EUPHEM

EUPHEM REPORT

Summary of work activities

Zoltán Kis

European Public Health Microbiology Training Programme (EUPHEM), 2013 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 2015

This report summarises the work activities undertaken by Zoltán Kis, cohort 2013 of the European Public Health Microbiology Training Programme (EUPHEM) at the National Center for Epidemiology (NCE), Budapest, Hungary. Zoltán Kis is a pharmacist from Hungary. Before and during the MS-track fellow he worked at the NCE as head of the Biosafety Laboratory and as head of the Department for Respiratory Viruses. He is responsible for the diagnosis of highly pathogenic viruses and for the laboratory background of the influenza surveillance.

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.

Material and 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 guide[1].

1. Epidemiological investigations

1.1. Outbreak investigations

A. Salmonella *Enteritidis outbreak among daycare centre employees in Budapest*

Supervisors: Ágnes Csohán, Ágnes Fehér, Katalin Krisztalovics, Judit Pászti

On 8 October 2014 the Public Health Office of Budapest was informed of gastrointestinal illness amongst employees from five day-care centres in Budapest. The fellow participated in the study design and conducted the epidemiological investigation to assess the extent of the outbreak, he also identified the mode and the vehicle of transmission, and initiated the appropriate recommendations and control measures. The outbreak investigation covered epidemiological, microbiological and environmental investigations. A case was defined as a person who worked in any of the day-care centres and developed any of the following symptoms between 6 and 8 October 2014: diarrhoea, vomiting, fever, abdominal cramps. All interviewed symptomatic people were asked to provide a stool sample. On 9 October, the National Food Chain Safety Office (NFCSO) inspected the day-care centres and the food leftovers. In the cohort study, the overall and food-specific attack rates (AR) and risk ratios (RR) were calculated using univariate analyses. Overall, 73.6% (64/87) of exposed persons participated in the study and 39 cases were identified (AR = 61.1%). Those who ate Vargabéles cake were 7.1 times more likely to be ill (33/42) than those who did not (2/18) (RR = 7.1; 95% CI: 1.9–26.3). Thirty-four stool specimens were collected and 97% were found to be culture-positive for *Salmonella* Enteritidis (phage type 8, PT8). The result of the environmental investigation showed that the Vargabéles cake was positive for *Salmonella* Enteritidis PT8. The investigation also revealed that the baking time and storage of the Vargabéles cake was inadequate. Thorough cleaning of the kitchen was recommended along with firm recommendations to educate the kitchen staff to adhere to the food safety regulations. The fellow participated in the ten steps of the outbreak investigation but also had a clear role in the phage typing tests. The fellow as a microbiologist had a notable role in the interpretation of the microbiological results and in broadening the microbiological knowledge of the epidemiologist.

[1] European Centre for Disease Prevention and Control. European public health training programme. Stockholm: ECDC; 2013. Available from: http://ecdc.europa.eu/en/publications/Publications/microbiology-public-health-training-programme.pdf

B. Gastrointestinal outbreak in a village in Tolna county, May 2014

Supervisors: Ágnes Csohán, Katalin Krisztalovics

On 23 May 2014 a paediatric general practitioner (GP) in a rural town informed the local municipal public health authority that several children had gastrointestinal symptoms in a village nursery school. The same day an investigation was launched to assess the extent of the outbreak, identify the mode and the vehicle of transmission and initiate appropriate control measures. The epidemiological investigation found more cases among students in the primary school retrospectively. The case definition was: anyone living in the village and having diarrhoea and at least one of either vomiting or nausea. Up to 13 June, 37 patients with gastrointestinal symptoms were identified and among them six were laboratory-confirmed cases of *Salmonella* Typhimurium (phage type 1). The fellow was involved with establishing the case definition, case finding (interviewing cases and controls, visiting GPs), descriptive epidemiology, and setting up recommendations. The contact tracing was unsuccessful, despite conducting personal interviews using a trawling questionnaire, because of recall bias (three weeks apart) so no clear epidemiological link between cases was found. The kitchen of the primary school investigated by the National Food Chain Safety Office (NFCSO) was negative for *Salmonella* Typhimurium. The stool samples of the employees of the school were also negative for *Salmonella* Typhimurium. During the interviewing the role of a butcher's shop and confectionery was raised and the NFCSO started to investigate. As a control measure the enteric surveillance was strengthened. This included the GP having to report any gastrointestinal cases immediately, the head of the primary and nursery schools having to report any absentees amongst the students and kept the food for 3 days. However, despite the negative environmental results, thorough cleaning of the kitchen and the nursery school was recommended.

C. Modules

The EPIET/EUPHEM introductory course familiarised participants with the methods and logistical aspects of outbreak investigations. The module 'Computer tools in outbreak investigations' in Berlin provided essential data management skills (entering, validating and cleaning data), dataset management and how to perform case–control studies (descriptive and cohort studies, including stratified analyses).

