Summary of work activities

Katarzyna Schmidt
European Public Health Microbiology Training Programme (EUPHEM), 2021 cohort

Background

The ECDC Fellowship Programme is a two-year competency-based training with two paths: the field epidemiology path (EPIET) and the public health microbiology path (EUPHEM). After the two-year training, EPIET and EUPHEM graduates are considered experts in applying epidemiological or microbiological methods to provide evidence to guide public health interventions for communicable disease prevention and control.

Both curriculum paths provide training and practical experience using the 'learning by doing' approach at acknowledged training sites across European Union (EU) and European Economic Area (EEA) countries.

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.

This final report describes the output of the fellow and the competencies they acquired by working on various projects, activities, theoretical fellowship training modules, other modules or trainings and international assignments or exchanges during the fellowship.

Stockholm, October 2023

Pre-fellowship short biography

Katarzyna Schmidt obtained a MSc degree in Biotechnology at the Agricultural University, Poznan, Poland (2001–2006) and a PhD degree in Biomedical Science at the University of East Anglia, Norwich, United Kingdom (UK) (2013–2017). To expand her skills in a diagnostic field and clinical microbiology, she completed a postgraduate study in Medical Analytics at the University of Health Scientists, Bydgoszcz, Poland (2006–2008) and a Medical Microbiology specialisation at the Medical University, Poznan, Poland (2010–2015). She applied this acquired knowledge working as a biomedical scientist specialising in microbiology at clinical laboratories in Poland and the UK. She participated and lead a wide range of research projects involving method development and validation of commercial/in-house assays towards improving diagnostics of clinical samples, as well as rapid detection of pathogens and their antibiotic resistances. Her passion is to broaden her knowledge in public heath microbiology and epidemiology in order to learn how to prevent and control infectious diseases and protect public health.

Results

The objectives of these core competency domains were achieved partly through project and activity work and partly by participating in the training modules. Results are presented in accordance with the EUPHEM core competencies, as set out in the ECDC Fellowship Manual[1].

1. Epidemiological investigations

1.1 Outbreak investigations

Retrospective investigation of a nosocomial outbreak of hepatitis C virus infection in Germany, 2017–2018

Supervisors: Sandra Niendorf, Ruth Zimmermann, Claus-Thomas Bock, Sebastian Haller

Category: Healthcare-associated infections and antibiotic resistance

In October 2018, an outbreak from south-east Germany (Bavaria) was communicated to the Robert Koch Institute (RKI) with suspected hepatitis C virus (HCV) infection with nosocomial transmission route. The local health authorities suspected an anaesthetist as the probable infection route, with patients becoming infected through invasive procedure during surgery. From almost 1 300 contacted cases who were treated by the doctor, and to whom HCV testing was recommended, 58 met the probable case definition criteria (person who underwent a surgical procedure involving the index anaesthetist in the hospital between May 2016 and April 2018 and who had a positive HCV result in the first HCV antibody test). In 51 of these 58 probable cases, HCV genotype 3/3a was confirmed. Serum samples from confirmed cases (n = 44) were sent to the Gastroenteritis and Hepatitis Viruses, Enteroviruses (FG15) unit at RKI for Sanger sequencing and further phylogenetic tree investigation. Sequencing data were available for 39 of these 44 samples. Descriptive epidemiological and phylogenic analyses were performed, including an attempt at Bayesian evolutionary analyses to better understand the course of the outbreak. The results of this investigation determined that all examined samples belonged to HCV genotype 3a. A further in-depth phylogenetic analysis revealed close genetic relatedness with maximum 36 single-nucleotide polymorphisms (SNPs) between the samples, indicating a high probability of infection by the same source. The temporal signal did not provide further information on the infection time point and there was no correlation between the number of SNPs and testing or surgery dates. A standardised procedure for molecular clock analyses was recommended to assess evolution rate in HCV genotypes in order to provide additional evidence when time of infection of this source-case truly occurred.

Role: The fellow conducted data cleaning, communicated with federal health authorities to confirm cases and linked epidemiological data with genotypic data. Additionally, the fellow conducted the descriptive and phylogenetic analysis. In order to estimate and narrow down the possible infection time, the fellow assessed temporal signal and familiarised herself with molecular clock analysis using BEAUTi and BEAST software. The fellow wrote the final report, which will be used as a template to writing a manuscript.

