, and was incorporated in the educational material provided to the MSc (PH) students in NSPH (core infectious diseases).

Educational outcome: The EUPHEM fellow learned and gained experience on planning and delivering lectures, including defining learning objectives, preparing lectures material, exercises and delivering/facilitating lectures and case studies to multidisciplinary audiences.

7. Public health microbiology management

A. Hellenic laboratory network Assessment on TB diagnostics implementation and recommendations (roles, placement and algorithms).

Supervisor: Dimitrios Papaventsis

TB incidence continues to decline across the European Union (EU) and European Economic Area (EEA). However, trends show that a strengthening of efforts is needed if the WHO End TB vision is to be realized by EU/EEA member states. To work towards TB elimination in this context due to the specific TB epidemiology in low-incidence countries, programs typically include interventions directed to vulnerable and high-risk groups alongside wider health system efforts to implement new diagnostic technologies, improve treatment and prevent resistance development. The END TB Strategy suggests that developing plans for laboratory strengthening leads to the introduction of indicators that measure the system's capacity to detect TB accurately and rapidly using new diagnostics (WHO-recommended rapid diagnostics, or WRDs), to provide universal DST, and to ensure the quality of testing. The GLI, a network of international partners dedicated to accelerating and expanding access to quality assured TB laboratory services, serves as a collaborative platform for the development and uptake of practical guidance and tools for building and sustaining high-quality TB diagnostic networks. GLI guidelines, recommended policies and strategies, have not been introduced in the Hellenic TB laboratory network yet, while a National Tuberculosis Programme (NTP) is still lacking. This project is providing the opportunity, through evidence, to identify the gaps and make recommendations on TB diagnostic services and on public health services management. A review of the available guidelines, policies and strategies, published data and reports with a description of the diagnostic techniques and technologies performed, as well as Quality Assurance and Biosafety Indicators, took place. The GLI Excel tool was implemented in order to calculate country specific targets for laboratory capacity and a comparison of the calculated requirements, also took place, along with a gap analysis register. Through the project, recommendations were made on public health management, upon which the adoption of guidelines and specific policies proposed, are based. This project could form the basis and a model for potential real-life future projects in order to develop a strong and efficient TB laboratory network at the national level in Greece. During this project, the EUPHEM fellow was familiarized with available guidelines, policies and global strategies for adopting TB diagnostics at the national level and contributing to health system strengthening. In order to determine appropriate placement of TB diagnostics to meet the country's need, she was acquainted with the laboratory network gap analysis methodology based on the latest World Health Organization (WHO) Europe/European Centre for Disease Prevention and Control (ECDC) joint TB surveillance Report and the obtained data from the Greek TB diagnostic network assessment, performed by another EUPHEM fellow, Dr Kyriaki Tryfinopoulou in 2016. The fellow was in a position to ascertain the TB cases underreporting at the local and national level and the lack of an NTP for tuberculosis disease in Greece. She was also able to make recommendations on the potential role of new diagnostics implementation and placement within the TB laboratory network, as well as of possible algorithms, considering mapping, infrastructure, algorithms, personnel, safety and current and future workload. Finally, she was engaged in the evaluation of the results, the production of the final report (see 8. Reports No3) and prepared a rapid communication manuscript, as a first author for a peer-reviewed scientific journal (see 8. Communication/will follow No3).

B. Public Health microbiology management components as part of regular projects

Public Health microbiology management was an integral component of all projects and activities during the fellowship. This included laboratory management, ethical and integrity considerations, team working, research collaboration, time management, and working in several multidisciplinary teams with microbiologists, biologists, physicians, veterinarians, epidemiologists, laboratory technicians, entomologists and epidemiologists. The fellow's communication output in terms of manuscripts, reports and presentations is listed below. The fellow interacted with different supervisors during her projects, while the changing of working environments among the Consortium departments, in the context of the Greek EUPHEM training site, gave the fellow insight to different leading strategies. Also, during the presentation on the "WGS in Greece" at ECDC (see 8. Other presentations No1), was very educational and challenging. She had the opportunity to encounter, some really tough questions from the ECDC higher authorities and defended Greece's WGS laboratory capacity.

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C. Training modules

The Management, Leadership and Communication in Public Health module, focused on principles, roles and responsibilities in public health management, topics like rational and emotional understanding of what Management, Leadership and Communication is within the Public Health environment, management skills of participants at different and distinct levels in order to effectively support their own personal development, understanding of what is required to motivate and manage individuals and teams successfully by using clear structures and tools, combine techniques to manage different situations, identify and prevent/control threats to the health of the public caused micro-organisms, construct evidence for polices and strategies that support improvement of the population's health, time management, how to apply different management styles, team building and team work, tasks delegation, provision of structured feedback and strategies for stress management.