Educational outcome: Application of microbiological and epidemiological knowledge in outbreak situations. Participation in a multidisciplinary outbreak team and involvement in outbreak investigations (case definitions, case-finding, data collection, data analysis, on-site visits, laboratory typing methods, communication), writing of reports and scientific publication, implementation of prevention measures.

1.2. Surveillance

A. Description and evaluation of the new STI surveillance system in Hungary

Supervisor: Mária Dudás

In Hungary, sexually transmitted infections (STIs) have been mandatorily reported by dermatovenerology dispensaries (DVD) as aggregated data since 1952. This reporting system does not permit the detailed and extended data required for submission to ECDC. Thus Hungary did not fulfil the obligation of international data reporting and therefore the introduction of a case-based surveillance system was required. In February 2014 a new surveillance system was launched; the aggregated data reporting was changed to mandatory case-based data reporting (Decree No 1/2014 (I. 16.) by the Ministry of Human Capacities on 'Reporting procedure of communicable diseases'). The project aimed to evaluate the current STI surveillance system during the period February 2014 – December 2014. The objective was to describe the current surveillance system and compare it with the previous system; to evaluate data completeness and timeliness of the system and to determine the improved efficiency in reporting. However, the numbers of data providers were extended, which may have resulted in an increase of the number of reported STIs, as not only the DVD but all healthcare providers and laboratories now send their reports. The reporting format was changed from a monthly paper-based collection to a continuous electronic web-based format. In the new system more epidemiological data, such as high-risk behavior, could be collected which assists the authorities in the determination of preventive measures. The data also contributed towards an overall increase in cost-effectiveness of the prevention measures and decrease of the disease burden, and informed the development and improvement of specific guidelines. The completeness of the new system is 100% for demographic data, and 86.8–96.1% regarding sexual behaviour. The completeness of 'working as sex-worker' or 'contact with sex-worker' was lower (67.3–78.2%) except for acute urogenital chlamydiosis where this information is not on the data collection form. In the new STI surveillance system only 'date of diagnosis' and 'date of reporting' are collected. More than 50% of the healthcare providers reported the STI cases within one week (56.8–62.9%). The most important limitng factor is that mainly the DVDs report the STI cases and we have a limited amount of data from other healthcare providers, such as gynaecologists and urologists. Moreover, only a few laboratories have reported laboratory results yet.

In conclusion, the new surveillance system can serve the national and international requirements better in terms of epidemiological data. However, completeness should be improved to have a better picture on the burden of STIs in Hungary. To improve the effectiveness of the new surveillance system, we recommend that NCE should increase the awareness and the willingness of the healthcare providers and laboratories to report the STI cases through more effective communication campaigns. The fellow worked together with epidemiologists in this project to combine laboratory, epidemiological and clinical data in order to have a complete picture of the system.

B. Modules

The EPIET/EUPHEM introductory course familiarised participants with the basic knowledge of development, evaluation and analysis of surveillance systems. Building on this course, the module on 'multivariable analysis' demonstrated the principles, application and interpretation of multivariable analysis and its role in field epidemiology. The 'vaccinology' module taught specific approaches to the surveillance of vaccine-preventable diseases (determination of vaccine coverage, efficacy and effectiveness). The 'rapid health assessment in complex emergencies and mass gatherings' module covered an introduction to the strategies for surveillance in complex emergencies, including nutritional, morbidity and mortality surveys.

Educational outcome: Participation in disease-specific networks at the national level; understanding analysis of laboratory-based surveillance systems at hospital, country and European level; understanding of the need to integrate microbiological and epidemiological data in disease surveillance; design data collection forms, evaluation of surveillance systems, identification of common goals; understanding ethical principles on data protection and confidentiality regarding information in databases; writing a study protocol and scientific paper.

2. Applied public health microbiology research

A. Molecular epidemiology and genetic characterisation of plasmid-mediated AmpC-type beta-lactamase-producing *Klebsiella pneumoniae* isolated from Hungarian hospitals, 2009–2013