Educational outcome

The fellow had an opportunity to be involved in several steps related to an outbreak investigation. Those included: defining probable and confirmed cases, generating and testing the hypothesis, as well as drawing conclusions and communicating findings with health authorities. Although it was a retrospective analysis, the fellow acquired epidemiological skills, such as how to perform descriptive analysis. Furthermore, the fellow gained skills in molecular analysis related to generating and interpreting a phylogenetic tree. Additionally, she familiarised herself with comprehensive molecular clock analysis.

[1] European Centre for Disease Prevention and Control. European public health training programme. Stockholm: ECDC; 2020. Available from: https://www.ecdc.europa.eu/en/publications-data/ecdc-fellowship-programme-manual-cohort-2021

1.2 Surveillance

A) Genomic surveillance of antibiotic resistance genes in patients with gastrointestinal infections in Sub-Saharan Africa (SSA), 2019–2021

Supervisors: Sara Tomczyk, Grit Schubert

Increasing antimicrobial resistance (AMR) poses a serious threat to human health. Sub-Saharan Africa (SSA) has been identified as a hotspot for AMR emergence, while surveillance data from this region are still scarce. We conducted a comprehensive human gut resistome study to characterise the antimicrobial resistance gene (ARG) composition among stool samples collected from patients that are part of the African Network for improved Diagnostics, Epidemiology and Management of Common Infectious Agents (ANDEMIA) surveillance network in SSA. Demographic data and stool samples (n = 116) from patients with acute gastrointestinal infections were collected from rural and urban hospital sites in Burkina Faso (BF) and Côte d'Ivoire (CIV). DNA extracts were used for high throughput sequencing via hybridisation capture, using 37 826 custom-designed, biotin-labeled probes targeting over 2 000 ARGs. Bioinformatic analyses were performed by a resistome pipeline (AmrPlusPlus). Statistical and epidemiological analyses were conducted with ResistoXplorer and R focusing on ARG compositional profiling, ARG diversity profiling and assessing high-risk ARGs. We identified 806 ARGs conferring resistance to 14 AR classes. The ARGs' compositions were assessed by country, hospital setting and sociodemographics. Genes conferring resistance to multiple drug classes were ubiquitous across the study population. Aminoglycoside and beta-lactames genes were found in higher abundance in CIV, while tetracycline determinants were highly prevalent across BF samples, the male population and the age group zero to one year old. Higher richness of ARGs within samples and differences between samples were seen in urban and rural sites in BF compared with CIV. ARGs' richness within the samples and dissimilarities of ARGs between the samples statistically differed between the countries and hospital settings, but not for age groups or gender. High-risk ARGs were frequently found in human gut resistomes. The study emphasised the need to monitor antimicrobial resistance and rational use of antibiotics in the selected countries, as well as further research.

Role: The fellow conducted laboratory work (generated data for sequencing) and comprehensive data analysis. This comprised bioinformatics analysis (supported by a bioinformatics team), as well as descriptive resistome investigation using R and the online tool ResistoXplorer. In terms of epidemiological investigation, the fellow performed the demographics analysis. Furthermore, the fellow wrote the draft of the study protocol, which was further extended to a final report. Additionally, the results of the study were submitted to the ECCMID conference held in Copenhagen in April 2023, and presented as a printed poster during resistance detection/prediction approaches session. The fellow prepared and delivered an oral presentation of the project results at the internal FG16 RKI seminar.

B) The impact of the COVID-19 pandemic on notifiable HIV infection case numbers in Germany: an analysis of surveillance data before and during the COVID-19 pandemic

Supervisors: Uwe Koppe

Timely diagnosis of HIV infection is crucial to prevent severe disease trajectories. The COVID-19 pandemic disrupted sexual health services, preventing people from accessing HIV testing. We analysed if certain groups were over- or underrepresented among individuals with new HIV diagnoses during the COVID-19 pandemic.
We compared HIV surveillance data during the COVID-19 pandemic (March 2020 to December 2021) with a corresponding pre-pandemic period (March 2018 to December 2019). Descriptive statistical and epidemiological analyses were conducted using a chi-squared test to assess changes in numbers of new HIV diagnoses between those periods by gender, age group, region, transmission route and late diagnosis. The overall number of new HIV diagnoses during the pandemic decreased by 24% (4 185 diagnoses) compared to the pre-pandemic period (5 521 diagnoses). This decline ranged from 6% to 38% in all federal states except one (Schleswig-Holstein), showing an increase of 13% (104 vs 120 reported cases). The proportion of male cases with new HIV diagnoses were comparable between periods (78.2% vs 78.4%; missing: 0.1%, p=0.882). Among all new HIV diagnoses, the distribution of age groups was similar, with only 0.1% to 1.7% differences between periods. During the pandemic, the proportion of people who inject drugs (PWID) increased from 6.7% to 8.5% (p=0.005), while the proportion of men having sex with men (MSM) (61.1% vs 61.3%) and heterosexuals (31.5% vs 29.5%) were comparable in both periods. The proportion of missing data regarding the probable route of transmission increased (20.9% vs 30.5%) during the pandemic. The proportion of late diagnoses increased from 15% to 18% (p<0.001; missing: pre-pandemic, 20.4% vs pandemic, 18.3%). There were not many obvious changes during the pandemic, except a reduction in the number of reported new HIV diagnoses and a decrease in data completeness for the probable route of transmission. Increased testing efforts, as well as monitoring the surveillance in order to identify individuals with late diagnosis, were recommended in order to reach people across all transmission groups and provide early diagnosis.