Educational outcome: The EUPHEM fellow was familiarized with available guidelines, policies and global strategies for adopting TB diagnostics at the national level and contributing to health system strengthening. In order to determine appropriate placement of TB diagnostics to meet the country's need, she was acquainted with the laboratory network gap analysis methodology based on the latest World Health Organization (WHO) Europe/ European Centre for Disease Prevention and Control (ECDC) joint TB surveillance Report and the obtained data from the Greek TB diagnostic network assessment (2016). Also, she gained experience in working in a multidisciplinary public health team, exercised communication skills with different audiences, higher authorities, public and media through simulation exercises. She understood the need of team management and close collaborations in planning, scheduling and organizing projects, realized the importance of laboratory database management ensuring security and integrity and strategies for stress management. The fellow understood the role and responsibilities to be an inspiring leader and an effective manager within the public health environment.

8. Communication

Publications accepted/published

1. Flountzi A, Georgakopoulou T, Balasegaram S, Kesanopoulos K, Xirogianni A, Papandreou A, Tzanakaki G; Members of the Hellenic network for Invasive meningococcal disease.Epidemiology of invasive meningococcal disease in Greece, 2006-2016. Eur J Clin Microbiol Infect Dis. 2019 Aug 15. doi: 10.1007/s10096-019-03668-y. [Epub ahead of print] Review. PMID: 31418100

Publications in preparation/will follow

1. Elina Horefti, Anastasia Flountzi, Andreas F. Mentis et al. Molecular investigation of the 2017-2018 measles outbreak in Greece. Manuscript for a peer-reviewed scientific journal in preparation (will follow).
2. Stavroula Beleri, Anastasia Flountzi, Nikolaos Tegos, Eleni Patsoula. Entomological surveillance in regional units of the East Macedonia-Thrace region in Greece and detection of West Nile Virus in mosquito pools collected during 2017-2018. Manuscript for a peer-reviewed scientific journal in preparation (will follow).
3. Anastasia Flountzi, Dimitrios Papaventsis et al. Hellenic laboratory network Assessment on TB diagnostics implementation and recommendations (roles, placement and algorithms) (Short communication manuscript for publication at the European Journal of Public Health, first draft sent to local supervisor).

Reports

1. Report of the external quality assurance (EQA) scheme 2017 for Mycobacteria Detection, Identification and Antimicrobial susceptibility testing.

2. 2018 Procedural Biorisk Management Report, Microbiology Laboratory & National Reference Laboratory for Mycobacteria (NRLM_GR).
3. Hellenic TB laboratory network Assessment on new diagnostics implementation and recommendations (roles, placement and algorithms).
4. Summary of influenza activity in Southern Greece during the 2018-2019 winter period (weeks 40/2018 - 05/2019).
5. Outbreak investigation report on a cluster of gastroenteritis cases during a school excursion to Athens from Larissa-Thessaly in Greece, in December 2018.
6. Evaluation report on the case study: West Nile virus outbreak in Greece, 2010.
7. Evaluation report on the: HIV surveillance in Spain, 2012, (No1).
8. Evaluation report on the: HIV surveillance in Spain, 2012, (No2).
9. EUPHEM-Quality report (BQM, ECDC, 2018)

Conference presentations

1. Anastasia Flountzi, Theano Georgakopoulou, Sooria Balasegaram, Konstantinos Kesanopoulos, Athanasia Xirogianni, Anastasia Papandreou, Pantelis Mavraganis, Georgina Tzanakaki and the Greek Meningitis study group. Epidemiology of Invasive Meningococcal Disease in Greece, 2006-2016. European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE), Saint Julian's, Malta, November 2018, (poster presentation, moderated session B-track 16.3).

2. Anastasia Flountzi, Panagiota Giakkoupi, Kyriaki Tryfinopoulou, Olga Pappa, Alikiviadis Vatopoulos, and the the Carbapenemases study group. Investigation of *Klebsiella pneumoniae* clinical isolates since 2015 for the putative presence of the plasmid-mediated *mcr*-1 gene for colistin resistance. 29th European Congress of Clinical Microbiology & Infectious Diseases (ECCMID), Amsterdam, Netherlands, April 2019, (poster presentation, P1405).