Supervisors: Ivelina Damjanova, Ákos Tóth, Tamás Tirczka

The first plasmid-mediated AmpC-type beta-lactamase producing *Klebsiella pneumoniae* (pAmpC-KP) isolate in Hungary was detected in December 2009 and during the next four years comprised 25% of all third-generation cephalosporin-resistant *K. pneumoniae* isolates that were submitted to the National Reference Laboratory at the National Center for Epidemiology on a mandatory basis. The aim of the study was to investigate the molecular epidemiology and routes of transmission of pAmpC-KP isolated from Hungarian hospitals. Therefore, a retrospective study was conducted on pAmpC-KP isolates from 312 clinical samples collected from November 2009 to December 2013 by healthcare units across the entire country. The objectives were a) to outline spatio-temporal distribution and susceptibility to antimicrobials of pAmpC-KP strains/clones in Hungarian hospitals over five years; and b) to reveal relationships between these isolates using molecular typing techniques. Phenotypic investigations were performed by the ESBL combined disc test and ESBL&AmpC ID test. PCR and sequencing was used to investigate the presence of different beta-lactamase genes. For molecular typing pulsed field gel electrophoresis (PFGE) and multilocus sequence typing (MLST) was performed. All isolates showed resistance to third-generation cephalosporins, aminoglycosides and fluoroquinolones and 77% were non-susceptible to at least one carbapenem. All isolates were positive for blaDHA-1, whilst 90% were positive for both blaDHA-1 and blaCTX-M-15. PFGE revealed twelve pulsotypes; two of these the KP053 (262/312, including the first isolates from 2009) and KP070 (38/312) belonged to sequence type ST11 and comprised 96% of isolates. The blaDHA-1 and blaCTX-M-15 producing KP053 clone affected 234 patients and spread to 55 healthcare centres across Hungary over the four years. This was the first time that the DHA-1 and CTX-M-15 co-producing *K. pneumoniae* epidemic clone in Hungary had been detected. The rapid countrywide spread of this multidrug-resistant 'high-risk' clone seriously endangers Hungarian healthcare facilities and warrants urgent strengthening of infection control practices and prudent use of carbapenems. It is very important to inform other EU Member States about this situation in order to prevent the possible cross-border transmission of this carbapenem non-susceptible DHA-1 and CTX-M-15 co-producing *K. pneumoniae* clone anticipating possible European outbreaks.

B. Crimean–Congo haemorrhagic fever virus seroprevalence amongst Hungarian blood donors

Supervisor: István Jankovics

The Crimean-Congo haemorrhagic fever (CCHF) virus is considered to be a major emerging disease threat spreading to and within the European Union following an expanding distribution of its main vector, ticks of the genus *Hyalomma*. Due to climatic, environmental and economic changes the tick has appeared in Hungary and there is serological evidence of CCHF virus infection in the European hare (*Lepus europaeus*) in the country. However, no seroprevalence data are available with regard to previous exposure of humans to CCHF virus infection in Hungary. The main aims of the study were a) to establish an in-house whole virus-based immunofluorescent assay (IFA) for serological diagnosis of CCHF virus in Hungary; and b) to determine the seroprevalence of CCHF virus infection using a retrospective panel of blood donor sera collected in 2008 from 14 of 20 regions in Hungary. A detailed protocol was developed for producing IFA slides determining optimal virus concentration, gathering day, infective/non-infective cell ratio and cross-reactivity for tick-borne encephalitis virus, Hantaan virus, cytomegalovirus, Epstein-Barr virus, *Leptospira* species and *Coxiella burnetii*. To determine the infective titre of the virus CCHF virus fluorescent forming unit (FFU) method was set up. The optimal parameters such us carboxymetil-cellulose concentration (1% in RPMI-1640), formaldehyde concentration (4%) and day of fixation (four days after infection) was determined. Six (four male, two female) of the 1 066 sera (selected according to age, gender and geographical region) were positive as very low titres (1:10) indicating an overall 0.6% prevalence. All six blood donors lived in six different counties. The results of this EUPHEM project will help to establish a more precise and extended serosurveillance using recently collected sera and targeting the risk population in the most affected counties. This and the future results from the repeated serosurvey will be used to elaborate CCHF modus operandi for healthcare providers because the CCHF virus can cause severe nosocomial infections and outbreaks. Moreover, the results will be used for dissemination of public information materials targeting at-risk populations. Together with accurate diagnostics these interventions constitute an important part of the management of CCHF. Additionally, during the project the fellow was responsible for design of the study, implementation of the experiments, reviewing workflow, and writing internal reports.

C. Modules

While the EPIET/EUPHEM introductory course focused on the development and presentation of study protocols, the module 'Initial management in public health microbiology' focused on laboratory aspects, time management and team collaboration during the execution of the studies and projects.

Educational outcome: Preparation of study protocols; methods of typing, interpretation of typing results; data analysis; development and assessment of laboratory methods (virology, bacteriology), evaluation of diagnostic assay, understanding the limitation of various diagnostic methods, bioinformatics and phylogenetic techniques, team coordination, writing scientific articles; delivering a scientific presentation at a conference.

