

The main title of the report, "Summary of work activities", followed by the author's name "Hilde Angermeier" and the program name "European Public Health Microbiology Training Programme (EUPHEM), 2018 cohort". The text is in a white, sans-serif font against a blue background.

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.

This report summarises the work activities undertaken by Hilde Angermeier, cohort 2018 of the European Public Health Microbiology Training Programme (EUPHEM) at the Institut Pasteur in Paris, France.

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

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Stockholm, August 2020

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Pre-fellowship short biography

Hilde Angermeier is a biologist with specialisation and PhD in Microbiology from the Julius-Maximilians-University of Würzburg in Germany. In addition to her PhD she obtained a postgraduate Master of Science degree in International Health from the medical faculty of the Ruprecht-Karls-University in Heidelberg, Germany in 2016. She gained international experiences first during an academic exchange year at the University of Texas at Austin in the USA. In 2013 she was an intern with the World Health Organization for the Western Pacific Region in the country office of Vietnam in Hanoi, where she supported the Emerging Diseases Surveillance and Response Unit. In 2016 she conducted during her Master's degree in International Health a research stay at the Oswaldo Cruz Foundation at Fiocruz Pernambuco in Recife, Brasil, in the framework of ZIKA-outbreak emergency research. Later on, she worked as a PostDoc in the Surveillance Unit (FG32) at the Department for Infectious Disease Epidemiology of the Robert-Koch-Institute in Berlin, Germany, before she started this fellowship programme in European Public Health Microbiology.

Methods

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

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

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

Results

The objectives of these core competency domains were achieved partly through projects or activities (on-job services) and partly through participation in the training modules. Results are presented in accordance with the EUPHEM core competencies, as set out in the EUPHEM scientific guide¹.

1. Epidemiological investigations

1.1. Outbreak investigations

SARS-CoV-2 associated with COVID-19

Supervisors: Isabelle Cailleau, Sylvie van der Werf, Arnaud Fontanet

In the framework of the SARS-CoV-2 outbreak associated with COVID-19 that has been threatening the world including France since January 2020 the fellow was involved at Institut Pasteur for France from 28th January until 5th May 2020 in the support of the Outbreak Investigation Taskforce. There she contributed to the ongoing preparedness activities (e.g. by translating documents from French into English on specimen shipment of 2019-nCoV samples for international partners) and updated the head of the Respiratory Viruses National Reference Laboratory (NRL) and other IP scientists with presentations on epidemiological and scientific information from websites and publications on the global outbreak situation of SARS-CoV-2. As a guest of the Outbreak Investigation Task Force (OITF) the fellow was allowed to join weekly meetings. The fellow created and regularly updated a website for the OITF on confluence which covered relevant information and publications on the SARS-CoV-2 and COVID-19 outbreak to inform the global International Pasteur Network (IPN) on the SARS-CoV-2 and COVID-19 situation to support ongoing emergency research activities. On top, she responded to evidence requests from IP scientists to assist ongoing epidemiological research on the SARS-CoV-2 and COVID-19 threat to support the scientific advisory board for the French government. During this time she learned about the SARS-CoV-2 outbreak associated with COVID-19 and she contributed to the French emergency response to confine the outbreak as soon as possible.

¹ European Centre for Disease Prevention and Control. European public health training programme. Stockholm: ECDC; 2017. Available from: <http://ecdc.europa.eu/en/publications/Publications/microbiology-public-health-training-programme.pdf>

Annually re-occurring infections caused by *Salmonella enterica* serotype Napoli in France

Supervisors: François-Xavier Weill, Elisabeth Njamkepo, Alexandre Boissinot

Uncommon infections due to *Salmonella enterica* serotype Napoli (in short: *S. Napoli*) have been observed to be annually re-occurring with hotspots in France, Italy and Switzerland besides countries that likely import those infections via returning travelers from those endemic countries (Fisher et al. 2009). The infections normally manifest gastrointestinally with diarrhea, fever and abdominal cramps, but can also cause life-threatening sepsis. This study was devoted to describe in detail the burden and geographic localization of the *S. Napoli* infections in France over the time span from 1970 to 2019 by applying descriptive epidemiology to identify potential risk groups, risk factors and sources or reservoirs of *S. Napoli* to design suitable measures for the prevention of *S. Napoli* outbreaks in the future. The fellow was involved in that project, that was at the same time the PH Microbiology research project (see text there for further details), in all aspects of the outbreak investigation starting with involvement in isolate preparation for WGS, historical and recent data collection and extraction, descriptive epidemiology, mapping, phylogenetic analyses, investigation of antibiotic resistance patterns as well as in field work for the investigation of potential *S. Napoli* reservoirs followed by extensive laboratory work for *Salmonella* subspecies identification.

Training modules

Introductory Course on Spetses, Greece, from 24th September to 12th October 2018: The EPIET/EUPHEM fellows obtained insights into the concepts of epidemiology and outbreak investigation, which were given in numerous lectures and interactive sessions by applying case studies and other group exercises. During the introductory course, also the ten steps of an outbreak investigation were taught to the fellows.

Outbreak Investigation Module in Berlin, Germany, from 03rd to 07th December 2018: This module taught fellows how to perform analytical epidemiological studies within outbreak investigations using various software packages. During the module fellows performed all steps involved in outbreak analysis from creation of a data entry file to the stratified analysis using EpiData, Stata and Microsoft Excel. They were also given practical training in when and how to perform analytical studies for an outbreak investigation, including descriptive, cohort and case-control studies.

Multivariable Analysis module in Madrid, Spain, from 25th to 29th March 2019: This module provided a more comprehensive understanding of the principles of statistical analyses by applying STATA or R to investigate outbreaks. It included the building of an optimal model using linear, logistic, Poisson and Cox regression.

Rapid Assessment and Survey Methods Module in Zagreb, Croatia, from 13th to 18th May 2019: This module focused on teaching survey and sampling methods that can be applied within outbreak situations. The fellows performed their own sampling during a field-trip by applying suitable software tools. In addition an exercise on the communication and conduction of a Rapid Risk Assessment of an autochthonous ZIKA outbreak in a European country was conducted. On top, the fellows got insights into the work of WHO GOARN and learned about behavior and security aspects during international deployments.

Management, Leadership and Communication in Public Health in Stockholm, Sweden, from 10th to 14th February 2020: In this module the fellows were involved in different outbreak-scenarios and gained experiences in the communication of emergency situations to higher authorities. The course also tackled different aspects of management, leadership and communication with a special focus on work in multidisciplinary teams.

Educational outcome: The fellow gained valuable insights into emergency research, management and communication to higher authorities by being involved in the support of the Outbreak Investigation Taskforce (OITF) at Institut Pasteur for France during the SARS-CoV-2 associated with COVID-19 response, that has been caused by an emerging virus creating a pandemic and WHO-PHEIC. On top, the fellow obtained valuable insights and experiences on a French Salmonellosis outbreak caused by *S. Napoli* that was observed even cross-border in two other European countries. This way, the fellow applied microbiological and epidemiological knowledge to outbreak situations, participated in a multidisciplinary outbreak team at Institut Pasteur and got involved in viral as well as bacterial outbreak investigations (case definition, case-finding, data collection, data analysis, data management, laboratory typing methods, communication and writing an outbreak report).