3. Anastasia Flountzi, Nikolaos Tegos, Stavroula Beleri , Eleni Patsoula. Detection of West Nile Virus (WNV) in mosquito pools collected during 2017-2018 from the East Macedonia-Thrace region in Greece. European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE), Stockholm, Sweden, November 2019, poster presentation (Abstract ID 455).

4. Athanasios Kossyvakis, Anastasia Flountzi, Maria Euagelidou, Vasiliki Pogka, Antonios Kalliaropoulos, Ioannis Karagiannis, Emmanouil Antalis, Theodoros Lytras, Dionyssios N. Sgouras, Sotirios Tsiodras, Andreas F. Mentis. HA sequence-derived phylogenetic and genetic characterization of A(H3N2) influenza viruses circulating during 2013-2019 winter seasons in Southern Greece. Clinical Virology Days 2019, with international participation, Athens, Greece, oral presentation (ID OP10).

Other presentations

1. Anastasia Flountzi. WGS in Greece. Oral presentation to ECDC Director, Chief Microbiologist and Chief Scientist during the MLCPHM, ECDC, Stockholm, February 2018.
2. Anastasia Flountzi. Whole Genome Sequencing Method (WGS) in *Legionella pneumophila* sg. 1 isolates. 3 minutes presentation of a topic of our choice, as a communication exercise during the IC in Spetses.

Certifications of achievement:
1. Certificate of International Transport of Infectious Substances, World Health Organization, 05-09/02/2018
2. Basic Security in The Field II, United Nations Department of Safety and Security, 03/05/2018
3. Advanced Security in The Field, United Nations Department of Safety and Security, 07/05/2018
4. The Global Outbreak Alert and Response Network and Working with GOARN in the Field, 09/05/2018

9. EPIET/EUPHEM modules attended

1. EPIET/EUPHEM introductory course, Anargýrios Korgialénios School of Spetses, Spetses, Greece [three weeks, 25.09–13.10.2017]

2. Outbreak investigation module, Robert Koch Institute, Berlin, Germany [5 days, 04–08.12.2017]
3. Biorisk and quality management module, European Centre for Disease Prevention and Control, Stockholm, Sweden [5 days, 05–09.02.2018]
4. Management, Leadership and Communication in Public Health module, European Centre for Disease Prevention and Control, Stockholm, Sweden [5 days,12–16.02.2018]
6. Multivariable analysis module, Medical University of Cyprus - Ministry of Health Cyprus, Nicosia, Cyprus, [5 days, 16–20.04.2018].
7. Rapid assessment module, National School of Public Health, Athens, Greece [6 days, 14–19.05.2018]
8. Project review module, Instituto de Higiene e Medicina Tropical, Lisbon, Portugal [5 days, 27–31.08.2018]
9. Project review module, Institut postgraduálního vzdělávání ve zdravotnictví (IPVZ), Prague, Czech Republic, [5 days, 26–30.08.2019] (upcoming module).

10. Other training

1. EUCIC Local Module, organized by the European Committee on Infection Control (EUCIC) of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the Microbiology Department of the Medical School of the National and Kapodistrian University of Athens, Greece. The topic: "The role of the clinical laboratory in preventing nosocomial infections due to MDR Gram-negative pathogens: a theoretical and practical approach". It included also 3 practical sessions. 20-22 May 2019.

2. Introduction to ISO 15189: Quality in the PH Laboratory- Measles & Rubella National Reference Laboratory at the Pasteur Institute of Athens. Sessions were delivered and discussion took place, with regards to the ISO 15189, by the local supervisor. Sessions included the Different Analysis Quality Control and Accreditation of Clinical Laboratories.

3. Three-months internship: a theoretical and practical training regarding all microbiological methods and techniques (conventional and molecular ones), which are being performed at the Hellenic National Reference Laboratory for Mycobacteria/Chest Disease Hospital "Sotiria". The training took place during the three ongoing TB projects at the Hellenic National Reference Laboratory for Mycobacteria/Chest Disease Hospital "Sotiria".

4. 9th National Conference in Clinical Microbiology and Infectious Diseases organized by the Hellenic Society for Microbiology, in Athens, Greece. Attendance of the Conference and in particular Seminars in "Syndromic Diagnosis of Infectious Diseases" and "Antibiogram-Lab Interpretation and Applications in patient therapy".

5. United Nations Department of Safety and Security (UNDSS) online training courses, on Basic Security in the Field II and Advanced Security in the Field, May 2018.

6. Global Outbreak Alert and Response Network (GOARN) online training courses, on The Global Outbreak Alert and Response Network and Working with GOARN in the Field, May 2018.