3. Applied public health microbiology and laboratory investigations

A. Serotype distribution and antibiotic profiles of invasive *Streptococcus pneumoniae* isolates from Hungary, 2012–2013

Supervisors: Tamás Tirczka, Ákos Tóth, Damjanova Ivelina, Ágnes Csohán

During the project, the aims were to monitor country-wide circulating serotypes and antimicrobial susceptibility patterns of invasive *Streptococcus pneumoniae* isolates across all age groups during 2012–2013 (PCV13 period) in comparison to previous years (2008–2010, PCV7 period). During the PCV7 period (282 isolates, 34 different serotypes) the most frequent serotypes were serotypes 3 (26.3%), 14 (6.8%) and 19A (6.0%). In the PCV13 period (403 submitted isolates, 43 different serotypes) the three predominating serotypes were 3 (26.4%), 19A (6.5%), 8 and 11A (4.7%). Amongst all age groups the proportion of cases of invasive pneumococcal disease caused by both PCV serotypes decreased (PCV7: 31.2% to 11.6%; PCV13: 77.8% to 56.3%). However, the frequencies of the PCV13-specific serotypes have not changed significantly. During the PCV13 period the number of isolates resistant to penicillin, ampicillin, erythromycin, clindamycin, meropenem and cefotaxime were 2.8%, 1.0%, 18.9%, 13.7%, 0.3% and 0.5%, respectively. The multidrug-resistance phenotype was not detected. The data have demonstrated the potential effect of PCVs in Hungary with a decrease of the serotypes included in PCV13 and partial serotype replacement. Maintaining laboratory-based surveillance, monitoring changing trends in serotype distribution and antimicrobial resistance are essential to measure the impact of a national vaccine programme.

B. Genotyping of *Toxoplasma gondii* detected in human toxoplasmosis in Hungary

Supervisors: Erika Orosz, István Kucsera

Toxoplasmosis is a potentially fatal disease of the developing human foetus and immunocompromised (e.g., AIDS and transplant) patients and can cause severe ocular disease in otherwise healthy individuals. The vast majority of *T. gondii* genotypes fall into one of only three distinct lineages. The aims were to determine the genotype of *T. gondii* diagnosed at the Department for Parasitology, National Center for Epidemiology, and to investigate the possible link between the genotype and the clinical findings. Twelve toxoplasmosis cases between 2005 and 2014 were included in the study. Different clinical materials were obtained from the patients (cerebrospinal fluid, EDTA-blood, sera/plasma, aqueous humour from eyes and amniotic fluid). Only eight of the 12 specimens contained sufficient parasite DNA suitable for restriction length fragment polymorphism of nested PCR product of SAG2 gene. The 5′ and 3′ end of the SAG2 gene were used to determine the genotypes. The PCR-RFLP analysis revealed that all toxoplasma detected directly from the clinical specimen belonged to genotype-II regardless of the clinical symptoms and immunological status. However, more locus should be used to analyse the genotype profile of the *T gondii* in Hungary to have insight into the population genetic structure of the parasite and the clinical manifestation of patients. Moreover, more human and animal samples are needed to confirm our results in order to get a better picture about the toxoplasma situation in Hungary. This is the first report about *T. gondii* genotypes in human toxoplasmosis in Hungary. The study contributes to a better understanding of the epidemiology and the association between the parasite genotype and human toxoplasmosis, especially in cases of congenital toxoplasmosis where treatment might be improved.

Educational outcome: Apply concepts of bacteriology, parasitology and immunology to public health disciplines, identification of the use and limitation of diagnostic methods and interpretation of the results at individual (patient diagnosis) and community (outbreak investigation, surveillance) levels; understand the importance of serosurveillance of *S. pneumoniae* isolates to assess the serotypes circulating and antibiotic resistance in the population in order to provide evidence to policy makers for decisions on immunisation policy; delivering a scientific presentation at a conference, writing a scientific paper.

4. Biorisk management

A. Biorisk management module, ECDC, Sweden

The 'Biorisk and quality management' module provided training on techniques for biorisk and biosafety risk assessment and mitigation, including WHO recommendations on biosafety management in laboratories. As part of the module the BSL4 laboratory at the Smittskyddsinstitutet, Stockholm, was visited. One day focused on international regulations for the transportation of dangerous goods, as set up by the International Civil Aviation Organization and certification was acquired on completion.

B. Laboratory support to the Ebola outbreak in Guinea, 2014

Laboratories and their provision of rapid and accurate diagnostics are a crucial and integral component of the Ebola outbreak response. The fellow, as a full member of the European Mobile Laboratory (EMLab) second team, participated in the establishment of molecular field diagnostics of the Ebola virus. Moreover, malaria, Lassa virus, dengue virus and *Vibrio cholera* diagnostics were also established. As an additional task the fellow participated in the validation of the experimental Ebola virus hand-held test, validation of new lots of Ebola molecular testing kits, testing for inhibition amongst specimens and preparation and organisation of safe BSL4 specimen transportation (with skills gained from the EUPHEM biorisk and quality management module) to send back to Europe for further characterisation. The fellow also participated in contact tracing in rural areas. He learned how to process specimens containing highly infectious materials under very basic conditions; how to manage unforeseen situations (electricity shortages during laboratory procedures, handling broken blood collection tubes), how to work in a limited space, how to use the limited resources in the most effective way.