1.2. Surveillance

Optimizing assay development by using antibody landscape signatures to conduct large-scale serosurveys of emerging vectorborne viruses: A nationwide representative serosurvey of Hantaviruses circulating in Bangladesh, 2014-2016

Supervisors: Jessica Vanhomwegen, Jean-Claude Manuguerra

Over the past decade there has been a growing number of hantavirus outbreaks. Therefore, serological tests are central for clinical diagnosis of hantavirus infections, understanding the immune status of populations, and for estimating levels of hantavirus circulations. Limited assay availability, cost barriers and the need for substantial volumes of blood mean that in both clinical and epidemiological settings, serological assays are nearly always done with just a single capture antigen. This means clinicians need to have an *a priori* assessment of the infecting pathogen, which is often difficult as the symptoms for different pathogens may be very similar. In response to these problems, the Pôle d'Identification Virale (PIV) of the Cellule d'Intervention Biologique d'Urgence (CIBU) at Institut Pasteur in Paris, France, has developed a low-cost multiplex Luminex-based assay, called MIA, that is able to simultaneously test serum for the presence of antibodies to a wide panel of different viruses, including arboviruses like DENV 1-4, ZIKV, CHIKV, Yellow fever, Japanese encephalitis, West-Nile virus or hantaviruses like Hantaan and Seoul virus. For this purpose, large amounts of recombinant viral antigens (envelope, glycoprotein and non-structural protein domains) have been produced and purified. A preliminary evaluation of the individual antigens has already been performed and demonstrated high clinical performances (specificity and sensitivity). By allowing the assessment of an individual's antibody response to a wide range of different pathogens, the assay can allow clinicians to discriminate between competing diagnoses as well as allow public health officials and epidemiologists to assess the circulation patterns of many different pathogens at the same time. The optimized assay and analytical tool will be a powerful means to estimate the level of infection different viruses are causing in outbreak situations. This will allow to take a fresh look at the epidemiology of a wide range of different viruses to assess their long-term circulation patterns in different settings of the world. In this study the fellow evaluated first time the seroprevalence of Hantavirus infections in Bangladesh to elucidate its local epidemiology and potential clinical relevance. Hantavirus infections can result in severe hemorrhagic fever with renal syndrome cases and fatalities. Serum samples were collected from 2448 individuals (non-travelers) in between 08/2014 and 01/2016 from an established nationally representative serum bank in Bangladesh to monitor the presence of IgG antibodies against the two main Hantaviruses circulating in Asia: Hantaan and Seoul virus. All 2448 samples were screened using an in-house bead-based multiplex immunoassay (MIA). A random subset of 76 MIA-seropositive serum samples was further tested by the fellow via a commercial enzyme-linked immunosorbent assay (ELISA) and an indirect immunofluorescent assay (IFA). Of 2448 samples, 358 (14.6%) were found seropositive for either Hantaan or Seoul virus by MIA. Among the retested MIA-seropositive sample subset, 66% (50/76) were confirmed to be seropositive by ELISA and/or IFA tests. These results from non-travelers indicate that the infections were acquired locally and that active Hantavirus circulation exists in Bangladesh. Serum samples with difficult serological interpretations probably result from cross-reactivity with an unidentified Hantavirus species (e.g. Thailand virus), which requires further investigations. Additional syndromic surveillance data of severe Hantavirus cases in Bangladesh could help supplement the results of this serosurvey. The long-term goal of this project is to facilitate the accurate diagnosis and surveillance of hantavirus infections in affected populations also in developing countries like Bangladesh.

Molecular epidemiology of leptospirosis in Tahiti, French Polynesia, during the 9-years-time span from 2011 to 2019

Supervisor: Linda Grillová

Leptospirosis, caused by spirochetes of the genus *Leptospira*, is the zoonosis with the widest global distribution causing more than one million severe cases resulting in 60.000 deaths every year. Rodents have been considered to be the main animal reservoir, however, leptospirosis is ubiquitously present within the animal kingdom. This project describes the molecular epidemiology of leptospirosis in Tahiti, French Polynesia - a hotspot for this disease - in the 9-years-time span from 2011 to 2019. In total 444 blood samples were collected from patients diagnosed with leptospirosis at the *Centre hospitalier* in French Polynesia. Using a combination of traditional and nested PCR followed by Sanger sequencing, the sequences for *secY* locus were determined in 244 samples (55%) by the fellow and colleagues at Institut Pasteur in Paris, France. In addition, 20 *Leptospira* strains isolated from patient blood were fully characterized at species and serogroup levels and used as references for the association of different phylogenetic branches with respective serogroups. The *secY* sequences were compared with sequences from wild rats, farm pigs and domestic dogs from a previous study in French Polynesia (Guernier et al. 2017). The phylogenetic analyses divided the sample set into 20 genotypes clustering into 4 lineages. Lineage 2 (*L. weilii*) associated with serogroup

Mini) was found exclusively in human patients. Its source remained unknown. Lineage 3 (*L. interrogans* associated with serogroup Canicola) was correlated with its co-isolation from human patients and farm pigs (*Sus scrofa*, p-value=0), while lineage 1 (*L. borgpetersonii* associated with serogroup Ballum) was correlated with its co-isolation from rats (*Rattus exulans* and *Rattus norvegicus*, p-value=0). The most prevalent lineage 4 (*L. interrogans*) consisted of two central genotypes, 9 (associated with serogroup Icterohaemorrhagiae) and 10 (associated with serogroup Australis). Remarkably, genotype 9 predominated each year (2007-2019). The ability to survive in a wide host range (dogs, rats and pigs) might facilitate its high prevalence and predominance over the 9-years period. This project shed light on the population dynamics of leptospires circulating among patients in Tahiti during 2011 to 2019 and on the role potential animal reservoirs (pigs, rats and dogs) play in leptospirosis transmission to humans. The long-term goal is to successfully stop the transmission to humans in FP by appropriate public health intervention measures (e.g. updated guidelines for Leptospirosis prevention and control). However, also the long-term conduction of leptospirosis surveillance in FP - in addition to awareness raising among medical staff and the general population – could be a first milestone to fight against this neglected tropical disease in French Polynesia. The fellow was conducting the laboratory work and was involved in sequence and data analysis as well as in abstract submission for a conference contribution and the writing of a joint first-authorship publication together with her project supervisors.

Seroprevalence study of Leptospirosis in Niger

Supervisor: Jean-François Mariet

As the information on zoonotic diseases and especially the Leptospirosis disease burden is still very limited for Niger, Africa, this project aimed to shed more light on the seroprevalence of leptospirosis in Niger by using Enzyme-linked Immunosorbent Assays (ELISA) on selected human serum samples from Niger to elucidate one of the causes of fever of unknown origin, to estimate the leptospirosis burden in the local population and to prevent death, as leptospirosis can be successfully treated with antibiotics. To test especially persons at risk, serum samples of butchers were primarily investigated. Due to its normal life cycle, leptospirosis has so far mostly been studied in temperate, warm and humid regions, while arid zones have been only very occasionally monitored for this disease. In particular, data for West African countries are extremely scarce. So far only one study has been published on Leptospirosis in Niger, Africa (Dobigny et al. 2015). This author could prove the presence of pathogenic leptospires in Niger for the first time and help the identification of their species in the Sahel, as they do circulate in Sub-Saharan Africa more extensively than currently thought (de Vries et al. 2014). However, their impact and virulence on human health still need to be investigated in detail. Shedding light on this public health problem could explain many fevers of unknown origin and prevent death among people living in one of the world's poorest societies. For these reasons, the fellow focused in this project on testing the seroprevalence of leptospirosis in 80 selected serum samples received at Institut Pasteur from persons at risk, who worked as butchers (n=79) in Niger and were therefore in contact with animals. The screening of these selected serum samples from Niger was performed via an in-house based IgM and IgG Enzyme-linked immunosorbent assay (ELISA) by the fellow. 10 of the tested serum samples were positive, five for IgM, stating a recent infection, and six for IgG, stating an infection that was already present longer ago, with one sample being positive for IgM and IgG. These 10 positive tested serum samples were all obtained from Niger and belonged all to men ranging in age from 28 to 52 years with a mean age value of 36.6 years. Nine of those positive tested persons were butchers and reported frequent contact to animals, mostly to cattle (n=8) or sheep and goats or also camels (n=1 each). One of the positive tested persons worked as a wood seller and not as butcher. Eight positive cases reported to have been exposed to a high-risk environment for leptospirosis (e.g. lakes, rodent and other animal contact, garbage exposure) and four had even reported to have taken a bath in fresh water. To conclude, the ELISA results for the 80 investigated human serum samples from Niger yielded 10 serum samples that contained antibodies against leptospirosis (12.5%). All of these samples belonged to men. Nearly all of them were butchers and had therefore a high-risk profession leading to regular contact with animals. Most of them reported also exposure to high-risk environment. It is therefore recommended that butchers protect themselves better against urine, blood and saliva of the animals they are handling by using protective clothing such as gloves, glasses, masks and suits to avoid any possible direct or indirect contact with animal body liquids. It is also recommended to avoid high-risk environments, if possible, and not to take baths in freshwater ponds, lakes or rivers where leptospirosis could be present within the animal populations. Further studies are needed to identify the exact animal reservoirs for leptospirosis in Niger and the associated transmission pathway to give even more precise Public Health recommendations.