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. Nancy came into the programme with extensive expertise in *Legionella.* This portfolio includes laboratory and epidemiological projects covering bacterial, parasitic and viral pathogens across a variety of disease programmes, such as vector-borne diseases, food and waterborne diseases, respiratory tract infections, vaccine preventable disease and antimicrobial resistance, but also shows her teaching on her previous expertise. All projects here described were in line with the 'learning by doing' and 'on-the-job' training service approach of the EUPHEM programme and followed the core competency domains described professionals in mid-career and above. Outbreak, surveillance and laboratory activities ranged from a localised food-borne outbreak and a national outbreak of measles to the analysis of national databases. All contributed to the understanding of important public health issues. 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 combining microbiological and epidemiological surveillance in the meningococcal analysis to the gap analysis of the TB diagnostic network for Greece using WHO and ECDC tools. The projects have been nicely selected to cover not only important public health topics such as entomological surveillance for the West Nile virus, national influenza surveillance and screening of Carbapenem-

resistant *K. pneumoniae* clinical isolates for the plasmid-mediated mcr-1 gene for colistin resistance, giving Nancy the opportunity to gain an outstanding training and increased resilience which we hope help her success in her future career. Those activities were complimented by nine training modules providing theoretical knowledge. Projects had a clear educational outcome, with results communicated in submissions to scientific journals and at conferences. The coordinator team concludes that the fellow has succeeded in performing all her tasks to a very high standard and with a professional attitude. It has been a pleasure working with Nancy and we wish her the very best in her career.

Supervisor's conclusions

Dr Anastasia (Nancy) Flountzi was the third MS EUPHEM fellow trained among the Greek EUPHEM Consortium. Those two years of training turned out to be very successful for the fellow as she was involved in a variety of Public Health activities as well as an added value for the country as the fellow through the training modules/projects contributed in very important Public Health issues. Namely, she was involved in the recent measles outbreak investigation by joining the reference laboratory team at Hellenic Pasteur Institute for the identification of possible routes of introduction and transmission of measles virus in Greece as well as in the seasonal influenza laboratory surveillance. Regarding to food-borne diseases, the fellow was actively involved in the investigation of a cluster of gastroenteritis cases during a school excursion in close collaboration with the epidemiologists from the Greek CDC. Furthermore, she analyzed the epidemiological and microbiological data of Invasive Meningococcal Disease (IMD) in Greece during 2006-2016 in order to describe the epidemiology of IMD in the country. In the field of health-care associated infections, a representative sample of Carbapenem-resistant *K. pneumoniae* clinical isolates was screened for the putative presence of the plasmid-mediated mcr-1 gene for colistin resistance. In addition, in the field of vector-borne diseases, she contributed to the entomological surveillance for the West Nile virus by investigating the presence of WNV in mosquito pools collected for a two year period (2017 and 2018) from a specific prefecture at which WNV human cases were recorded during the year 2018. Moreover, the fellow was involved in the assessment of the Hellenic TB laboratory network on TB diagnostics implementation by conducting a gap analysis and she helped to formulate the recommendations on TB diagnostic services and their management. On teaching and pedagogy, the fellow has had the chance of implementing the methodology taught during the EPIET/EUPHEM Introductory Course through case studies by translating and facilitating one case study to the MSc Public Health students.
In conclusion, during the two year fellowship, Nancy developed both personally and professionally and gained new skills through her involvement in a variety of public health activities both in microbiology and epidemiology. The Consortium and the supervision team wishes her every success for the future.