C. Crimean-Congo haemorrhagic fever training

The fellow received five-day training at the World Health Organization Collaborating Centre for Haemorrhagic Fever Viruses, Bernhard-Nocht-Institute for Tropical Medicine, Hamburg, Germany. The course included an overview of local and international regulations, with theoretical and practical training. During the training CCHF molecular and serological diagnostics were practised.

Educational outcome: Understand processes associated with BSL3/BSL4 laboratories; experience different personal protective equipment; understand the principles and practices of biorisk management; biorisk assessment and biorisk mitigation, writing publications, communication to higher authorities, media and the public.

5. Quality management

A. External quality assurance study for diphtheria identification and characterisation

Supervisors: Tamás Tirczka, Ivelina Damjanova, Judit Pászti

As part of the European Diphtheria Surveillance Network and as the ECDC contact point for diphtheria at the National Center for Epidemiology, the Department of Bacteriology was asked to participate in the diphtheria EQA (DIPEQA) to determine its current laboratory capabilities for diagnostics and the methods used for corynebacteria identification and characterisation. The fellow was responsible for: 1) reception of the EQA simulated specimen panel and cultivation; 2) examination of primary plate cultures and subcultures for any potentially toxigenic *Corynebacterium* spp. that may be present; 3) isolation of corynebacteria; 4) identification and characterisation of *Corynebacterium* spp. using phenotypic l tests (APICoryne, Micronaur-RPO) and MALDI-TOF; 5) using PCR for detection of the diphtheria toxin gene; 6) using the Elek immunoprecipitation test to detect toxin production; 7) reporting results (isolated *Corynebacterium* spp., biotype, toxigenicity status, time taken to achieve the final results, and problems encountered; 8) evaluation of results and recommendations for future improvements.

B. Participation in an internal and external audit for the Virology Division and the Bacteriology Division

Supervisor: Mária Takács, Judit Pászti

Laboratories at the National Center for Epidemiology are currently accredited under the EN ISO 15189 by the National Accreditation Body. The fellow participated in the internal and external audits of protocols and procedures used in the laboratories. The fellow also participated in the laboratory meeting to evaluate and provide feedback based on the results of the audits.

C. Modules

The module 'Biorisk and quality management' in Stockholm, Sweden provided an overview of quality management concepts in diagnostic laboratories in accordance with the ISO 15189 standard. The topics discussed were: factors influencing quality in laboratories, internal and external quality control, norms and accreditation, assessments and audits, documentation and record keeping, sample management, stock purchase and inventory management, management of equipment and temperature-controlled devices, process improvement, customer service and international health regulations.

Educational outcome: Apply concept of bacteriology and immunology, understanding specialised methodologies related to diphtheria diagnostics; understand the principles and practices of EQA in accordance with national and international directives, efficacy of quality assurance systems; prepare and analyse an internal quality assessment; evaluation of results and making recommendation.

6. Teaching and pedagogy

A. Biorisk and quality management module

Lecture on 'Introduction into laboratory quality management system' for EUPHEM fellows and invited supervisors as part of the biorisk and quality management module, Stockholm, Sweden. In the same module the fellow facilitated the lectures on 'International shipment of dangerous substances'.

B. Lectures on 'Biorisk management in microbiology laboratories' and 'Microbiological techniques'

Two 90-minute lectures were delivered to labour protection inspectors on five occasions concerning the biosafety in microbiology laboratories, specimen transportation and specimen collection. Lecture on microbiology techniques: conventional (cultivation, isolation), serological (IFA, ELISA, (haem)agglutination, etc., and molecular (PCR, real-time PCR, RFLP, sequencing). Preparing material (slides) and revision of the questions in final examination tests.

C. Teaching on Filovirus, Ebola virus and Ebola outbreak

The fellow participated in teaching (theoretical and practical) on the Ebola virus and Ebola outbreak, and Ebola modus operandi for people with different backgrounds (epidemiologists, microbiologists, disinfection specialists, infectologists). He delivered a two-hour lecture 'Filoviridae' for medical students at Szeged University on filoviruses (in English and Hungarian). Also a two-hour lecture at ELTE University on 'Role of the field laboratories in humanitarian crisis – focusing Ebola outbreak in Africa', And a one-hour lecture on 'Newest biological agent causing occupational health diseases' in an accredited training session of the Occupational Health Office of the Chief Medical Officer.

D. Outbreak investigation training course at the National Center for Epidemiology

Elaboration of the three-day programme for the training course. Lecture on 'Identification of bacterial pathogens in outbreak situations', facilitating case studies of outbreak investigations.

E. Practical training about biosafety

During the two years the fellow performed theoretical and practical training about biosafety and biosecurity, using PPE, packaging infectious substances according IATA rules, disinfection procedures, biosafety level 3-4 regulations (entry, exit, emergency situations, don-doff PPE, etc.) for infection disease specialists, biologists, disinfection specialists, epidemiologists and the special anti-terrorist unit.