Training modules

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Educational outcome: The fellow obtained first hands-on experiences with the sero-surveillance of hantaviruses in Bangladesh and leptospires in French Polynesia or Niger respectively by applying laboratory work (IFA, ELISA) and data work as well as drafting the Project Proposal Forms (PPF), abstracts for conference contributions and a first co-authorship publication.

2. Applied public health microbiology research

Genomic investigation of annually re-occurring infections caused by Salmonella enterica serotype Napoli in France, 1970-2019

Supervisors: François-Xavier Weill, Elisabeth Njamkepo, Alexandre Boissinot

Uncommon infections due to *Salmonella enterica* serotype Napoli (in short: *S. Napoli*) have been observed to be annually re-occurring with hotspots in France, Italy and Switzerland besides countries that likely import those infections via returning travelers from those endemic countries (Fisher et al. 2009). The infections normally manifest gastrointestinally with diarrhea, fever and abdominal cramps, but can also cause life-threatening sepsis. This project was devoted to describe in detail the burden and geographic localization of the *S. Napoli* infections in France over the time span from 1970 to 2019 by applying descriptive and genomic epidemiology to identify potential risk groups, risk factors and sources or reservoirs of *S. Napoli* to design suitable measures for the prevention of *S. Napoli* outbreaks in the future. For these reasons, an observational, retrospective study on French *S. Napoli* isolates and their case-associated epidemiological patient data obtained at the French National Reference Laboratory for Salmonella at Institut Pasteur was initiated by the fellow for the respective time period. Whole-genome sequencing (WGS) was applied to all isolates obtained at Institut Pasteur via convenient sampling followed by descriptive and genomic epidemiological, mapping as well as phylogenetic analyses comparing the different hierarchical clustering (HC) of cgMLST thresholds. In addition, a search for resistance patterns was conducted. Three field-trips to the *Réserve Naturelle Régionale Bocage des Antonins* in the *Deux-Sèvres Nature Environnement* were conducted by the fellow to sample cloaca swabs or faeces from French snakes, frogs, snails, slugs and lizards. Salmonella isolation and species identification trials were conducted by the fellow at Institut Pasteur in Paris, France, by applying suitable Salmonella cultivation techniques, MALDI-TOF, biochemical galleries for Salmonella sub-species testing and serotyping. Unfortunately, not a single *S. Napoli* bacterium could be obtained after extensive efforts. However, the applied methodology proved appropriate, as numerous other expected or non-expected Salmonella species were successfully isolated from the environmental samples. Currently, PCR tests on these samples are ongoing to definitely rule out any presence of *S. Napoli*. This retrospective study helped to rule out potential environmental reservoirs and sources of infection for *S. Napoli* in France. It showed via genomic epidemiology and phylogeny that not a single source outbreak is attributable to all endemic *S. Napoli* infections in France and abroad. Therefore, to avoid further salmonellosis cases caused by *S. Napoli* the normal hygiene measures should be considered to avoid salmonellosis

(e.g. hand washing before the ingestion of food, after toilet use etc.) until the exact reservoir for the many *S. Napoli* outbreaks in France can be identified in detail that might hint to even more tailored prevention and control measures of endemic *S. Napoli* transmission events in France and beyond.

Training modules

Introductory course on Spetses, Greece, from 24th September to 12th October 2018: In this module the fellows learned via an intense multidisciplinary group work on a gastrointestinal protozoa outbreak in Spain how to best plan and draft the proposal of a Public Health Microbiology Research Project to answer a research question. We also obtained lectures on important concepts of laboratory-based standard microbiological techniques including concepts of phylogenetic analysis. In addition, case studies were facilitated that were designed for public health microbiologists to help interpret laboratory results.

Outbreak Investigation Module in Berlin, Germany, from 03rd to 07th December 2018: During this module at the RKI lectures and workshops for sequence analysis and phylogenetic investigations were implemented for EUPHEM students only to help during their projects.

Educational outcome: The fellow learned how to conduct all stages of a Public Health Microbiology research project by drafting a study proposal including the research question, planning the project, working in multidisciplinary team, performing the according laboratory and field work as well as data analysis. The fellow learned standard microbiological techniques for the diagnosis and subspecies identification of *Salmonella* species, which cause every year numerous cross-border food-borne outbreaks worldwide.

3. Applied public health microbiology and laboratory investigations

Biochemical description of seven putative novel species of the genus *Yersinia* identified by core-genome multilocus sequence typing

Supervisors: Anne-Sophie Le Guern, Bich-Tram Huynh, Javier Pizarro-Cerda

In France about 740 cases of Yersiniosis are reported per year (ECDC report). As *Yersinia* strains can be isolated from clinical materials, they have to be identified on the species and subgroup level to estimate their pathogenicity. In that context it is highly important to describe newly discovered *Yersinia* species to be able to distinguish them from the already described *Yersinia* species to assess their pathogenic potential. As the species discrimination by applying solely phenotypical methods of characterization is difficult, the molecular method enables elucidation on a species level. Therefore, a phylogenetic analysis based on cgMLST of the genomes of 238 strains belonging to 18 *Yersinia* species was performed by the French National Reference Laboratory and evidenced seven putative novel *Yersinia* species. Those were mainly derived from human stool samples (91.7%) besides veterinary (4.2%), environmental (1.4%), alimentary (0.7%) or undefined origin (2.0%). The new species were called by then *Y. frederiksenii* 2 and 3, *Y. kristensenii* 2 and 3 as well as *Y. new* 2, 3 and 4 with the last two species clustering phylogenetically at the root of the *Y. enterocolitica* strains. The aim of this project was the biochemical characterization of these 7 new species of the genus *Yersinia*. As those species have not been described at the start of the project, it was of relevance for public health to better distinguish them phenotypically from the disease-causing *Yersinia* strains for a first estimation of their pathogenic potential. In order to describe these 7 new species, the EUPHEM fellow analysed the YNRL database and identified the specific microbial characteristics of these strains. As a next step, the fellow performed biochemical tests to describe the phenotypical characteristics of the putative new *Yersinia* species (presence of lipase activity, pyrazinamidase activity, motility and the utilisation of sugars/chemicals as identified by the application of the tests API 50 CH and API 20E). Additional O-serotyping was performed to characterize the species. The obtained results of those 7 new species were compared to the described *Yersinia* species in the surveillance database to identify the differences that characterize the new species. The significance of the observed biochemical patterns was tested via Fisher's exact test. The strains of the putative novel species were highly variable in sample size: *Yersinia new* 2 (n=2), *Y. new* 3 (n=3), *Y. new* 4 (n=35), *Y. frederiksenii* 2 (n=11), *Y. frederiksenii* 3 (n=62), *Y. kristensenii* 2 (n=5) and *Y. kristensenii* 3 (n=6). The new *Y. kristensenii* species showed differential characteristics in D-arabitol ($p \leq 0.0109$), indole ($p \leq 0.0311$), L-fucose ($p \leq 0.0411$), lipase ($p \leq 0.0137$), gluconate and 5-colo-gluconate ($p = 0.0049$). Within the new *Y. frederiksenii* species lipase ($p < 0.0001$) and citrate ($p \leq 0.002$) varied. Strains of *Y. new* 4 differed in VP ($p = 0.0019$), L-fucose ($p = 0.0183$) and D-arabitol ($p = 0.0071$).