Role: The fellow conducted data cleaning and descriptive epidemiological and statistical analysis using R. Additionally, the fellow submitted an abstract to the ESCAIDE 2023 conference, which was accepted as an online poster. The outcome of the project was summarised in a report that will be used as a template for writing the manuscript.

C) The impact of the COVID-19 pandemic on notifiable syphilis infection case numbers in Germany: An analysis of surveillance data before and during the COVID-19 era

Supervisors: Klaus Jansen

Early diagnosis and treatment of syphilis is crucial to prevent the progression to the late latent stage. In recent years, in Germany and globally, the rate of syphilis infection has been growing. The COVID-19 pandemic disrupted an increasing trend in syphilis infection, leading to a decline in the number of reported syphilis cases in 2020 and 2021. We assessed the impact of the pandemic on syphilis notifications in order to identify changes during this period. We compared syphilis surveillance data during the COVID-19 pandemic (March 2020 to December 2021) and a corresponding pre-pandemic period (March 2018 to December 2019). Descriptive statistical analyses were conducted using a chi-squared test to determine variation in syphilis notification rates between defined periods by gender, age group, region, transmission route and clinical indicators (e.g. syphilis stage, co-infection, time between infection and diagnosis). Overall, the number of syphilis cases decreased by 9% during the pandemic (12 689 cases) compared to the pre-pandemic period (13 999 cases). This reduction ranged from 2% to 21% in all federal states, except Mecklenburg–Western Pomerania and Saxony, which showed increases of 21% (141 vs 178 cases) and 12% (573 vs 649 cases), respectively. In both periods, the male population accounted for 94% (p=0.070; total missing: 0.2%) of cases and the age group 30 to 39 years was the most affected. The distribution of syphilis cases among all age groups was comparable, with only 0.1% to 2.1% differences between the pre-pandemic and pandemic periods. The number of heterosexual cases increased by 1% (1 543 vs 1 556 cases; p=0.008), while the number of MSM cases decreased by 9% (9 431 vs 8 580 cases; p=0.014; total missing: 20.7%) during the pandemic. The proportion of syphilis cases in the primary stage decreased (40% vs 37.7%; p=0.002) during the pandemic, while the proportion in the early latent stage increased (32.4% vs 34.4%; p=0.002; total missing: 29%). Chlamydial and gonococcal co-infections increased during the pandemic (chlamydia: 6% vs 7%; gonococcal: 4.8% vs 5.9%). Increased syphilis screening and health campaigns to promote prevention measures were recommended to effectively reduce syphilis infections and provide early access to treatment.

Role: The fellow conducted data cleaning and descriptive epidemiological and statistical analysis using R. The outcome of the study was provided as a final report, which will be used as a template for writing the manuscript.

Educational outcome

The fellow was involved in three surveillance projects that delivered different educational outcomes. These included interpretation of data to generate information for action (ANDEMIA genomic surveillance) and comparison of various indicators from the COVID-19 pandemic and pre-pandemic periods to identify any changes in total numbers of two notifiable diseases (HIV and syphilis). For the first project, the fellow used her previous laboratory skills to generate sequencing data and characterise antimicrobial resistance genes' composition. Moreover, when conducting the projects, she also acquired skills in descriptive epidemiological analysis and gained confidence using R software.