Educational outcome: Planning and organisation of lectures and training courses both theoretical and practical; guiding case studies, defining learning objectives and teaching laboratory and microbiology topics to people with different backgrounds.

7. Public health microbiology management

A. 'Initial management in public health microbiology', ECDC, Stockholm, Sweden

This one-week module focused on understanding roles and responsibilities in public health management. Topics included the identification of different management styles, team roles and team evolution, the delegation of tasks and the provision of structured feedback.

B. Ebola modus operandi

The fellow was involved in the working group responsible for setting up a Ebola modus operandi and for modifying the Ebola viral disease part of the First Annex of Decree No 18/1998 (VI.3) by the Ministry of Welfare on 'Epidemiological measurements necessary for the prevention of communicable diseases and outbreaks'. It involved participation in national and international teleconferences, meetings with representatives of the ministry, the office of chief medical officer, specialised hospitals, the police, the policy administration services of public health, and the national ambulance service. The fellow was fully responsible for the microbiological diagnosis of Ebola virus disease in Hungary, managing the BSL4 laboratory and its specialised group. As an expert the fellow gave more than fifty interviews (TV, radio, press) to communicate the Ebola situation and preparedness to Hungarian citizens.

C. 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 building and coordination, research collaboration, time management, management of cultural differences in international contexts and working in a multidisciplinary team with people from different backgrounds (microbiologists, physicians, laboratory technicians, epidemiologists, statisticians, government officials including high-level authorities, public health officers, and logisticians.

Educational outcome: Obtaining experience with working in a multidisciplinary public health team; understanding team management; understanding roles and formal responsibilities, designing, scheduling and organising research projects, communication with the media.

8. Communication

A. Publications

1. Pályi B, Bognár Zs, Kis Z. Az Ebola vírus – kell-e félnünk tőle? IME, 2014, 13(8):23-25
2. Pályi B, Kis Z. Az Ebola-Járvány. Természet Világa Természettudományi közlöny, 2014, 146(3): 98-101.
3. Pályi B, Kis Z. Challenge of the Ebola diagnostic in the field. Bulletin of National Center for Epidemiology, 2014 September.
4. Kis Z. The Ebola outbreak from a field lab. EAN News, Special Issue: Ebola. p6
5. Kis Z, Tirczka T, Damjanova I, Csohán Á, Krisztalovics K, Molnár Zs, Efstratiou, A. Serotype distribution and antibiotic profiles of invasive *Streptococcus pneumoniae* isolates from Hungary, 2012 – 2013. Submitted to Epidemiology and Infection.
6. Ruibal P, Oestereich L, Lüdtke A, Becker B, Wozniak D, Cabeza-Cabrerizo M, Bore JA et al. Unique human immune signature of Ebola virus disease in Guinea. Submitted to Nature.
7. Kis Z, Tóth Á, Janvári L, Pászti J, Damjanova I. Molecular epidemiology of plasmid-mediated AmpC-type β-lactamase-producing *Klebsiella pneumoniae* isolated from Hungarian hospitals, 2009-2013 – Epidemiological stage 5 spread of DHA-1 and CTX-M-15 co-producing *K. pneumoniae* ST11 high-risk clone. (In final preparation).
8. Pályi B, Farkas Á, Szalai B, Kiszely N, Takács M, Kis Z. Crimean-Congo hemorrhagic fever virus seroprevalence amongst Hungarian blood donors. (In preparation).
9. Orosz E, Kis Z, Danka J, Kucsera I. Genotyping of *Toxoplasma gondii* detected in human toxoplasmosis in Hungary. (In preparation).

B. Reports

1. Kis Z, Fehér Á, Bodzay Samrák Zs, Damjanova I, Csohán Á. Salmonella Enteritidis outbreak among day care center employees in Budapest, National Center for Epidemiology.
2. Kis Z, Damjanovai I, Tirczka T. External Quality Assurance study for diphtheria identification and characterization, National Center for Epidemiology.
3. Kis Z, Strecker T, Günther S. Laboratory support to the Ebola outbreak in Guinea, 2014.

C. Conference presentations

1. Pályi B, Kis Z. Az Ebola-vírus és a 2014-es nyugat-afrikai Ebola járvány. Hungarian Society of Zoonoses, September 2014, Budapest, Hungary (invited speaker).
2. Pályi B, Szalai B, Farkas Á, Zoltán Kis. Facing Ebola - Lessons learnt from the field. Hungarian Society for Microbiology. October 2014, Keszthely, Hungary (invited main speaker).
3. Kis Z, Berta B, Csohán Á, Damjanova I, Molnár Zs, Krisztalovics K, Tirczka T. Serotype distribution and antibiotic profiles of invasive *Streptococcus pneumoniae* in Hungary, 2012 – 2013. ESCAIDE 2014, November 2014, Stockholm, Sweden.
4. Pályi B, Kis Z. Field laboratory experience based on the Ebola outbreak in West-Africa. 3rd Croatian Epidemiology Congress, May, 2015, Šibenik, Croatia. (invited speaker).
5. Pályi B, Kis Z. Ebola járvány. Helyszíni tapasztalatok. XI. Young Hygienists Forum, Hungarian Hygienists Association, Young Hygienists Section. May 2015, Eger, Hungary (invited speaker).