They were strongly associated with the O:10,34 serotype. Sample sizes of the species *Y. new* 2 and 3 were too low to determine significant characteristics. However, *Y. new* 2 was found to be negative for pyrazinamidase-activity which is usually associated with virulence in *Yersinia*. To conclude, biochemical characteristics were successfully applied by the fellow to discriminate the putative novel *Yersinia* species, as strong associations with phenotypical characteristics were found. However, the low number of strains in some species requires larger studies. As a final step, the association of these species with their epidemiological and clinical characteristics will be evaluated to further assess their pathogenic potential. The description of six of those above mentioned novel species is going to be published in the International Journal of Systematic and Evolutionary Microbiology (see publications).

Training modules

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Project Review Module in Prague, Czech Republic, from 26th-30th August 2019: In this module all fellows present one of their projects to a small group for a detailed discussion on the presentation and project. This module serves to draft, train and improve conference contribution on scientific projects. The EUPHEM fellow presented the *Yersinia* project to her colleagues. On top, the fellows obtained lectures on the interpretation of laboratory results of vaccine-preventable diseases.

Educational outcome: The fellow learned a lot about *Yersinia* as potential gastrointestinal pathogens and extended her skills in the application of standard laboratory methods for the identification and characterization of *Yersinia* species. She gave presentations, drafted an abstract and contributed to a publication in the International Journal of Systematic and Evolutionary Microbiology.

4. Biorisk management

Mandatory Biosafety trainings at Institut Pasteur for laboratory and BSL-3 work: Training courses on general and laboratory prevention, biological and chemical risks in the laboratory, autoclave training and on biosafety in the BSL-3 laboratory

At the fellow's arrival at Institut Pasteur mandatory online safety trainings as offered by Kaptitude needed to be passed for being allowed to work at the institute and in the laboratories. Those trainings were about prevention as well as biological and chemical risks that one can encounter in the laboratory: Prevention at Institut Pasteur - General 2018, Prevention at Institut Pasteur – Laboratory, Biological risks in the laboratory and Chemical risks in the laboratory. For being able to learn the methods for rabies diagnosis to perform the research work under BSL-3 conditions, the fellow was undergoing BSL3-Training including a mandatory autoclave training in 2018 and 2019.

Applied Biorisk project: A *One Health* workshop for improved rabies diagnosis and control in Harare, Zimbabwe, in December 2019 - a hands-on experience

Supervisors: Laurent Dacheux, Florian Liégeois, Lambert Fadzai Gwenhure, Hervé Bourhy

Rabies surveillance and diagnosis capacities are insufficient in many rabies enzootic countries like Zimbabwe in Southern Africa, leading to an under-reporting of the disease and delayed post-exposure prophylaxis. Therefore, the specific objectives of this project were to plan and conduct a One Health workshop for improved rabies diagnosis and control in Zimbabwe in order to strengthen its existing diagnostic capacities and to implement new diagnostic tools for enhanced rabies surveillance even in rural settings. The following standard diagnostic techniques for rabies, as applied in the Rabies National Reference Laboratory and WHO Collaborating Center at Institut Pasteur, Paris, France, were first learned by the fellow including a training to work under BSL-3 conditions and then taught jointly under MIC conditions in the workshop in Harare, Zimbabwe: Fluorescent Antibody Test (FAT), Rapid Immunochromatographic Diagnostic Test (RIDT), Enzyme-linked Immunosorbent Assay (ELISA) as well as conventional (RT-PCR) and real-time Reverse Transcription Polymerase Chain Reaction (RT-qPCR). The 4-day long workshop took place from 17th to 20th December 2019 at the Veterinary Department and University of Zimbabwe in Harare. It was attended by 18 Zimbabwean veterinarians and molecular biologists involved in the field of rabies research and diagnostics, both from the Health and Veterinary sectors, and achieved to present an update on the major state-of-the-art techniques for rabies diagnosis in humans and animals by combining plenary lectures, performing hands-on training and discussing the endemic rabies situation in Zimbabwe. The fellow was involved in all of these steps. As a result, the workshop contributed to diagnostic capacity building by enhancing laboratory surveillance of rabies in Zimbabwe following a One Health approach. It gave guidance and support to the national Public Health workers involved in rabies diagnosis, surveillance and control. On top, it underlined the high importance of dog control and dog vaccination programs as the preventive measure of choice to stop the vicious circle of dog-mediated rabies transmission to animals and humans in Zimbabwe.

Applied Biorisk- and Quality Management research project: Evaluation of different storage techniques for reliable rabies diagnosis under low- and middle income (LMIC) settings

Supervisors: Laurent Dacheux, Hervé Bourhy

From January to March 2020 the fellow performed a biorisk and quality management (QM) research project under BSL-3 conditions in the National Reference Laboratory and WHO Collaborating Center at Institut Pasteur (IP) with the goal to improve reliable rabies diagnosis of human saliva and animal skin samples - especially in low and middle-income settings (LMIC) as those samples are often transported or stored under suboptimal conditions in rabies endemic countries. For the BSL-3 work she used independently personal protective equipment, conducted by herself safe handling of highly pathogenic rabies virus, waste management and safe discharge of contaminated material. She understood and applied the entry and exit procedures for the BSL-3 and P2+ labs. She was involved in experimental project design, conduction of infection experiments as well as RNA isolation of rabies virus (RABV) for rabies diagnosis method evaluation. For the QM experiments human saliva, obtained from the IP biobank, was pooled and spiked by the fellow with Thai rabies virus. The fellow performed also the excision of skin punches of dead Thai rabies virus infected mice. These saliva samples and skin punches were then stored under different storage conditions with respect to media, time and temperature. The experiments included storage of rabies-positive and negative samples in different media (RNA later, RNA/DNA shield, no medium) at different temperatures (-80°C, 4°C, RT, 37°C) for varying time periods (6h, 24h, 1 week, 1 month). The respective viral RNA of these samples was extracted by the fellow under BSL-3 conditions. The long-term goal of this project is to assess the diagnostic test performances, as especially time and temperature play a key role for successful rabies detection in tropical enzootic countries. This project is going to identify the best possible way of the storage of rabies samples (medium, temperature and duration) to secure reliable and accurate diagnosis of rabies positive samples in LMIC and for remote settings beyond. In addition, the fellow was involved in the diagnosis of a rabies-positive human brain sample sent to Institut Pasteur by WHO to molecularly confirm and trace back phylogenetically the differential diagnosis.

Training modules

Biorisk and Quality Management Module: ECDC provided in 2020 lectures on Biorisk and Quality Management as well as Biorisk scenarios online to teach their fellows on biorisk mitigation, QM and EQAs.

Educational outcome: The fellow learned at Institut Pasteur a lot about prevention and biorisk for being able to work in normal and BSL-3 laboratories: She was trained in biosecurity to identify and mitigate risks, to use personal protective equipment, perform waste management and safe handling of infectious agents as well as autoclaves. The fellow used these skills to work with rabies-positive samples independently under BSL-3 and P2+ conditions. During that time she learned all WHO-recommended rabies diagnostic techniques while participating in the daily routine tasks at the Rabies National Reference and WHO Collaborating Center for Rabies at Institut Pasteur in Paris. These encompassed the performance and interpretation of Fluorescent Antibody Tests (FAT), direct Rapid Immunohistochemical Tests (dRIT), Rapid Immunodiagnostic Tests (RIDT), Enzyme-linked Immunosorbent Assays (ELISA) and molecular techniques (RT-qPCRs and conventional RT-PCRs followed by gel-electrophoresis). Last but not least, she had the chance to participate at an international One Health mission to jointly teach these methods within the framework of capacity building and enhancing laboratory surveillance in Zimbabwe.