2. Applied public health microbiology and laboratory investigations

A) Virulence and resistance patterns of **Vibrio cholerae** *non-O1/non-O139 from Germany and other European countries*

Supervisors: Susann Dupke, Holger Scholz

Global warming is an important driver for the emergence of *Vibrio* species in marine and estuarine environments. Freshwater could also be affected. Furthermore, in recent decades *Vibrio* species have developed antimicrobial resistance towards various antibiotics commonly used to treat such infections. We assessed virulence and resistance patterns of *Vibrio cholerae* non-O1/non-O139 strains derived from Germany and other European countries, collected between 2011 and 2021. Sequence data from clinical and environmental *Vibrio* strains (n = 87) were analysed using virulence (vFDB) and antibiotic resistance (AMRfinder) databases. Genotypic results were compared with resistance phenotypes according to EUCAST breakpoints. Genetic relatedness between isolates was assessed by an ad hoc cgMLST scheme (SeqSphere+) and pubMLST scheme. Both cgMLST schemes yielded comparable results, with high genetic diversity among *Vibrio* isolates. A few isolates showed very close relationship (allelic distance <20) and clustered together. Thirty-seven virulence genes (VGs) were identified. Virulence profiles were similar between clinical and environmental isolates, except for one stool sample, where the majority of VGs were detected, and a cluster of 11 environmental isolates, where the lowest number of VGs were found. Among all strains, the predominant VGs were quorum sensing protein-*luxS*, repeats-in-toxins-*rtxC/rtxD*, hemolysin-*hlyA,* and different type VI secretion proteins genes. Genotypic profiles disclosed antibiotic resistance genes conferring resistance to beta-lactames, quinolones, macrolides, tetracycline, antifolate, aminoglycosides,

fosfomycin, phenicols and sulfonamide. Carbapenemase gene-VCC-1 was detected in ten meropenem-resistant *Vibrio* isolates derived from surface water in Germany. The proportion of resistance among *Vibrio* isolates against first-line treatment (3rd generation cephalosporin, tetracycline and fluoroquinolone) was low. Empirical treatment would have been effective for all clinical *Vibrio* isolates. Nevertheless, carbapenem-resistant isolates have been present in freshwater in Germany and might represent a reservoir for antimicrobial resistance genes. The study concluded that monitoring antimicrobial resistance is crucial for public health authorities to minimise its risk to the human population.

Role: The fellow conducted laboratory work (DNA extraction for whole genome sequencing and antimicrobial susceptibility testing) and data analysis. The fellow wrote the study protocol, which she also used as a guide for writing the manuscript. Additionally, the fellow presented the study results as a printed poster at the ECCMID conference in Copenhagen in 2023, during the resistance surveillance and epidemiology (Gram-negatives) session. The fellow also prepared and delivered an oral presentation of the project results at the FG16 internal RKI seminar. A peer-reviewed manuscript (first author) was submitted to *Frontiers in Microbiology*.

B) Assessment of genomic diversity of **Mycobacterium avium** *in a patient with cystic fibrosis in Germany, 2017–2020*

Supervisors: Jennifer Bender, Astrid Lewin

In cystic fibrosis (CF) patients, *Mycobacterium avium* infections may cause chronic pulmonary disease. To date, little is known about genetic diversity of *M. avium* in patients with chronic lung infections. We conducted whole genome analyses to assess genomic diversity of *M. avium* subspecies *hominissuis* isolates derived from one chronically infected CF patient to guide therapeutic strategies. DNA isolated from 29 *M. avium* isolates from eight respiratory samples collected between 2017 and 2020 were sequenced on Illumina and one isolate on MinION. Hybrid assembly was performed to provide a patient sample reference. Genetic relatedness was assessed by an ad hoc core genome multi-locus sequence type (cgMLST) scheme and an SNP-based approach. Virulence and resistance determinants were sought in the vFDB and AMRfinder databases. Functions and pathways of genes affected by SNPs were identified using the KEGG database. The cgMLST scheme revealed 3 964 target genes and two clusters (allelic distances <5). Year-specific clustering of isolates and specific clonal clusters were not observed. All isolates were closely related, with maximum 20 allelic differences. The SNP-based approach identified three clusters, two of which indicated year-specific clustering of samples originally isolated in 2017. The numbers of SNPs affecting proteins were diverse (average: 17 SNPs/genome) and present in 56 protein coding regions associated mainly with metabolic pathways. Antibiotic resistance genes were not found, while five virulence determinants (*eccCa5, esxN, icl, ideR, relA*) linked to metabolic functions and transportation were detected in all isolates. The study revealed genetic diversity among *M. avium* isolates from one CF patient. The low number of SNPs indicated single-strain infection. Although resistance genes were not detected, in-host diversity must be acknowledged and therapeutic strategies should be adjusted for bacterial populations rather than for single isolates. More studies and patients are needed to understand the genetic diversity of *M. avium* during chronic lung infection.

