EUPHEM

EUPHEM REPORT

Summary of work activities

Umaer Naseer
European Public Health Microbiology Training Programme (EUPHEM), 2014 cohort

Background

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'.

The ECDC Fellowship Training Programme therefore includes two distinct curricular pathways: Intervention Epidemiology Training (EPIET) and Public Health Microbiology Training (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 paths that provide competency based training and practical experience using the 'learning by doing' approach in acknowledged training sites across European Union (EU) and European Economic Area (EEA) Member States.

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 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.

Stockholm, August 2016

This report summarises the work activities undertaken by Umaer Naseer, cohort 2014 of the European Public Health Microbiology Training Programme (EUPHEM) at the Norwegian Institute of Public Health (NIPH), Oslo, Norway.

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

Pre-fellowship short biography

Umaer completed his PhD in medical microbiology from the University of Tromsø, Norway in 2009, building upon his Masters in Technology (Molecular Biotechnology) from the same institute in 2005. During his PhD he worked on the molecular epidemiology of antimicrobial resistance, focusing on the dissemination of extended spectrum beta-lactamases (ESBLs), plasmid mediated AmpCs and carbapenemases produced by Enterobacteriaceae. His postdoctoral research focused on the identification of virulence factors, mutation potentials, and mechanisms of resistance and their transfer, with special focus on plasmid biology using tools related to whole genome sequencing. Since 2013, he has been working at the Norwegian Institute of Public Health at the Department of Foodborne Infections, where he has overseen the activities of the National Reference Laboratory for Enteropathogenic Bacteria in Norway, including surveillance, outbreak detection, molecular typing and method development.

Fellowship assignment: Public health Microbiology (EUPHEM) path

Methods

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

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

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

Results

The objectives of these core competency domains were achieved partly through project or activity work and partly through participation in the training modules. Results are presented in accordance with the EUPHEM core competencies, as set out in the EUPHEM scientific guide[1].

1. Epidemiological investigations

1.1. Outbreak investigations

Supervisors: Emily MacDonald, Anneke Steen, Bernardo Guzman, Karin Nygård, Katrine Borgen, Line Vold

A. Outbreak of gastroenteritis at the Radisson Blu Hotel Gardermoen, Oslo 2014

On the 21st of November 2014, the Norwegian Food and Safety Authorities (NFSA) notified the department of infection control at the NIPH about an outbreak of gastroenteritis at Radisson Blu Hotel Oslo. NIPH constituted a team to investigate the circumstances of the outbreak. Eighty-seven cases reported gastrointestinal symptoms (diarrhoea OR at least two other symptoms; vomit, nausea, stomach pains) after consuming lunch at the hotel on the 19th and/or 20th of November 2014. NIPH performed a retrospective cohort study among the hotel guests, and NFSA performed environmental screening. No patient samples were available for analyses. A detailed questionnaire was sent out, response rate was 50% (n=316). Both males and females were equally affected. Most frequently reported symptom was diarrhoea (99%), with symptom onset 12 hours after exposure and duration of illness 24 hours. Hypothesised source of the outbreak was a common dish served at lunch on both 19th and 20th of November. Clinical picture was compatible with enterotoxins produced by *Bacillus cereus*, *Clostridium perfringens*, *Staphylococcus aureus* or Enterotoxigenic *Escherichia coli* (ETEC). Epidemiological results were inconclusive, however a vegetable casserole was assumed as a possible source of illness RR 2.57 [95% CI 1.93-3.42, p <0.05].

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

NFSA recommended the hotel to conduct an audit of the internal control system to ensure that procedures were according to existing guidelines to minimize the risk of illness among its guests in the future, with special emphasis on procedures related to heating, cooling and storage of dishes served at the buffet. NIPH compiled an outbreak report and distributed it to the authorities and all the concerned parties. The fellow conducted all part of the outbreak investigation, from designing and sending out an online questionnaire, collecting and collating data, framing case definitions, performing descriptive and analytic statistical analyses, communicating with NFSA and the authorities, and writing the outbreak report.

B. Training modules

29.09.2014 - 17.10.2014 - The EPIET/EUPHEM introductory course: Three weeks of lectures, interactive sessions, case studies, group work, problem based learning (PBL), and writing of a research protocol as training in public health microbiology and intervention epidemiology. The course introduced fellows to the ten steps of an outbreak investigation.