D. Submitted abstracts

1. Kis Z, Tóth Á, Tirczka T, Jánvári L, Pászti J, Damjanova I. Molecular epidemiology of plasmid-mediated AmpC beta-lactamase producing *Klebsiella pneumoniae* in Hungary, 2009-2013. ESCAIDE 2015, Stockholm, Sweden.
2. Kis Z, Fehér Á, Bodzay Samrák Zs, Damjanova I, Csohán Á. *Salmonella* Enteritidis outbreak among day care center employees in Budapest. ESCAIDE 2015, Stockholm, Sweden.

E. Other presentations

1. Kis Z, Pályi B, Farkas Á, Szalai B, Herpay M, Mag T, Szabó Zs, Tóth Sz, Visontai I. Diagnostic capability of the highly pathogenic microorganism at the Hungarian National Biosafety Laboratory at National Center for Epidemiology – results of international proficiency tests. Directorate of National Institute for Quality- and Organizational Development in Healthcare and Medicines (GYEMSZI), Human Resources Ministry (EMMI). November 2013, Budapest, Hungary.
2. Kis Z, Pályi B, Farkas Á, Szalai B, Herpay M, Mag T, Szabó Zs, Tóth Sz, Visontai I. Why is the Hungarian Biosafety Laboratory important? 'The National Center for Epidemiology is 15 years old' Ceremony. National Center for Epidemiology, November 2013, Budapest, Hungary.
3. Kis Z. Ebola outbreak in Guinea. Epidemiology day, National Center for Epidemiology, May 2014, Budapest, Hungary.
4. Kis Z. Lesson learnt about the Ebola outbreak in Guinea. EMLab in the field. National Center for Epidemiology, May 2014, Budapest, Hungary.
5. Kis Z. The Hungarian suit-based National Biosafety Laboratory Level-4 at National Center for Epidemiology. Meeting of the Visegrad Group. May 2014, Szilvásvárad, Hungary.
6. Kis Z. 'Veni. Vidi.' An outbreak of Ebola virus disease in Guinea. ECDC, August 2014, Stockholm, Sweden.
7. Kis Z. Pályi B. Ebola outbreak. Institute of Medical Microbiology, Semmelweis University, October 2014, Budapest, Hungary.
8. Kis Z. Press conference in the Biosafety Laboratory: 'Ebola preparedness in Hungary'.
9. Kis Z, Palyi B. All day press conference: Ebola outbreak - field experience from the witnesses.
10. Pályi B, Farkas Á, Szalai B, Kis Z. Ebola outbreak and the RG3-4 pathogen diagnostic in Hungary. National Food Chain Safety Office. November 2014, Szekszárd, Hungary.
11. Pályi B, Kis Z. Tapasztalatok a helyszínről. Ebola járvány Nyugat-Afrikában. Semmelweis University. November 2014, Budapest, Hungary.
12. Pályi B, Kis Z. Jelentés az Ebola járvány helyszínről. Matrica Museum – Ebola day. February 2015, Szászhalombatta, Hungary.
13. Kis Z. Az Ebola járvány szemtanúja voltam. National Vaccinology Training Course. April 2015, Debrecen, Hungary.
14. Kis Z. Hungary's preparedness for public health threats caused by highly pathogenic agents. Meeting of the Visegrad Group. April, 2015, Bratislava (Pozsony), Slovakia.
15. Kis Z, Pályi B. Molekuláris módszerek alkalmazása a virológiában. Scientific day at Hungarian Army Hospital, May 2015, Budapest, Hungary.
16. Pályi B, Kis Z. Az Ebola járvány. Scientific day, Hungarian Army Medical Center, May 2015, Budapest, Hungary.

9. International missions

Supervisors: Thomas Strecker, Stephan Günther, Aftab Jasir

A. Laboratory support to the Ebola outbreak in Guinea, 2014

The fellow is a member of European Union Mobile Laboratory Consortium (EMLab) which is an EU-funded project with the overall objective of setting up a collaborative network involving European and African institutions able to operate in common mobile laboratory units during outbreak situations. When the World Health Organization launched an international response the EMLab offered to deploy the laboratory in Guinea. The EMLab has been providing a mobile laboratory team for the diagnosis of Ebola virus disease from 24 March 2014. The fellow was a member of the second team in Gueckedou, Guinea from 16 April to 8 May 2014. His activities were diverse and are described in Section 4.