Role: The fellow performed bioinformatics analysis, including quality control and genome assembly, for all isolates sequenced on the Illumina platform. Additionally, the fellow performed hybrid assembly for the isolate sequenced on the MinION platform to generate a patient sample reference for the ad hoc cgMLST and the SNP-based approach. The fellow generated an ad hoc cgMLST scheme using the SeqSphere+ software, aligned and mapped sequence reads to the reference sample to identify SNVs, and assessed genetic divergence over time (temporal signal). The fellow presented the draft of the results during a Project Review Module and submitted the abstract for the ESCAIDE 2023 conference. The fellow wrote the final report, which will be used as a template for writing the manuscript.

Educational outcome

The fellow had an opportunity to familiarise herself with methods used for bacterial identification and molecular characterisation of virulence and antimicrobial resistance factors. Previous experience in clinical microbiology allowed her to conduct and interpret antimicrobial susceptibility testing in the *Vibrio* study. Additionally, the fellow gained skills in bioinformatics and genome analysis by using different softwares (SeqSphere+Geneious, pubMLST). The fellow also learned how to conduct and interpret the results from commercial and publicly available cgMLST schemes. She gained confidence in R software, which was used to create graphical presentation of the results.

3. Biorisk management

Biosafety practices for handling prions

Supervisor: Achim Thomzig

Due to the fellow's previous work experience in Biosafety Level 3, the biorisk management competency was achieved by performing an activity on biosafety practices for handling prions. Prion diseases or transmissible spongiform encephalopathies (TSEs) initiate or transmit neurodegenerative processes in the central nervous system, leading to death of neurons. Transmission takes place enterally (via the intestinal track) or parenterally (intravenously, intracerebrally or intraperitoneally). An abnormal, misfolded conversion of normal prion protein (PrP^C) is the infectious agent and causes Creutzfeldt-Jakob disease (CJD), scrapie and other related human and animal neurodegenerative diseases. The aim of

this activity was to become familiar with biosafety and biosecurity practices for handling prions. The objective was met by demonstrating the laboratory workflow in a Biosafety Level 3* (BSL3*) setting, and demonstrating the appropriate use of decontamination strategies and personal protection to safely process high-risk specimens.

Role: The fellow performed a literature review and wrote a reflective note.

Educational outcome

The fellow gained not only theoretical knowledge regarding prions and prion diseases, but also came to understand the specific nature of this agent. The fellow refreshed her knowledge and skills of how to work safely with BSL3* organisms. The fellow became familiar with the risk assessment associated with the hazard and which protective measures should be implemented in a BSL3* laboratory to minimise the risk of contamination and infection. The lab tour allowed her to view microscopy slides depicting the misfolded structure of prion proteins and broaden her knowledge in diagnostic methods used to identify these specific infectious agents.

4. Quality management

A) External Quality Assurance for detection of **Cryptococcus neoformans** *and* **Cryptococcus gattii** *antigen in human serum: participation in the ring trial sample preparation and results evaluation*

Supervisor: Ilka McCormick Smith

Quality Assessment (QA) refers to all activities and procedures undertaken by medical laboratories to improve quality and clinical usefulness of laboratory test results. QA is a critical aspect of laboratory quality management, and it can be conducted in several ways. Here, we performed an external quality assurance (EQA) for detection of *Cryptococcus neoformans* and *Cryptococcus gatti* capsular polysaccharide antigen in human serum. The main objective of this project was to prepare human serum (negative and positive samples) for EQA and further evaluate the results from medical laboratories participating in the ring trial. The detection of *Cryptococcus* antigen in serum was performed by three immunological tests: i) lateral flow assay, ii) polyclonal latex assay, and iii) monoclonal latex assay. Additionally, ELISA was performed in order to evaluate a new method for future testing. All tested serum was negative for the presence of *Cryptococcus* antigens. In a serious of dilutions of serum with antigen, the cut-off point for positive serum was <1:640 using lateral flow assay, and <1:64 using polyclonal and monoclonal latex assay. The tested serum by ELISA showed OD: 2.84-3.22 for positive samples, and OD <0.264 for negative samples. The prepared positive and negative serum was sent to the German reference institution INSTAND and then further distributed to 92 medical laboratories for examination and data interpretation. The target values of the different splits were defined by the median of the results from the participants. The accepted range was defined as two dilutions above and beneath this median value. From all participants, 94% interpreted the results correctly and were awarded the certificate. Screening for cryptococcal antigen in serum may shorten time to diagnosis, especially for high-risk patients and lead to earlier specific therapy.