08.12.2014 – 12.12.2014 - The outbreak module: An interactive course methodologically going through the steps required in an outbreak investigation, form data entry and management (in Excel), designing of questionnaires (in EpiData), descriptive and analytical data analyses (in STATA), communication of the findings and implementation of control measures.

23.03.2015 – 27.03.2015 – The multivariable analysis module: An interactive statistic course introducing multivariable analysis, stratification, interactions of variables, how to build logistic regression and binominal regression models (in STATA).

28.09.2015 – 02.10.2015 - Better training for safer food (BTSF): An European Commission initiative aimed at organising a training strategy in the areas of food law, feed law, animal health and animal welfare rules, as well as plant health rules. The course provides training into investigation of food-borne outbreaks aimed at improved cooperation, communication, collaboration and data control management between veterinarians, food protection agencies and the public health institutes. Organised by; Consumers, Health, Agriculture and Food Executive Agency (CHAFEA).

10.12.2015 – 24.12.2015 – Outbreak responsible: A two week long mandatory responsibility entrusted upon EUPHEM and EPIET fellows to monitor national and international outbreak notifications and weekly summarise for the institute orally and in a written report.

02.05.2016 – 13.05.2016 – Outbreak responsible: A two week long mandatory responsibility entrusted upon EUPHEM and EPIET fellows to monitor national and international outbreak notifications and weekly summarise for the institute orally and in a written report.

Educational outcome

The fellow received first-hand experience of an outbreak investigation, from determining the existence of an outbreak to implementation of control measures. He was involved in all steps during the outbreak investigation and applied his microbiological and epidemiological knowledge to frame and test hypothesis. As principal investigator, the fellow was required to coordinate a team of epidemiologist and communicate efficiently with all the stakeholders.

1.2. Surveillance

Supervisors: Ulf Dahle, Susanne G Dudman, Kirsti Vainio, Katrine Borgen, Oliver Kacelnik

A. Routine surveillance of enteropathogenic bacteria in Norway, 2014-date

The reference laboratory performs real-time molecular surveillance of the food-borne pathogens *Campylobacter, E. coli, Listeria, Salmonella, Shigella* and *Yersinia*. Molecular surveillance contributes significantly to the understanding of how these pathogens spread, by identifying their reservoirs and routes of transmission. In order to improve the surveillance systems ability to monitor trends and allow for a timely detection of outbreaks, we introduced standardised data entry forms compatible with real-time trend monitoring and data import into the BioNumerics platform. We completed data curation and entry forms for all pathogens under surveillance except *E. coli*, and developed a real time trend monitoring system that compares data on a monthly basis to the last five-year data. We imported data into BioNumerics for integrated data analysis of phenotypic and genotypic tests, as well as biological data management. The work has been automated, and has improved the surveillance system of enteropahtogeneic bacteria in Norway, by allowing for an early warning and response system, and fast and accurate comparability with historical data. Work is ongoing to format *E. coli* data entry in lines with the improved surveillance system. We recommend the reference laboratory to prepare internal reports on monthly bases, to

summarize the trend analysis. The fellow designed the project, performed data curation, designed and implemented data entry forms, applied trend analysis algorithms, and data import and analyses templates for BioNumerics.

B. Laboratory-based surveillance system for rotavirus infections in Norway, 2015, Part I – Setting up the system

Rotavirus (RV) infection is the most frequent cause of hospitalisation for gastroenteritis in children <5 years in Norway. In September 2014, rotavirus vaccine was included into the national immunization programme. In January 2015, The Department of Virology at the NIPH was assigned reference laboratory for RV-infection. The objective of this study was to implement a nationwide laboratory based surveillance systems for RV-infection in order to monitor the effects of the vaccine on the number of cases and circulating RV-strains. We performed an inventory of all RV-detection methodologies in use in Norway. We devised sampling, handling, shipment and reporting procedures, and communicated it to the laboratories. We devised sample reception, RV-confirmation and RV-typing procedures and implemented them at the reference laboratory. We instructed all laboratories (n=17) to submit a monthly electronic report summarizing all RV-tested samples and positive findings to the reference laboratory stratified by age groups and methods, and to collect and send the first ten RV-positive samples (stool/rectal swabs) each month to the reference laboratory. We instructed the reference laboratory to confirm RV-positive diagnosis with ELISA (WHO gold standard) and genotype strains (G-type and P-type) using an in-house RT-PCR upon reception of isolates. We implemented the surveillance system during March 2015, allowing for isolate and data collection from January to March 2015 in retrospect. An in place laboratory based surveillance system provides the NIPH with a unique opportunity to monitor the effects of the vaccine on the public health. The surveillance system enables comparisons of RV-infections and its outcomes before and after vaccination in terms of reduction in the total number of RV-cases, hospitalisations for acute gastroenteritis, risks or rates for different age groups, and monitoring shifts in the circulating RV-strains. The fellow contributed to the design of the surveillance system, described the steps required for its implementation, created data submission forms and devised submission and reporting procedures. Furthermore, he communicated with the laboratories and wrote the surveillance system protocol.