5. Quality management

Laboratory proficiency evaluation: Participation at an External Quality Assessment programme for Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and West Nile Virus (WNV) diagnostics

Supervisors: Christophe Batéjat, Jean-Claude Manuguerra

The Laboratory for urgent response to biological threats (CIBU) was created to respond to “specialized biological urgencies” in France. These urgencies are dealt with in the event of epidemics, accidents, or terrorist attacks using biological weapons which can endanger public health. The CIBU is divided into 3 major poles (Bacteriology, Virology and Pathogen genotyping) and intervenes 24/7 in the detection of a wide array of pathogens in particular for the following microbiological agents. For Bacteria it is responsible for agents of botulism, anthrax, plague, tularemia, glanders, melioidosis. For viruses it performs the detection of influenza A(H5N1) and (H7N9) viruses, MERS-Coronavirus, orthopoxviruses and arboviruses. It is also involved in the detection of class 4 infectious agents by molecular biology without virus amplifications in cell culture: Ebola and Marburg, Crimean Congo, Lassa and Nipah viruses. In order to ensure the quality of the diagnostic results, the unit follows the same Insurance Quality standards (ISO 15189) as the French National Reference Centers and WHO-Collaborative Centers. In this context, the CIBU participates in at least 4 different EQA programs per year, as well as an annual exercise on the laboratory response to biothreats. The objective of this “quality management” project was for the fellow to coordinate, perform and/or follow as well as report the results of the experiments of the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and West Nile Virus (WNV) External Quality Assurance (EQA) test that took place at the Virology Unit at the Laboratory for the urgent response to biological threats (CIBU) at Institut Pasteur in spring 2019. As an audit was performed at that time as well, the fellow was also able to attend and observe its ongoing procedures.

Training modules

Biorisk and Quality Management Module: ECDC provided in 2020 lectures on Biorisk and Quality Management as well as Biorisk scenarios online to teach their fellows on biorisk mitigation, QM and EQAs.

Educational outcome: The fellow was involved in the External Quality Assessments (EQA) of West Nile Virus (WNV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and witnessed a national audit at the PIV of CIBU at Institut Pasteur in spring 2019. Thereby, she learned about quality standards and guidelines, developed a good understanding of quality control processes, learned to perform EQAs, manage their associated biorisks and to write their reports.

6. Teaching and pedagogy

Global education by e-learning via Massive Open Online Courses (MOOCs) on public health issues targeted for low and middle income countries (LMIC)

Supervisors: Dominique Franco, Monica Sala

It is a high priority of Institut Pasteur (IP) to provide global access to education on infectious disease topics of relevance for public health. As fair access to state-of-the-art science is often unequally distributed on a global scale, IP is strongly investing in e-learning and creates since 2014 Massive Open Online Courses (MOOCs) to grant high-level online-education to a large worldwide audience including low- and middle-income countries (LMIC) (www.pasteur.fr/moocs). Since 2014, IP has realized 17 MOOCs with free global access on the French platform *FUN* and partially on the platforms *XuetangX* and *UVS* targeting scientists, students, health care and public health employees. This project was based on the realization of the newest IP MOOC on *Emerging Viruses* (MOOC-EV) since September 2018. All steps of the MOOC development were performed by the fellow. This included the outline design following a careful definition of objectives, the choice of directors and speakers, the recording of video lectures, the drafting of multiple choice questions, the community management, the broadcasting of the MOOC and the final statistical evaluation of its learners. As a result, the MOOC on *Emerging Viruses* has been successfully developed and one Hangout was performed by the fellow. The MOOC-EV has been available for 11 weeks from 17th February to 4th May 2020 on the platform FUN and reached 6224 learners from 130 countries. The majority of learners, 4425 (71.1%), originated from HIC with France ranking first (3789; 60.9%). However, the proportion of the 1299 learners from LMIC was 20.9%. 500 learners (8%) did not reveal their country. The MOOC-EV encompassed 39 English lectures with French and English subtitles given by 33 speakers in seven chapters covering the most important aspects of EV. The chapter content met the objectives and ranged from a general introduction to the topic to explanations on the molecular mechanisms and conditions that drive virus emergence, epidemiological aspects to One Health. The MOOC also shed light on prevention, detection, early management, infection control and international response mechanisms towards emerging viruses. The MOOC-EV is a very good example for the costly and timely efforts of IP spent in equalizing worldwide access to quality scientific education. It has had an immense global outreach towards a diverse professional audience and aimed to reach as well as teach this audience to be better prepared for EV outbreaks, which can - just like the SARS-CoV-2 pandemic associated with COVID-19 - appear anytime in the future.

Other teaching activities:

1. **Problem-based Learning (PBL)-Presentation** of EUPHEM Cohort 2018 on Antimicrobial Resistance in the Introductory Course on Spetses, Greece, in October 2018
2. **Performance of in total eight hangouts** for the MOOCs *HIV Science* (four hangouts), *Viruses and Human Cancers* (three hangouts) and *Emerging and Re-emerging Viruses* (one hangout). A so-called hangout is a live Question and Answer (Q&A) online session that addresses questions that have been posted in the discussion platform of the respective MOOC community. The Hangouts have been recorded and can be found on YouTube.
3. **Presentation in the Journal Club 2019 of the Department for Microbiology on 5th February 2019:** "Acute encephalitis cases in Germany associated with Bornavirus infections"
4. **Presentation in the Rabies Laboratory Meeting on 27th March 2020:** "Acute encephalitis cases associated with Bornavirus infections in Germany" including a short presentation on the rabies One Health workshop given in Harare, Zimbabwe, in December 2019 and on other ongoing activities in the rabies unit
5. **Presentation in the online Rabies Laboratory Meeting on 4th May 2020:** Selected publications covering "Central nervous system involvement of SARS-CoV-2"

Training modules

Introductory course on Spetses, Greece, from 24th September to 12th October 2018: In this module the fellows obtained lectures on pedagogics and teaching. The topic of the Problem-based Learning (PBL)-Presentation was introduced and the group work facilitated. At the end, the group work presentation was held in front of the ECDC coordinators and supervisors.

Project Review Module in Prague, Czech Republic, from 26th-30th August 2019: In this module all fellows present one of their projects to a small group for a detailed discussion on the presentation and project. This module serves to draft, train and improve conference contributions on scientific projects. The EUPHEM fellow presented the *Yersinia* project to her colleagues. This way the fellows learn about the correct presentation styles.

Management, Leadership and Communication in Public Health Module in Stockholm, Sweden, from 10th to 14th February 2020: In this learning by doing module information was obtained via lectures on presentation and management styles and group exercises were performed to train how to present to different types of audiences (journalists, higher authorities like Ministry of Health (MOH) etc.).

Educational outcome: The fellow learned a lot about teaching in these two years. The gained knowledge ranges from designing the MOOC-EV, being a lecturer and co-director for this MOOC to the performance of one Hangout. She gave presentations alone or as part of group work: The latter was for example the case during the One Health Workshop in Harare, Zimbabwe, in December 2019, where the fellow held lectures and taught state-of-the-art techniques of rabies diagnostics in a middle-income setting for capacity building and enhanced laboratory surveillance in a rabies endemic country. However, the fellow also used the stage to present topics that were of interest to her (e.g. human encephalitis cases caused by bornavirus infections; selected SARS-CoV-2 publications) during a Journal Club at the Institut Pasteur, the MOOC lecture and during laboratory meetings.

