Summary of work activities
Jessica Vanhomwegen, European Public Health Microbiology Training Programme (EUPHEM), second cohort

Background

Public health microbiology (PHM) 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. PHM laboratories play a central role in disease detection, disease 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. This includes the design of prevention strategies as well as treatment and infection control. A broad range of expertise is necessary to fulfil these requirements, for example in epidemiology and public health microbiology. PHM is required to provide access to experts with expertise/experience of 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 or assist in the development of microbiological guidelines, evaluate/develop new diagnostic tools, arbitrate on risks from microbes or their products, and provide pertinent information to policy makers related to the above issues from a microbiology 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'. Therefore, ECDC has initiated a two-year training programme (EUPHEM) which 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.

This report summarises the work activities undertaken by Jessica Vanhomwegen, a EUPHEM fellow based at the Institut Pasteur in Paris.

All 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 of the outcome of different activities conducted during the EUPHEM fellowship. Activities were comprised of specific projects and theoretical training modules (not summarised in this report). The specific projects included laboratory surveillance, risk assessments, outbreak investigations, quality management, research, summarising and communicating scientific evidence, and activities with a specific microbiological focus, such as biosafety or different laboratory techniques. The outcome included 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 specific projects and work activities can be summarised as follows:

Risk assessment of influenza virus exposure through aerosols and surfaces from an urban environment during a seasonal flu outbreak

The aim of this study was to assess the survival of influenza viruses in the urban environment in order to develop suitable control strategies to reduce the risk of infection. For this purpose, the presence of respiratory viruses, particularly human influenza viruses or respiratory syncytial virus, was determined in the air and on inert surfaces of subway trains at the peak of the H1N1 2009 pandemic in a major European capital city. This project included the design of a study protocol, field sampling, environmental data collection, molecular testing of samples, viral inoculation and data analysis. The results of this study were addressed to the European Commission as part of a final project report and communicated to the deputy director of the public transport operator in the city where the samples were taken.

Educational outcome: wrote a study protocol for a laboratory-based research project; identified the use and limitations of laboratory sampling methods; interpreted results from a public health point of view.

Multicenter evaluation of molecular and serological diagnostic tests for Crimean-Congo hemorrhagic fever

The aim was to conduct a multi-centre evaluation of Crimean-Congo hemorrhagic fever (CCHF) diagnostic tools in order to select the best-performing methods and give recommendations in the event of an outbreak. Published diagnostic tools for CCHF (quantitative reverse transcription-polymerase chain reaction, low-density DNA macroarray, enzyme-linked immunosorbent assay and indirect immunofluorescence slide) and were selected based on a systematic review of the literature and the experiences of the collaborators of the study. Selected diagnostic tools were tested in the facilities of five European reference laboratories on a panel of collected sera. Specific datasheets and questionnaires were designed to collect the test results and data on operational characteristics. The performances (sensitivity, specificity and reproducibility) of the diagnostic tools were estimated.

Educational outcome: wrote a study protocol for a multicentre study; critically appraised published data and information; identified the use and limitations of molecular and serological diagnostic methods and their interpretation in patient diagnosis; coordinated a multicenter study involving laboratory specialists and commercial companies.

Development and validation of a bead-based multiplex immunoassay for diagnostic and surveillance of viral hemorrhagic fevers and arboviruses

Control of viral hemorrhagic fevers (VHF) outbreaks depends crucially on the rapid detection and accurate identification of the agent to define and the implementation of timely and appropriate action. The aim was to develop a rapid tool for VHF outbreak investigations and seroprevalence studies, namely a fluorescent bead-based multiplex flow cytometric immunoassay for the detection of serum immunoglobulin M and G for seven hemorrhagic fever viruses in a single test. This project involved developing a technical protocol, validating the method technically (with reference antibodies) and clinically (with animal and human sera).

Educational outcome: developed a technical protocol; identified the use and limitations of multiplex serological methods and their interpretation in outbreak investigations; understood the requirements for technical and clinical validation of diagnostic methods.

Molecular epidemiology of tuberculosis among US- and foreign-born residents of Rhode Island

Molecular typing and epidemiological data from tuberculosis patients in Rhode Island were combined to describe transmission patterns and identify possible risk factors for recent tuberculosis transmission. Results of two independent genotyping techniques, spoligotyping and 12-loci mycobacterial interspersed repetitive unit typing, were combined to identify patient isolates sharing identical fingerprinting patterns. These isolates, described as clustered, were defined as resulting from recent transmission. Multivariable logistic regression was performed to identify independent demographic or clinical predictors of recent TB transmission. Our data suggested that many incident cases have arisen from reactivation or acquisition of TB infections outside of Rhode Island. Nevertheless, transmission occurred among the US- and foreign-born population, as well as between communities, suggesting the need to improve public health interventions in both populations. The results of this study were published and shared with the Rhode Island Department of Health in order to reorient control strategy.