C. Laboratory-based surveillance system for rotavirus infections in Norway, 2015, Part II – Analysing the results

In January 2016, the RV-surveillance system completed its first year of running. The aim of this study was to examine laboratory participation, describe its findings and identify deficiencies in the system in order to improve the overall performance of the system. We collected data from monthly RV-diagnosis reports submitted from the individual laboratories, and confirmation and genotyping data of RV-isolates from the reference laboratory. During 2015, the laboratories (15/17) reported 986 RV-positive diagnoses. Each reporting laboratory provided data for 8.4 months and 11.9 laboratories submitted a report every month of the year. Children <5 years accounted for 74% of all reported cases, with an incidence of 22.9 per 10,000 for 2015. Most laboratories used a single method for RV-detection (n=10). At the reference laboratory 155/211 samples, from 15 primary laboratories tested positive for RV with ELISA and 165/211 by RT-PCR. The isolates typed into seven different G-genotypes (G1, G2, G3, G4, G9, G10 and G12) and three different P-genotypes (P4, P8 and P10). The genotypes with the highest prevalence was G1 (42%) and P8 (64%). We observed an overall good compliance to the surveillance system, although two laboratories failed to notify and submit isolates. Data from the first three months were lagging and incomplete due to the delayed implementation. The first year results formed a baseline for the following years to measure the effects of the rotavirus vaccine. We informed the laboratories failing to notify to ensure future participation. We advised the reference laboratory to include RT-PCR as a routine confirmatory test in addition to ELISA. We completed a report on the results and distributed it to the laboratories. The fellow collected and analysed the data, presented the data at scientific forums and wrote the annual report for distribution to the laboratories.

D. Setting up a syndromic surveillance system for asylum seekers in Norway, 2015

Due to the refugee crisis in Europe during autumn of 2015, there was a need to house the increasing number of people entering Norway. In Råde municipality (75km south of Oslo), a reception and registration centre was established, with a capacity to lodge 1000 people at any one time. The National Institute of public health (NIPH) assessed this centre to be a considerable health threat, as it involved the assembly of distressed and fatigued people with an unknown medical history. The NIPH recommended putting in place a syndromic surveillance system at this centre to complement the existing Norwegian notification based surveillance system, to enable rapid identification of potential outbreaks and enforce appropriate infection control measures. The EPIET and EUPHEM fellows of Norway, under guidance of a team of supervisors, were tasked to develop a protocol for a syndromic surveillance system at this registration centre, with a built-in flexibility to adjust the protocol for use at any other

locations if needed. We assessed the needs and requirements of the system through multiple onsite visits, meetings with health care providers and discussions with national and international experts with experience from similar work, and adapted a passive syndromic surveillance system for Råde. We based the registration of syndromes on the current coding system (IPCP-2) at the registration centres' health clinic, provided data collection tools in excel, examples of automated data analyses and reports, and provided tools that could be used to respond to alerts in the system. The established system served the recommendation of ECDC experts on prevention and control of communicable disease in Europe following the refugee upsurge. Complementing disease screening upon entry, public health follow-up, vaccination, general hygiene measures and the existing mandatory infectious disease notification system, the established syndromic surveillance system enabled a timely response to possible outbreaks and improved the public health. The fellow together with other EPIET and EUPHEM fellows wrote the protocol, developed data collection and data entry tools in collaboration with stakeholders, developed an example of automated data analyses and reporting system. The fellow presented the data at a national public health conference in 2015 (oral).