Role: The fellow conducted the laboratory work (preparation of positive and negative serum) and data interpretation from medical laboratories participating in the ring trial. The outcome of the study was presented as a final report written by the fellow.

B) Internal audit of the Mycology laboratory at RKI

Supervisor: Ilka McCormick Smith

The audit was performed in the Mycology laboratory at RKI, after the Biorisk and Quality Management Module. The main aim of this activity was to refresh the fellow's knowledge in the procedure and documentation involved in an internal audit. The fellow had previous experience as an internal accessor and also completed an Internal Audit course in the past. The audit was performed using the tool from BQM as a one-day meeting in which indicators related to 'Process and Quality Control' and 'Documentation' were discussed in detail. This short assessment showed that the Process Management, Quality Control and Documentation are very well registered in the Mycology laboratory. The laboratory fulfilled the requirements of accreditation (PL-13113-01, ML-13113-01). Almost all indicators were assessed at 100%, except one pre-analytical process and specimen management. However, it is based on the results from the BQM tool and not an internal audit by the RKI body. The laboratory did not record 'time of sampling', 'name of sampler', 'name/sex/age and address of patient', but instead used a unique number that allows matching of patient records, which is well accepted at RKI. There is no dedicated room for collection of specimens. However, sample collection does not take place onsite. In terms of accommodation/environment conditions, quality management and assurance, the laboratory has achieved 100%. Only authorised persons have access to the laboratory, all rooms are well organised for laboratory work, and all activities in the laboratory are very well documented. Overall, the audit team (two PAE fellows) concluded that the Mycology laboratory successfully passed the internal audit.
Role: The fellow conducted the internal audit with two PAE fellows (cohort 2020). The fellow summarised the results, sent them to the supervisor and wrote a reflection note.

Educational outcome

Participating in both quality management activities broadened the fellow's knowledge in quality assurance and quality management. The ring trial allowed the fellow to understand the workflow of the methodology required to prepare positive and negative samples for further assessment by medical laboratories and also how to evaluate the results. The internal audit helped the fellow to understand the quality management system, as well as the structure and function of the mycology consultant laboratory at RKI.

5. Public health microbiology management

A) Update on national polio and enterovirus surveillance in Germany

Supervisor: Kathrin Keeren

Polio (poliomyelitis) is an endemic infectious disease caused by the RNA virus (poliovirus). It is a highly contagious virus that spreads through person-to-person contact, mostly affecting children under five years old. There are three serotypes of Wild polioviruses (WPVs) that cause infection: type 1, type 2 and type 3. WPV type 1 is currently the only remaining wild type circulating in some regions of the world (Pakistan and Afghanistan). WPV type 2 and 3 were declared eradicated in recent years (2015 and 2019, respectively). Nowadays, circulating vaccine-derived poliovirus (cVDPV) has caught the attention of public health authorities, as there have been many outbreaks in several countries where immunisation coverage was low. Therefore, implementing appropriate interventions (e.g. enhanced laboratory and environmental surveillance), raising awareness among physicians to identify relevant cases, increasing polio vaccination coverage, minimising the risk of spread of polioviruses and eradicating WPV type 1 are the most important goals for public health. The aim of this activity was to become more familiar with poliovirus circulation in the framework of the Global Polio Eradication Program (GPEI) in Germany, as well as with the German enterovirus surveillance system. The objective of the activity was met by self-studying, preparing data for the National Certification Commission for Polio Eradication (NCC) meeting, participating in the NCC meeting and updating the German annual progress report on polio eradication for the World Health Organization (WHO). Additionally, a laboratory visit to the National Reference Centre for Poliomyelitis and Enteroviruses at RKI was initiated to demonstrate the laboratory workflow of polio/enterovirus detection and typing.

Role: The fellow reviewed the literature, prepared the data for the NCC meeting and updated the German annual progress report on polio eradication. The fellow wrote a reflection note.