Educational outcome: took part in a multidisciplinary team effort, combining microbiology and epidemiology; identified the use and limitations of genotyping methods; conducted a descriptive and analytical epidemiological study.

Design of a pan-virologic DNA resequencing microarray for the detection of emerging viral agents

The ability to simultaneously screen for a large panel of pathogens in clinical samples, especially viruses, represents a major development in the diagnosis of infectious diseases and in surveillance programmes for emerging pathogens. For this purpose, a high-density DNA resequencing microarray (PathogenID v3.0) was designed, with roughly 800 viral sequences from a wide range of viruses. One of objectives was to be able to detect and type common and potentially emerging human and animal *Caliciviridae* with a minimum of sequences tiled on the array. For this design, all available sequences of the capsid gene were retrieved by data-mining of genomic databases and aligned to identify conserved regions. From the alignments, a small number of clusters gathering sequences with <10% variation were determined. For each cluster, one consensus sequence was computed and used for tiling.

Educational outcome: collected data from genomic databases; understood principles of viral taxonomy and phylogeny; understoond emerging pathogen dynamics.

Evaluation of a broad-spectrum DNA resequencing microarray for the rapid recognition and characterisation of listeriosis and botulism outbreaks

The rapid and accurate identification and characterisation of pathogens is critical in the control of infectious disease. To this end, we analysed the capacity of a recently described high-density resequencing microarray (RMA) to identify known *Listeria* (sub-)species and *Clostridium botulinum* toxinotypes. The RMA, containing probes for the detection of up to 124 bacteria and 673 toxin or antibiotic resistance genes, was designed for multiple pathogen detection using database similarity searching. The approach was first assessed using purified DNA from a panel of *Listeria* and *Clostridium* reference strains. As this approach was successful for discrimination of *C. botulinum* toxinotypes, we proceeded to the clinical validation using uncharacterised *C. botulinum* strains isolated from contaminated food extracts collected during a botulism outbreak in France.

Educational outcome: identified the use and limitations of bacterial typing methods and their interpretation; understood the steps in the validation of a bacterial genotyping strategy.

Outbreak alert and response activities in the North and North East departments in Haiti (one-month WHO-GOARN mission)

The aim of the mission was to take part in cholera control activities, as part of the PAHO/WHO Haiti Alert Field Team covering the North and North East departments. Responsibilities included epidemiological investigations of cholera outbreaks, organisation/coordination of response, day-to-day epidemiological surveillance of cholera cases, writing of weekly epidemiological surveillance reports, organisation of stool sample collection/transport and laboratory testing, assessment of epidemiological, medical and local laboratory capacity for surveillance and response to cholera or other mandatory reportable diseases and monitoring of antimicrobial resistance of *Vibrio cholerae* strains. Experiences from the field and final recommendations were addressed to PAHO/WHO in a mission report and during the GOARN operational review meeting.

Educational outcome: understood the roles and responsibilities of local, national and international organisations involved in infectious disease control; coordinated the response by communicating effectively with persons from a multidisciplinary background, the authorities and the public; applied combined microbiological and epidemiological knowledge in order to analyse different situations; to distinguish the strengths and weaknesses of surveillance systems (syndromic and laboratory-based systems).

Tick survey of Crimean-Congo hemorrhagic fever virus for exposure risk assessment in France

During recent years, new foci of Crimean-Congo hemorrhagic fever (CCHF) have emerged in several Balkan countries, southwest Russia, and Turkey. Given the abundance of the tick vectors *Hyalomma* and *Ixodus*, the numerous animals that can serve as hosts, and the favourable climate and ecologic parameters in other southern European Mediterranean countries, CCHF is an example of a vector-borne disease that may emerge in this area. The objective of this project was to use molecular techniques (RT-PCR) to screen tick populations collected in France (Auvergne, Normandy and Ile de France) for the presence of CCHF viruses, and assess the potential public health threat. This work included the design of a tick survey, the selection and technical validation of methods for RNA extraction from ticks, and the selection of a molecular CCHF detection method.

Educational outcome: developed a protocol for a tick survey, understood transmission dynamics of vectorborne diseases and the importance of entomological surveillance.

Microbiological, environmental, and epidemiological investigations of a norovirus outbreak in a long-term care facility in Tarn, France

From the end of June through July 2011, a prolonged outbreak of acute gastro-entiritis affected the residents and employees of a 60-bed long-term care facility. An outbreak investigation was conducted using epidemiological and molecular diagnostic methods to identify the likely mode of transmission and risk factors for illness, and to evaluate environmental contamination. This investigation included testing of stool samples for norovirus by RT-PCR and sequencing, descriptive epidemiology, redaction of questionnaires, drafting of surface and water sampling protocols, and giving recommendations on appropriate decontamination strategies and products.