Educational outcome: Application of concepts of virology, practice of appropriate measures for safe transport of infectious materials, appropriate use of PPE and decontamination strategies, using communication techniques to communicate with people from different backgrounds.

10. EPIET/EUPHEM modules attended

- EPIET/EUPHEM introductory course, Spetses, Greece (three weeks)
- Computer tools in outbreak investigations, Robert Koch Institute, Berlin, Germany (one week)
- Biorisk and quality management, ECDC, Stockholm, Sweden (one week)
- Initial management in public health microbiology, ECDC, Stockholm, Sweden (one week)
- Vaccinology, Public Health England, London, United Kingdom (one week)
- Rapid health assessment in complex emergency situations and mass gatherings, Athens, Greece (one week)
- Project review, ECDC, Stockholm, Sweden (one week)
- ECDC stay – meeting with ECDC experts, ECDC, Stockholm, Sweden (four days)
- Project review, Lisbon, Portugal (one week).

11. Other courses

Theoretical and practical one week biosafety level 4 (BSL4) training at Bernhard-Nocht-Institute for Tropical Medicine, Department of Virology.

Discussion

Coordinator's conclusions

Zoltán was the first EUPHEM fellow in Hungary in addition to being part of the first cohort of MS-track EUPHEM fellows.

During the two-year fellowship, the fellow, supervisors and training site have demonstrated the capability of addressing communicable disease threats of national, European and international concern in a structured joint approach between public health microbiology and epidemiology. It is often the combination of specialised diagnostics and epidemiology that produces credible evidence for decisions on interventions. This is particularly well illustrated by the examples of the outbreak investigation of *Salmonella* Enteritidis and the gastrointestinal outbreak in Tonya county in Hungary. In addition, this portfolio includes many examples of public health microbiology studies on topics that have relevance for public health in other EU Member States, such as genetic characterisation of plasmid-mediated AmpC-type beta-lactamase-producing *Klebsiella pneumoniae*, and an external quality assurance exercise for diphtheria identification and characterisation. In March 2015, the Ministry of Health in Guinea notified WHO about a rapidly evolving outbreak of Ebola virus disease; in April, Zoltán was the first fellow deployed with the European mobile lab to Guinea in order to contribute to setting up the mobile laboratory and detection of Ebola, Malaria and Lassa virus among the suspected cases. He also contributed with contact tracing and training activities during his deployment in Guinea.

The involvement of fellows and supervisors in such projects within the context of an EU-wide training programme offers valuable opportunities for sharing good practice, knowledge and experience.

Supervisor's conclusions (Ivelina Damjanova and Ágnes Csohán on behalf of the supervision team)

This was the first time the National Center for Epidemiology (NCE) participated in the EUPHEM programme and Dr. Zoltán Kis was our first fellow. He has been working at the NCE for years and leading the Hungarian Biosafety Laboratory and the Department of Respiratory Viruses. Accordingly he started the fellowship as highly qualified virologist who was very interested and curious about all aspects of microbiology and epidemiology. During the fellowship Zoltán gained high-level experience in bacteriology, parasitology and even more virology and in epidemiology as well. He really enjoyed all of his projects and was always full of constructive ideas. Zoltán is a sharp-witted and quick-minded person with excellent managerial capabilities but he is also very good team player. He is committed to public health microbiology as evidenced by his international mission – Zoltán was the first EUPHEM fellow involved in the field laboratory investigation of the Ebola outbreak in Guinea. The results of Zoltán 's projects had a significant impact on the improvement of public health microbiology in Hungary, e.g. elaboration of Ebola modus operandi, setting up of FFU method for CCHF, the first report on genotypes of *T. gondii* in human toxoplasmosis in Hungary, detection and characterisation of an international 'high-risk' multidrug-resistant *K. pneumoniae* epidemic clone, evaluation of STI surveillance systems, etc. On our own behalf and on behalf of our supervisor's team, we would like to thank Zoltán for his excellent work and we are grateful to the EUPHEM programme for the very well-organised high quality training in the field of public health microbiology.

Fellow's conclusions

The EUPHEM programme provided me with an excellent opportunity to work in several projects within different areas of public health microbiology and the field of communicable diseases. During the fellowship I was able to improve my knowledge and skills in virology, bacteriology and parasitology in the context of public health. Networking is one of the most important values of the programme which gave me a unique opportunity to be part of national and international networks and working groups and I met specialists and experts from different areas. The bridge created by EUPHEM qualified me to understand better and communicate more effectively with epidemiologists. During my projects and mission I could improve my communication and management skills which are important to fulfil one of the EUPHEM objectives, i.e. to foster future leaders in public health microbiology.

The structure of the training programme with all the projects and modules together with the 'learning-by-doing' philosophy serves the goals of EUPHEM well. Expanding the programme would contribute greatly to better European public health and to a better Europe.

Acknowledgements of fellow

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