7. Public health microbiology management

Rabies management and communication by the creation of a website dedicated to the French network of anti-rabies clinics in cooperation with Santé Publique France and the French Ministry of Health

Supervisor: Hervé Bourhy

The epidemiology of rabies in France and Western Europe has changed during the past 22 years. In France, rabies in non-flying terrestrial mammals was declared to be eliminated in 2001, and the risk of rabies is now limited to contact with bats, rabid animals that were illegally imported from rabies-enzootic countries and travelers' exposure in enzootic areas. However, the healthcare professionals' perception of the rabies risk is slowly changing in France. The risk of being infected is extremely low or even negligible in mainland France and rabies is now perceived as a threat only if exposure takes place outside Western Europe. The decline of Post-Exposure-Prophylaxis (PEP) administration over the past 22 years illustrates the growing understanding of the changing risk by both, the public and healthcare professionals. However, adapting medical practice to the actual rabies risk is a long and difficult process, in the field of potentially lethal and rare communicable diseases, especially in the absence of any active curative treatment. Therefore, information and education are needed at different levels to allay patients' and healthcare professionals' unjustified concerns and emphasize real risks.

The aim of this project was the creation of a website to provide training courses to physicians in charge of anti-rabies clinics including knowledge assessments. It should also provide access to all national and international guidelines needed for rabies counseling. This website should serve as a forum for the exchange of information, alerts and experiences (e.g. the management of difficult situations arising during rabies counselling). The project was initiated by the EUPHEM fellow in February 2020. She joined twice the counselling sessions as performed at the Institut Pasteur's anti-rabies clinic (CAR). There numerous persons living in France are treated before or after potential rabies exposure (e.g. vaccinations for travelers who are going to visit rabies endemic countries in the frame of travel medicine as well as administration of PEP to persons at risk of rabies virus exposure, if applicable). The fellow got an excellent insight into the problematic situations that can arise during counselling, if for example patients do not understand the risk assessments of the medical staff. Unfortunately, this project had to be stopped due to the SARS-CoV-2 pandemic and an associated shift in the allocation of resources.

Public Health Management for IP's Massive Open Online Courses

Supervisors: Dominique Franco, Monica Sala

The MOOC project involved besides teaching a lot of management skills of the fellow that can be considered as Public Health Microbiology Management due to the scientific topics and public health contents of the MOOCs: First hand, the fellow was responsible for designing the outline of the *Emerging and Re-emerging Viruses* MOOC (MOOC-EV) finding suitable content together with her main supervisor and the MOOC co-directors. This included planning of lectures and speakers as well as inviting them to give a lecture, travel organization and assistance during broadcasting, when needed. This all occurred in teamwork with her supervisor Dominique Franco of course. For the MOOC *Emerging and Re-emerging Viruses* she was organizing and performing one hangout by herself.

In addition, the fellow was also involved in the community management of the MOOC *HIV Science and Viruses and Human Cancers*, where she performed seven Hangouts. From 5th November to 31st December 2018, the MOOC on *HIV Science* reached 4455 learners from 131 countries with a proportion of 29.9% learners from LMIC. The MOOC on *Viruses and Human Cancers* gained from 7th January to 8th April 2019 3665 learners from 122 countries, with 20% of LMIC learners. For the community management of the MOOCs *HIV Science* and *Viruses and Human Cancers*, she

organized and performed in total seven hangouts that had to take part in congruence with the MOOC directors' timelines. She organized during these two years MOOC meetings, performed phone calls, contacted colleagues at Institut Pasteur and from other prestigious research facilities in France or abroad e.g. for the hangout sessions.

On top, the fellow was involved in proof-reading and revising MOOC flyers for the MOOCs *Medical Entomology* and the presentation page of the MOOC *Epigenetics*. She was giving an ECDC statement in the trailer of the MOOC on *Antimicrobial Resistance* as well as in briefing new community managers on the MOOC Community Management tasks. The fellow also helped to facilitate the cooperation between ECDC and Institut Pasteur to offer IP's Vaccinology MOOC as a SPOC to the EPIET/EUPHEM fellow and supervisor community in the framework of the Fellowship's Vaccinology module 2020.

Training modules

Management, Leadership and Communication in Public Health Module in Stockholm, Sweden, from 10th to 14th February 2020: This module taught the fellows in many lectures and interactive sessions how to best lead, manage and communicate in the Public Health working environment.

Educational outcome: The fellow learned to apply Public Health Microbiology management and the necessary skills to perform her EUPHEM projects. She used it among other projects for designing and performing all tasks involved in the MOOC project, for presenting scientific projects to diverse audiences (e.g. lecture in the MOOC-EV, One Health workshop in Zimbabwe, presentations at IP or in the modules) and for reaching her fellowship objectives as good as possible.

8. Communication

Publications

*shared first authorship

Le Guern AS, Savin C, **Angermeier H**, Brémont S, Clermont D, Mühle E, Orozova P, Najdenski H, Pizarro-Cerdá J: *Yersinia artesianiana* sp. nov., *Yersinia proxima* sp. nov., *Yersinia alsatica* sp. nov., *Yersinia vastinensis* sp. nov., *Yersinia thracica* sp. nov. and *Yersinia occitanica* sp. nov., isolated from humans and animals. *International Journal of Systematic and Evolutionary Microbiology (IJSEM)* 2020 Oct; 70(10):5363-5372. (<https://www.microbiologyresearch.org/content/journal/ijsem/10.1099/ijsem.0.004417#tab2>)

Grillová L*, **Angermeier H***, Levy M, Giard M, Lastère S, Picardeau M: Circulating genotypes of *Leptospira* in French Polynesia: An 9-year molecular epidemiology surveillance follow-up study. *PLoS Neglected Tropical Diseases* 2020 Sep28;14(9):e0008662. (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7544043/pdf/pntd.0008662.pdf>)

Angermeier H*, Franco D*, Sala M: Massive Open Online Courses (MOOC) of the Institut Pasteur as a tool for worldwide access to knowledge. Planned to be published.

Weill FX, Njamkepo E, **Angermeier H** et al.: *Salmonella* Napoli outbreak in France. Planned to be published.

Dacheux L, **Angermeier H** et al.: Rabies diagnosis under low-resources settings. Planned to be published.

Reports

1. **EQA Report:** West-Nile-Virus and Middle East Respiratory Syndrome Coronavirus EQAs performed at the CIBU/PIV at Institut Pasteur in March 2019
2. **Biorisk-Training Report:** Prevention, biological and chemical risks as well as BSL-3 and autoclave training at Institut Pasteur, 2018-2019
3. **Workshop Report:** One Health Workshop for teaching rabies diagnosis in Harare, Zimbabwe, December 2019
4. **Reflective Note for Teaching:** MOOC project
5. **Outbreak Investigation Report:** Annually re-occurring infections caused by *Salmonella enterica* serotype Napoli in France (currently in preparation)

Conference presentations

1. **Angermeier H**, Grillová L, Lastère S, Levy M, Picardeau M: *Molecular epidemiology of leptospirosis in Tahiti, French Polynesia, during the 13 years-time span from 2007 to 2019*. Accepted Poster Presentation: ECCMID 2020, abstract available in the ECCMID 2020 abstract booklet.
2. **Angermeier H**, Le Guern AS, Bremont S, Savin C, Pizarro-Cerda J: Biochemical description of seven putative novel species of the genus *Yersinia* identified by core-genome multilocus sequence typing (cgMLST). Accepted Poster Presentation: ECCMID 2020, abstract available in the ECCMID 2020 abstract booklet.
3. **Angermeier H**, Fadzai Gwenzure L, Guerrini L, Bourhy H, Parize P, Liégeois F, Dacheux L: A hands-on experience - a *One Health* workshop for improved rabies diagnosis and control in Harare, Zimbabwe, in December 2019. Plenary presentation at the Project Review Module 2020.