E. Training modules

29.09.2014 - 17.10.2014 - The EPIET/EUPHEM introductory course: Three weeks of lectures, interactive sessions, case studies, group work, problem based learning (PBL), and writing of a research protocol as training in PHM and intervention epidemiology.

23.03.2015 – 27.03.2015 – The multivariable analysis module: An interactive statistic course introducing multivariable analysis, stratification, interactions of variables, how to build logistic regression and binominal regression models (in STATA).

14.06.2015 – 20.06.2015 - Rapid assessment and survey methods module: An interactive course in sampling strategies and how to select appropriate sampling methodology adapted to the studied population and how to apply epidemiological skills to serve public health interventions as contributors in a multidisciplinary and international response to a complex emergency situation (CES).

Educational outcome

The fellow developed understanding of the importance of accurate data entry, how to implement relevant data comparison algorithms and perform data comparison. In addition, the fellow developed understanding of the need to integrate microbiological and epidemiological data in disease surveillance. In the process, the fellow acquired skills and experience in the planning and implementation phase of a surveillance system and data analysis.

2. Applied public health microbiology research

Supervisors: Ulf Dahle, Lin Brandal, Hilde Kløvstad, Øivind Jul Nilsen, Blystad Hans, Georgia Mandilara, Alkis Vatopoulos

A. Whole genome sequencing of the major listeria MLVA-cluster in Norway, 2005-2015

Multilocus variable number of tandem-repeats analysis (MLVA) is used for genetic fingerprinting of *Listeria monocytogenes* in Norway. From 2005 to 2015, 302 isolates have been distributed into 97 different MLVA-types. The most common type; 7-7-10-10-6 account for 30% of all isolates, and this strain was responsible for the largest outbreak of listeriosis in Norway, involving 21 cases and five deaths (2007). With low discrimination of the most frequently occurring MLVA-type, MLVA appears to be inadequate to allow timely and effective outbreak detection. The aim of this study was to investigate whole genome sequencing (WGS) as a tool for typing the most frequent *L. monocytogenes* MLVA-type by comparing three different analytical approaches in order to identify the most appropriate approach and to establish a working pipeline for routine WGS based surveillance of listeria. We selected 29/82 *L. monocytogenes* MLVA-type 7-7-10-10-6 (n=25) isolates and its single locus variants (n=4) according to; i) isolates previously associated with an outbreak (n=8), ii) isolates from cases with epidemiological links (n=4), and iii) isolates of supposed unrelated cases distant in geography and time (n=17). The isolates were sequenced and analysed using Reference Genome Mapping (RGM), Core Genome Mapping (CGM) and Gene-by-Gene mapping (GbG). All methodologies clustered the isolates belonging to an outbreak, confirmed a suspected mother to child transmission, and uncovered two new clusters of related isolates. This study demonstrated that a superior discriminatory power of WGS over MLVA regardless of analytical approach. However, before implementation of WGS, each method must be adapted to its intended use. The optimal approach to WGS analysis must have the ability to adapt to the required level of resolution to enable surveillance and outbreak detection. We recommend introducing WGS into routine surveillance of *L. monocytogenes* for accurate and timely detection of

future outbreaks in Norway. The fellow designed the study, wrote the protocol, established methodology, performed the experiments, analysed the data, disseminated the findings, presented data at ESCAIDE 2016 (oral) and at a national public health conference 2015 (oral), and wrote a manuscript.