B) Retrospective investigation of a nosocomial outbreak of hepatitis C virus infection in Germany, 2017–2018

Supervisors: Sandra Niendorf, Ruth Zimmermann, Claus-Thomas Bock, Sebastian Haller

The outbreak investigation required good management skills, including time management and project management. The investigation required communication with the local health authorities in Bavaria and the Hepatitis C National Reference Laboratory (NRZ) in Essen. Each stakeholder was responsible for different aspects of the investigation. Local health authorities conducted an extensive case search and NRZ performed the viraemia testing for the anti-HCV positive samples. All of these steps were communicated with the fellow who managed the whole investigation. Each step of the investigation was communicated and discussed in detail with the project supervisors. The summery of the outbreak report was shared with the stakeholders.

C) Organisation and implementation of the Laboratory Module (Lab4Epi) for fellows of the Postgraduate Training for Applied Epidemiology (PAE) and EPIET programmes based in Germany

The training module for German PAE/EPIET fellows (described in more detail in Section 6: Teaching and pedagogy) required drafting the PAE module agenda, as well as planning laboratory activities. The structure of the module, timeline and preliminary schedule (including an example of laboratory activities) was discussed extensively with other PAE team organisers. Upon agreement on the training module content, the final version of the agenda was shared with RKI presenters and participants.

Educational outcome

Each of these projects and activities strengthened the fellow's management and communication skills, as well as built her confidence. The fellow learned how to plan, organise, communicate, manage and lead projects from a different field. She also learned how effectively deliver outcomes with third parties, how to prioritise tasks and how to effectively manage a timeline. The activity performed on national polio and enterovirus surveillance in Germany indicated how important public health preparedness, response and management are, as well as communication with WHO.

6. Teaching and pedagogy

Organisation and implementation of the Laboratory Module (Lab4Epi) for fellows of the Postgraduate Training for Applied Epidemiology (PAE) and EPIET programmes based in Germany

The PAE Laboratory Module (Lab4Epi) is organised every year by the current EUPHEM fellow at RKI in collaboration with multiple units from the institute. The format of this course was delivered as a three-day, face-to-face and hybrid module. The course included plenary lectures, RKI unit's presentations, hands-on laboratory activities and description of an outbreak scenario that was used to put diagnostic methods into context. The main goal of the laboratory module was to familiarise fellows with the laboratory work, scientific content and projects at the RKI, as well as various microbiological methods used across the different RKI departments with laboratory capacity. Additionally, the aim of the module was to create and promote close cooperation between epidemiologists and microbiologists.

Role: The fellow was responsible for all steps related to organising, implementing, communicating and moderating the module. Additionally, the fellow delivered a lecture regarding diagnostic methods used for bacterial identification, presented an interactive outbreak scenario including an interactive quiz (Slido). She also evaluated the module based on the online questionnaires and summarised her experience in a reflective note.

Educational outcome

The fellow learned how to organise and manage all stages of a training module. Additionally, she improved her skills in delivering scientific content to public health professionals and evaluating participant feedback in the context of improving the module. Organising the module required communication with a multidisciplinary team and with presenters; therefore, involvement in that part strengthened the fellow's communication and management skills and improved her ability to communicate effectively and successfully.

7. Communication

7.1 Publications related to the EUPHEM fellowship

7.1.1 Manuscripts published in peer-reviewed journals

Paper 1: Katarzyna Schmidt, Holger Scholz, Sandra Appelt, Jana Michel, Daniela Jacob, Susann Dupke. Virulence and Resistance patterns of *Vibrio cholerae* non-O1/non-O139 acquired in Germany and other European countries. **Manuscript was submitted to *Frontiers in Microbiology.***

7.1.2 Other reports

Report 1: Outbreak Investigation: Retrospective investigation of a nosocomial outbreak of hepatitis C virus infections in Germany, 2017–2018.

Report 2: Surveillance: Genomic surveillance of antibiotic resistance genes in patients with gastrointestinal infections in Sub-Saharan Africa (SSA), 2019–2021.

Report 3: Surveillance: The impact of COVID-19 on notifiable HIV and syphilis infections numbers in Germany: An analysis of surveillance data during pre-and COVID-19 era.

Report 4: Quality Management: External Quality Assurance for detection of *Cryptococcus neoformans* and *Cryptococcus gattii* antigen in human serum.

Report 5: Laboratory Investigation: Assessment of genomic diversity of *Mycobacterium avium* in a patient with cystic fibrosis in Germany, 2017–2020.

Reflective note 1: Teaching: PAE Laboratory Module (Lab4Epi).

Reflective note 2: Bio-risk Management: Biosafety practices for handling prions.

Reflective note 3: Management & Communication: Update on national polio and enterovirus surveillance in Germany.