Educational outcome: applied combined microbiological and epidemiological knowledge in order to analyse the outbreak; designed safe sampling strategies; comprehended principles and practices associated with decontamination strategies.

Development of a course on epidemiological and microbiological aspects of outbreak investigations, Bangkok, Thailand

The aim was to develop a course on epidemiological and microbiological aspects of outbreak investigations for Thai field epidemiologists and laboratory specialists of the NIH in Bangkok, Thailand. A curriculum was proposed, based on personal practical experience with EUPHEM and the curriculum of similar modules. The project included the preparation of the module programme together with the Thai FETP coordinators (objectives, lecture topics, case study topic, order and timing of sessions, facilitators/lecturers, evaluation); preparation of three lectures ('Overview of diagnostic methods', 'Overview of typing methods' and 'Development and validation of diagnostic methods'); modification of an existing case study; facilitation of the case study (topic: 'Q fever') during the module and preparation of a questionnaire for the final examination.

Educational outcome: identified training needs for planning and organising courses; moderated case studies, gave lectures and used pedagogically appropriate teaching methods; understood important laboratory/microbiology concepts for epidemiologists; translated the laboratory approach to epidemiologists.

Promotion of the EUPHEM fellowship programme.

The objective was to promote the EUPHEM programme through presentations to different audiences. The activities consisted of the following: oral presentation 'EUPHEM training activities', ENIVD annual meeting, Stockholm, Sweden, 2010; poster presentation 'European Public Health Microbiology (EUPHEM) Training Programme: objectives and activities', Institut Pasteur departmental days, Paris, France; oral presentation 'EUPHEM training activities', ENIVD annual meeting, Antalya, Turkey, 2010.

Educational outcome: oral and written communication.

Publications

Vanhomwegen J, Kwara A, Martin M, Gillani FS, Fontanet A, Mutungi P, Crellin J, Obaro S, Gosciminski M, Carter EJ, Rastogi N. Impact of immigration on the molecular epidemiology of tuberculosis in Rhode Island. 2011. J Clin Microbiol. 2011. 49:834-44.

Vanhomwegen J, Berthet N, Guigon G, Mazuet C, Popoff MR, Caro V, Manuguerra JC. Application of high-density Resequencing Microarray for detection and characterisation of neurotoxin producing Clostridia. 2011. (In preparation)

Discussion

The objective of the EUPHEM training programme is to enable the fellows to carry out a broad range of activities related to the specific areas of public health microbiology: development and evaluation of methods for pathogen detection and characterisation, laboratory-based surveillance and risk assessments, project management and outbreak investigations. This multidisciplinary approach allows the fellow to comprehend the roles and responsibilities of all the public health specialists and organisations involved in infectious disease control. In particular, the close collaboration with epidemiologists in the context of EPIET training activities or specific missions and projects is extremely valuable and allows the fellow to acquire a unique perspective on the many aspects of public health work.

This report summarises the different activities and projects conducted by a EUPHEM fellow from cohort 2 based at the Institut Pasteur in Paris. All activities were in line with the learning-by-doing approach of the EUPHEM programme, and all projects had a clear educational outcome contributing to the development of a wide range of experience and expertise. The activities provided the fellow with a variety of skills required in the field of public health microbiology and strengthened her ability to work in a multidisciplinary team.

Conclusion

Public health microbiology is presently a recognised discipline only in few European countries. Public health microbiology, as defined by ECDC (national microbiology focal points), is a cross-cutting area that spans the fields of human, animal, food, water and environmental microbiology, with a focus on human health and disease. Public health microbiologists should be able to work effectively across disciplines, particularly with epidemiologists and professionals of clinical medicine. Strengthening the collaboration and networking within and between public health institutes in national and international levels is vital to respond to the future demands of public health. Bringing together specialists representing different disciplines in public health, such as epidemiologists and microbiologists, is one of the key issues in this networking effort. In particular, it seems there is a lack of microbiologists with a solid knowledge and understanding of public health needs, and who can combine these areas in a productive way. Furthermore, the structures of the healthcare systems in many European countries do not as yet recognise the discipline of public health microbiology, resulting in challenges to an effective collaboration between microbiology and related disciplines. The EUPHEM programme launched by ECDC aims to increase expertise in this cross-cutting discipline. Already during the first two years of the programme, the importance of fruitful collaboration between microbiologists and other public health professionals has been acknowledged, and the programme will continue to increase awareness and expertise in this area.

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