Other presentations

1. **Problem-based Learning (PBL) presentation of EUPHEM Cohort 2018**: "Importance of AMR as PH threat" in the Introductory Course on Spetses, Greece, in October 2018
2. **Journal Club 2019 of the Department for Microbiology at Institut Pasteur**: "Acute encephalitis cases in Germany associated with Bornavirus infections", 5th February 2019
3. **Yersinia Unit Lab Meeting**: "Description of strains belonging to 8 new species of *Yersinia*", 6th February 2019
4. **Project Review Module 2019**: "Biochemical description of eight new species of the genus *Yersinia*", 28th August 2019
5. **PIV/CIBU Laboratory Meeting**: "Nationwide representative serosurvey of Hantaviruses circulating in Bangladesh, 2014-2016", 19th September 2019
6. **Lecture in the Emerging and Re-emerging Viruses MOOC**: "Bornavirus & Borna Disease", 25th October 2019
7. **One Health Workshop on rabies diagnostics in Harare, Zimbabwe**: "Rabies laboratory surveillance and diagnostic experiences in humans and animals", 17th-20th December 2019
8. **One Health Workshop on rabies diagnostics in Harare, Zimbabwe**: "Facts on rabies: From Europe, Africa and the world", 17th-20th December 2019
9. **Rabies Laboratory Meeting**: Presentation, updated for 2020: "Acute encephalitis cases associated with Bornavirus infections in Germany" including presentation of the "Rabies One Health Workshop" in Harare, Zimbabwe, 27th March 2020
10. **Rabies Laboratory Meeting**: Presentation of selected publications covering "Central nervous system involvement of SARS-CoV-2 and caused neurologic features", Rabies Laboratory Meeting, 4th May 2020
11. **Project Review Module 2020**: A hands-on experience - a *One Health* workshop for improved rabies diagnosis and control in Harare, Zimbabwe, in December 2019.

Other

1. **Creation and maintenance of a Confluence website on the SARS-CoV-2 outbreak associated with COVID-19** for the Outbreak Investigation Taskforce (OITF) at Institut Pasteur and the International Institut Pasteur Network (RIIP) from February to May 2020
2. **Translation of SARS-CoV-2 laboratory diagnostics/surveillance documents from French into English** of the Respiratory Viruses National Reference Laboratory for France
3. **Development of a Massive Open Online Course (MOOC) on Emerging and Re-emerging Viruses**
4. Conduction of **eight MOOC hangouts**: Four hangouts for the MOOC HIV Science, three hangouts for the MOOC Viruses and Human Cancers and one hangout for the MOOC Emerging and Re-emerging Viruses.
5. Involvement in the **creation of other MOOC documents** (e.g. flyers, presentations pages, trailers)

Training modules

Introductory course on Spetses, Greece, from 24th September to 12th October 2018: In this module the fellows obtained hints, ideas and tools for teaching and presenting on conferences (posters or orally).

Project Review Module in Prague, Czech Republic, from 26th-30th August 2019: In this module all fellows presented one of their projects to a small group for a detailed discussion on the presentation and project. This module served to draft, train and improve conference contributions on scientific projects. This way the fellows learn about the correct presentation styles.

Management, Leadership and Communication in Public Health Module in Stockholm, Sweden, from 10th to 14th February 2020: This module taught the fellows in many lectures and interactive sessions how to best lead, manage and communicate in the Public Health working environment.

9. EPIET/EUPHEM modules attended

1. **EPIET/EUPHEM Introductory Course** on Spetses, Greece, from 24th September to 12th October 2018
2. **Outbreak Investigation Module** in Berlin, Germany, from 03rd to 07th December 2018
3. **Multivariable Analysis Module** in Madrid, Spain, from 25th to 29th March 2019
4. **Rapid Assessment and Survey Methods Module** in Zagreb, Croatia, from 13th to 18th May 2019
5. **Project Review Module** 2019 in Prague, Czech Republic, from 26th-30th August 2019
6. **Management, Leadership and Communication in Public Health Module** in Stockholm, Sweden, from 10th to 14th February 2020
7. **Vaccinology Module** in cooperation with the Vaccinology SPOC of Institut Pasteur, online, May-June 2020
8. **Project Review Module 2020**, online, from 24th to 28th August 2020

10. Other training

1. Attendance of **French Language Courses**: Conduction of 31 hours of WEFIT-French Language Training
2. Attendance of **Institut Pasteur PPU French Courses** from 2018 to 2020
3. **Biosafety in the BSL-3 laboratory** at Institut Pasteur
4. **Autoclave Training** at Institut Pasteur (for being able to enter the BSL-3 laboratory for work)
5. Online-Trainings at Institut Pasteur given by Kaptitude: **General and laboratory prevention; Biological risks in the laboratory, Chemical risks in the laboratory**
6. **UNDSS "BSAFE" Training Certificate**, 7th May 2019
7. Training in rabies laboratory diagnostic techniques by the Rabies National Reference Laboratory and WHO Collaborating Center at Institut Pasteur in Paris, France, in order to participate as a facilitator at the "*One Health Workshop on rabies diagnosis*" in Harare, Zimbabwe, 17th-20th December 2019
8. Institut Pasteur Workshop "**Bibliographic tools / Atelier outils bibliographiques au banc d'essai**" on 24th April 2020
9. Institut Pasteur Workshop "**ZOTERO Training**" on 19th May 2020
10. Institut Pasteur **Vaccinology Massive Open Online Course (MOOC) / SPOC**, May 2020

Discussion

Coordinator's conclusions

One of the main goals of the EUPHEM programme is to expose fellows to diverse and multidisciplinary public health experiences and activities, thus enabling them to work across different disciplines. This report summarises all activities and projects conducted by Hilde Angermeier during her two-year EUPHEM fellowship (cohort 2018) as an EU-track fellow at the Institut Pasteur in Paris, France. Hilde is the third appointed EU-EUPHEM fellow in France. The projects described in this portfolio demonstrate a diversity of public health microbiology projects. The epidemiological studies consisted from outbreak investigations at national level (including a central role in the response to the COVID-19 pandemic) to surveillance activities including optimizing assays to conduct sero-surveys of Hantaviruses in Bangladesh or the study of the epidemiology of leptospirosis in Tahiti and Niger. All projects covered a diverse range of disease programmes involving multidisciplinary working and teamwork. Hilde has shown a high capacity of public health management by working with an active role in interdisciplinary groups and bringing different professionals together. She has strongly supported the teaching activities in the Institute Pasteur by actively participating in the organization of the Massive Open Online Course (MOOC) on Emerging Viruses. Activities were in line with the 'learning by doing' of the EUPHEM programme and fulfilled the core competency domains described for professionals in their mid-career and beyond. Activities were complimented by nine training modules providing theoretical knowledge.

Projects had a clear outcome, with results communicated in scientific journals and at conferences. The contributions made by Hilde to IP's work indicate the importance of developing a future critical mass of highly skilled field public health microbiologists within Member States to contribute towards national preparedness as well as being available for responses in the interest of the EU. The EUPHEM Coordinator Team concludes that the fellow has succeeded in performing all her tasks to a very high standard and with a professional and critical attitude. We wish the fellow every success in her future career.