Reflective note 4: Quality Management: Internal audit in RKI Mycology laboratory.

7.2 Conference presentations

Conference 1: Schmidt K, Michel J, Scholz HC, Jacob D, Dupke S. 2023. Phenotypic and genotypic characterization of *Vibrio cholerae* non-O1/non-O139 strains from Germany and other European countries. In ECCMID 2023, Denmark. 15–18 April 2023. Onsite poster presentation.

Conference 2: Schmidt K, Schubert G, Ulrich M, Ouedraogo AS, Akoua-Koffi C, Traoré A, et al. Genomic surveillance of antibiotic resistance genes in patients with gastrointestinal infections in Sub-Saharan Africa (SSA), 2019–2021. In ECCMID 2023, Denmark. 15–18 April 2023. Onsite poster presentation.

Conference 3: Schmidt K, Jansen K, Gunsenheimer-Bartmeyer B, Bremer V, Koppe U. The impact of COVID-19 on notifiable HIV infection numbers in Germany: An analysis of surveillance data during pre-and COVID-19 era. In ESCAIDE 2023, Spain. 22–24 November 2023. Online poster.

7.3 Other presentations

1. Bacterial diagnostics. Oral presentation, PAE Laboratory module, June 2022 and March 2023.
2. Outbreak Scenario. Oral presentation, PAE Laboratory module, June 2022 and March 2023.
3. Midterm review. Oral presentation, July 2022.
4. Molecular characterisation of *Mycobacterium avium* in a CF patient. Oral presentation, Project Review Module, August 2022.
5. Surveillance of gastrointestinal pathogens and antimicrobial resistance (AMR): Resistome study. Oral presentation, RKI FG16 internal seminar, September 2022.
6. Virulence and resistance patterns of *Vibrio cholerae* non-O1/non-O139 acquired in Germany and other European countries. Oral presentation, RKI FG16 internal seminar, May 2023.
7. The impact of COVID-19 on notifiable HIV infection numbers in Germany: An analysis of surveillance data during pre-and COVID-19 era. Oral presentation, Project Review Modul, August 2023.
8. A trip from African countries to the Baltic Sea – an overview of public health-related EUPHEM projects. Oral presentation, RKI internal seminar, September 2023.

8. EPIET/EUPHEM modules attended

1. Introductory Course Part 1 (20/09/2021–08/10/2021), virtual.
2. Inject Day 1 – Phylogeny and Whole Genome Sequencing (20/10/2021), virtual.
3. Virtual Inject Day 2 – Operational Research (27–28/10/2021), virtual.
4. Outbreak Investigation (6–10/12/2021), virtual.
5. Biorisk and Quality management (17–18/01/2022), virtual.
6. Multivariable Analysis (14–18/03/2022), virtual.
7. MVA Inject Day (30/03/2022), virtual.
8. Introductory Course Part 2 (20–29/04/2022), Spetses, Greece.
9. Rapid Assessment Method (6–10/06/2022), Stockholm, Sweden.
10. Project Review Module (29/08/2022–02/09/2022), Lisbon, Portugal.
11. Times Series Analysis (7–11/11/2022), Utrecht, the Netherlands.
12. Vaccinology (13–17/02/2023), virtual.
13. Management, Leadership and Communication in Public Health (8–12/05/2023), Stockholm, Sweden.
14. Project Review Module (28/08/2023–1/09/2023), Lisbon, Portugal.

9. Other training

1. Epidemiology in healthcare settings (combined module with UK FETP and German PAE) (18–20/05/2022), Cardiff, United Kingdom.

2. Advanced Epidemiologic Methods: Mastering R for Epidemiologic Research (22/08/2022–02/09/2022), virtual.

3. CLC Genomics Workbench (29/04/2023–20/05/2023), virtual.

4. Conducting systematic reviews for complex (public health) interventions – a hands-on introduction (03–06/07/2023), Berlin, Germany.

5. Whole-genome sequencing-based (WGS) detection of antimicrobial resistance (AMR) in bacteria (04/09/2023; 08/09/2023), virtual.

10. Missions

The fellow did not apply to participate in missions.

11. Other activities

1. Participation in an Infodemic Management group meeting.

2. TB Surveillance Systems Workshop (31/03/2022), virtual.

3. OHEJP Diagnostic Satellite Workshop (14/04/2022), virtual.

4. UKHSA Update on the national polio and enterovirus surveillance webinar (02/02/2023), virtual.

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