Personal conclusions of fellow

The EUPHEM Fellowship is a very demanding, challenging and advanced training experience, a very well organised educational programme, as it is a once in a lifetime opportunity to have so many experts from all around Europe to teach and share their valuable knowledge and experience. The EUPHEM programme was for me a unique opportunity to work on diverse projects across various laboratories, many of which were unfamiliar to me from my working experience at clinical settings and departments covering the entire field of public health microbiology, in a continuous interaction with epidemiologists. The fellowship significantly improved the personal capacities giving at the EUPHEM fellows the opportunity to become expert not only among microbiology, but also to open their view in a multidisciplinary, dynamic and international setting. I strongly consider this programme as a milestone of my career and feel blessed for all the wonderful people I have met and helped me broaden my perspectives in Public Health. I strongly believe that the structure of the programme, with all the modules and the projects provided by my training site, along with the "learning by doing" approach and multitasking everyday reality serves the objectives of EUPHEM in the most efficient way. The teaching approach by EUPHEM facilitators and project supervisors during the modules, case studies and projects allowed me to learn by experience, gain new knowledge and expertise, opening my views on public health microbiology and epidemiology. Moreover, the feedback approach was fundamental to identify any weaknesses and strengths. In addition, the interaction with epidemiologists (facilitators, EPIET-fellows and local supervisors) during the modules, through case studies and simulation exercises, as well as during various projects was effective in building bridges between epidemiology and laboratory colleagues. Because of this close collaboration, the added value in public health was shown in the most practical way. Local supervisors provided me with all the guidance, opportunity and support needed to complete my fellowship within the two years. The fellowship has undoubtedly broadened my perspectives on public health microbiology and instilled confidence in my competencies for the years to come. I am proud to be part of the growing public health microbiology community and I will work on maintaining and strengthening my personal network between European epidemiologists and public health microbiologists. I hope to have the opportunity, in the future, to be involved in international projects and settings and further improve my skills and competencies.

Acknowledgements of fellow

The fellowship to me was a great adventure that for two years drove me towards new knowledge, skills, people, cities and great memories. No adventure will be possible without sharing of new experiences with someone who supports and shares your goals. Therefore, there are a great number of people I had the honor of meeting during the EUPHEM adventure that I really would like to thank.
My thanks go to all coordinators, supervisors, facilitators and administrators who hosted the introductory course and continued to guide us during the two-year fellowship. First and foremost, Prof Dr Aftab Jasir as the Head of EUPHEM, who provided me great support and encouragement, a high quality of scientific advice through her expertise and of course her rigorous but motherly attitude! I will always be grateful for her mentorship and involvement in all different aspects of my fellowship, her constructive feedback on all project proposals, reports, manuscripts and availability for any urgent issue. I would like to especially express my gratitude to my front-line Coordinator, Dr Sooria Balasegaram, for her constant support, encouragement and her strong commitment to the fellowship. She is a great teacher, a really wise and noble person, available in providing her scientific knowledge and expertise with great pleasure. I am grateful for receiving her constructive feedback, support and encouragement in stressful situations. I would like to especially express my gratitude and thank my supervision team, Prof Georgina Tzanakaki, Prof Alkiviadis Vatopoulos and Dr Kiki Tryfinopoulou, for their continuous support and guidance. Prof Georgina Tzanakaki, whose comments, guided me towards a higher level of search and scientific investigation on the field of Public Health Microbiology and her very efficient coordination of the whole EUPHEM consortium in Greece. Prof Alkiviadis Vatopoulos, for trusting me with this wonderful EUPHEM journey and who provided me with his inspiring vision and his mentoring in Public Health principles and culture, my friend and supervisor Dr Kiki Tryfinopoulou, for her constant encouragement, support, availability and precious scientific advice. Thank you for believing in me! I am really grateful! I would like to acknowledge all local project supervisors, namely, Dr A. Mentis, Dr T. Kossyvakis , Dr E. Horefti, Dr P. Giakkoupi, Dr K. Kesanopoulos, Dr A. Xirogianni, Dr E. Patsoula , Dr S. Beleri , Dr E. Vassalou, Dr S. Karabela, Dr D. Papaventsis, Dr M. Kotsianopoulou and Dr N. Tegos who worked with me with great enthusiasm and professional attitude, gave me the possibility to be part of their interesting work and shared with me their expertise. Also, I would like to mention the excellent cooperation and support from my EPIET supervisor Dr K. Mellou during the outbreak investigation projects, Dr A Lambrou for her cooperation and last but not least, Dr. Theano Georgakopoulou for her guidance, great support, and the overall supervision, as Head of Department of Epidemiology, Surveillance and Intervention at the Hellenic CDC.
I also would like to thank the staff of all the laboratories, which have helped me in the rotations. I wish to thank all members of the EUPHEM forum, the ECDC training section, the fellowship programme office for their excellent administrative assistance, the EUPHEM and EPIET coordination team and all the people who have contributed with their hard work in delivering modules and trainings during these last two years.
I am thankful to all my EUPHEM and EPIET co-fellows, with who we created a network for life beyond comparison, for their friendship, support, amazing team-spirit and hilarious company and especially Elisavet Mouratidou, my EPIET co-fellow and friend, for her support and encouragement in the difficult times.
Last but not least, my thoughts and gratitude go to my family, my husband, my parents and my amazing, wonderful daughter, for their love, understanding and endurance in my absence throughout my EUPHEM fellowship.