Supervisor's conclusions

In 2018, when I re-met Hilde at the Market, I was happy to select her to come to Institut Pasteur, as I already had the occasion to appreciate her at a previous selection interview. At that time, the match did not work out. This is to say that our common history as EUPHEM fellow and supervisor had begun already more than 2 years ago. Then, at the 2018 Market, we both expressed again the will to work together and this time it matched: she was selected to come to our Institut Pasteur. Now, two years after, I can say that it was worth to put my confidence in her twice. She has brought a lot to our Institute. She has a serious, rigorous and calm personality associated to a lot of energy put at working. All this is essential to overcome problems which is the daily life in dealing with public health and field microbiology research. She always shows a real quiet strength in the midst of tempest. The live test was directly performed at Institut Pasteur in Paris, when the SARS-CoV-2 outbreak showed up in France resulting in a major pandemic. She asked to be on the frontline at the Institute to be part of the Institut Pasteur Outbreak Investigation Task Force (OITF) to face the coronavirus outbreak, when most of the Institute was undergoing lockdown at home. Her contribution to the task force was remarked and thanked by one of the members, Professor Arnaud Fontanet, of the Scientific Council of the French President and by Vincent Richard, member of the International Directorate of Institut Pasteur as well as Isabelle Cailleau, member of the IP Medical Department. I am grateful and proud of her for that. Along these two years, Hilde has gained the trust of the renowned Institut Pasteur scientists and tightly collaborated with them as shown by her publications. She was an active member of the IP Teaching Center, the Biological Emergency Response Unit (CIBU) as well as the Yersinia-, Leptospira-, Salmonella- and Rabies National Reference Centers and partly even WHO-CCs located at the Institut Pasteur. There she showed valuable ability in learning and applying new experimental methodologies to be used in field microbiology and outbreak investigations. The feedback that I received from all these research entities is that Hilde was always very constructive, hard-working and showed a greatly appreciated team-player attitude. For all this, Hilde is the kind of person that can scientifically and psychologically be an efficient actor on the frontline of any major infectious disease outbreak. The enormous amount of work she has accumulated along these two years shows her great motivation and ability to assimilate new knowledge on public health microbiology, but also in communicating public health topics. Indeed, aside to this intense research work, Hilde invested major energies in modern Public Health communication means to professionals working in the field, deeply believing that knowledge has to be shared globally for international collaboration on public health issues. She was an active part of many Institut Pasteur Massive Open Online Courses (MOOCs) as a Community Manager (animation of the online community and creation of hangouts addressing international scientific debates) of the MOOC on "HIV Science" and "Viruses & Human Cancers", speaker of the trailer for the MOOC "Antimicrobial Resistance", facilitator for the cooperation with ECDC of the MOOC/SPOC "Vaccinology" and she was involved in the design of the newest IP MOOC on "Emerging and Re-emerging Viruses", where she played a major role as a MOOC Director and lecturer. As said by the Head of the MOOC Team of the Institut Pasteur, Hilde brought to Institut Pasteur's digital education a new breath and MOOCs like "Emerging Viruses" would have never been so scientifically solid without her intelligent contribution". Scientific collaborations and interdisciplinary communication on public health topics were possible also thanks to Hilde's great networking abilities. Thanks to her engagement and seriousness in dealing with public health issues, she was considered by Pasteurians as a member of the IP community consolidating long-term scientific connections that will be useful for her professional future. As supervisor, I had a great pleasure to work with Hilde for both the professional and personal aspects. As professional, it is great when you know that the person you work with is reliable, efficient, clever and constructive, especially in the context of this program where your name is engaged with the name of the fellow in your Institute, as the fellow works in different research entities of your own Institute. Finally, I would like to thank the ECDC EUPHEM program for allowing Institut Pasteur to participate to this excellent training program in field microbiology. A great experience that we are willing to renew.

Personal conclusions of fellow

I am personally very grateful that I got the opportunity to participate in ECDC's Program in European Public Health Microbiology (EUPHEM), which enabled me to dive into the cross-cutting world of Public Health, microbiology and applied infectious disease epidemiology under a One Health umbrella in the renowned National Reference Laboratories and WHO Collaborating Centers at Institut Pasteur in Paris, France. Through the fellowship I could extend my knowledge in Microbiology and Public Health by building up core competencies in Public Health diagnostics, research and epidemiology including work on a range of diverse pathogens that one can encounter in medical, tropical or clinical microbiology. I gained a lot of expertise, professionally and personally, in the last two years by being positively challenged in a French-speaking country with handling diverse projects in a multidisciplinary, international working environment at the same time. My special highlights were the possibility to work with renowned experts on such an impressive spectrum of pathogens - partly even under BSL-3 conditions – while applying a wide range of diagnostic state-of-the-art techniques not only in Paris, but also in near and far areas. These field missions ranged from swabbing reptiles, amphibians and molluscs in a French National Park for Salmonella to remote places like Harare, Zimbabwe, where I was involved in the conduction of a One Health workshop for improved rabies diagnostics, laboratory surveillance and control in this endemic middle-income-country. All my fellowship's outcomes and experiences would have been never possible without ECDC's EUPHEM program and the great and knowledgeable people behind it at Institut Pasteur, ECDC or within its global network. Certainly, a remarkable experience was to be a piece of the Public Health puzzle during the SARS-CoV-2 pandemic in the last year of the fellowship, where one could feel the fellow's team spirit on a daily level. Therefore, I truly believe that the ECDC fellowship program and its Alumni network (EAN) are paramount for the future of International Health Microbiology and Field Epidemiology to protect and improve the health of entire nations.

Acknowledgements of fellow

First of all, I would like to thank my site supervisor, Monica Sala, for offering me the great opportunity to work at Institut Pasteur in Paris, France, and for her always excellent supervision and support throughout the entire fellowship time. Due to her I felt immediately home in Paris. I had a fantastic time as well as experience at Institut Pasteur in Paris, not only professionally but also beyond. Monica was always optimistic, helpful and motivating. I really appreciate her efforts in searching and handing over to me at my arrival so many interesting EUPHEM projects, which just underlines her devotion to ECDC's EUPHEM program and trust in me.

My deepest gratefulness goes above that to all my different project supervisors and mentors in those two years: Dominique Franco, Anne-Sophie Le Guern, Javier Pizarro-Cerda, Bich-Tram Huynh, Jessica Vanhomwegen, Christophe Batéjat, Jean-Claude Manuguerra, Linda Grillová, Jean-François Mariet, Laurent Dacheux, Hervé Bourhy, François-Xavier Weill, Elisabeth Njamkepo, Alexandre Boissinot, Arnaud Fontanet, Sylvie van der Werf and their associated team members among others from the different National Reference Laboratories (NRL) and WHO Collaborating Centers (WHO-CC) at Institut Pasteur in Paris, France, who were offering me generously the possibility to dive into their current projects. It was an absolute honor to get insights into your daily working activities as well as responsibilities and to learn from you, not only state-of-the-art Public Health microbiology and epidemiology, but also beyond including some French. I am truly happy to have met you all and I had wished it would have been possible to stay longer for every single project, as there is always so much more to discover in science. On top, it was an excellent opportunity to improve my French in France's capital for two years.

I am also thankful to Isabelle Cailleau, Monica Sala and her administrative assistants for their support during my first steps settling as a working citizen in France with all of its associated administrative and financial challenges as well as when leaving France again. Isabelle involved me in the SARS-CoV-2 associated with COVID-19 outbreak support at Institut Pasteur that I am really grateful for.

Moreover, I would like to honor my frontline coordinator Silvia Herrera León for her excellent, reliable and trustful supervision during my fellowship. I really enjoyed working and meeting her every single time. A big thank you goes also to Aftab Jasir for sharing with me her professional wisdom and experience as an interim frontline coordinator. Thank you both for the mentoring, constructive feedback and guidance throughout the fellowship. The fellowship was a very enriching professional and private experience that will stay in my heart forever as will Institut Pasteur and France.

On top, I also highly appreciate the good work of the ECDC fellowship office and the ECDC staff to make the fellowship and its numerous real-life and virtual modules happen. Thus, I would also like to express my gratitude to all ECDC EPIET and EUPHEM supervisors/coordinators involved in my fellowship program for their commitment to high-quality education. A special thank you goes also to my friends, the EUPHEM and EPIET fellows of Cohort 2018, for their never-ending motivation and support throughout the fellowship, no matter where they were in Europe or on the globe. At the end, I would like to thank Aftab Jasir for her strong commitment to Public Health Microbiology and its associated training opportunities which made this fellowship experience possible for me. I am pleased and proud to have entered the EPIET/EUPHEM family and to be a part of it by now.

Above all, I would like to thank my parents for supporting me in all my professional life endeavors that had led me to Paris, France, which would all not have been possible without their global vision and trust.