B. Estimating the incidence of HIV in Norway, 2015

HIV infections remain of major public health importance, as there is no clear indication of a decline in the number of cases diagnosed each year. In the last decade, Norway has seen a threefold increase in the number of HIV reported cased. The aim of this study was to estimate the total population living with HIV in Norway, including those not yet diagnosed, in order to understand the burden of HIV and HIV associated to the MSM risk group. We calculated the overall HIV incidence, and HIV incidence in the MSM group using the incidence method for maximum likelihood (HIV modelling tool) developed by ECDC. We used national surveillance data from 1984 to 2015 of cases diagnosed with HIV, AIDS and HIV with a concurrent AIDS. We estimated 6348 HIV infections in Norway from 1980 to 2015, of which 5763 alive and diagnosed, and 563 (8.9%) alive and undiagnosed in 2015. For the MSM group, it was estimated that 2054 HIV infections from 1980 to 2015, of which 1905 alive and diagnosed, and 140 (6.9%) alive and undiagnosed in 2015. The MSM risk group accounted for 33% of the alive and diagnosed, and 25% among the alive and undiagnosed HIV population in Norway in 2015. An undiagnosed HIV-population of 8.9% was lower than expected, and among the lowest in Europe (12-50%). Undiagnosed HIV among the MSM group was on a downward trend and the increase of HIV-reported cases over the last decade suggested an increase in other risk groups. We recommend continued efforts to target the MSM group to decrease the HIV-undiagnosed population among MSM, and to enhance efforts to reach out and screen other potential risk groups, such as the immigrant population to uncover increasing trends of undiagnosed HIV. The fellow was involved with the designing of the study, wrote the protocol, identified methodology, performed the experiments, analysed the data and wrote a report on the findings.

C. Plasmid-mediated colistin-resistant Escherichia coli detected from 2014 in Norway

Since its first description, plasmid mediated colistin resistance (*mcr-1*) has been documented on a large scale among community-acquired and hospital-acquired pathogens. The aim of this study was to characterise the first *mcr-1* carrying *E. coli* strain detected in Norway during retrospective screening of non-enteropahtogenic *E. coli* from 2006 to 2015, in order to understand its potential for further spread. We performed antimicrobial susceptibility testing, sequencing and plasmid conjugation experiments. The strain was isolated in 2014 from a traveller returning from India, symptomatic with traveller's diarrhoea. The isolate was resistant to colistin (MIC 4 µg/mL.), ampicillin, nalidixic acid and ciprofloxacin. The *mcr-1* gene was identified on an Inc*I2* plasmid (pIP2-01), which displayed 99% similarity to pHNSHP45. Plasmid IP2-01 was transferable, with transconjugants conferring a 4- to 8-fold increase in colistin MIC while remaining susceptible to other antibiotics. There should be no selection pressure present in the community, and it is therefore likely to assume that the fitness cost associated with *mcr-1* would results in a rapid eradication of *mcr-1* from the normal gut microflora. However, travel and the constant influx of new and better-adapted strains is a continuous cause of concern. We did not detect any co-resistance linked to pIP2-01, but since *mcr-1* is located on an Inc*I2* plasmid, our biggest concern is that the evolutionary paths of ESBLs and *mcr-1* may converge, and the plasmid may find its way into nosocomial species causing severe outbreaks in the future. We recommend future studies on travellers to endemic countries to identify risk factors/behaviours and implement intervention strategies. The fellow participated in study design, identified appropriate methodology, supervised data analysis and contributed to writing of a manuscript for publication.

D. Characterization and sequencing of ESBL and AmpC encoding plasmids isolated from human and poultry Salmonella entérica and Escherichia coli isolates in Greece from 2008 to 2014

Salmonella and *E. coli* are widely distributed foodborne pathogen and one of the most common causes of bacterial foodborne illnesses worldwide. Resistance to first-line treatment antibiotics limit the choice of effective antimicrobial agents and delay the initiation of the adequate antimicrobial therapy. Since 2000, reports on the presence of ESBL- and plasmid-mediated cephalosporinases (AmpC) producing *Salmonella* and *E. coli* in animals and food is increasing. The aim of this study is to characterise and sequence plasmids, identified in ESBL or AmpC producing *Salmonella* and *E. coli* from human and poultry sources isolated in Greece from 2008 to 2014 in order to identify common transmission vehicles and their potential for spread. We collected 3,199 *Salmonella enterica* isolates; 2556 human isolates and 643 isolates from food (n=132) and food producing animals (n=511). In addition, three extended cephalosporin resistance (ESC) *E. coli* isolates from poultry recovered during an AMR

National monitoring programme in 2014 were included in this study. The isolates for ESC were screened, using resistant isolates as donors in conjugation experiments and sequenced transconjugants to obtain the plasmid sequences. Reads were assembled into circular plasmids and annotated the open reading frames, before performing a plasmid comparison. Finally, sequenced plasmids from 11 *Salmonella enterica* (9 human, 2 poultry) were assigned to ten different serotypes, and two *E. coli* isolates (poultry). Circulation of plasmids and comparisons are currently ongoing. This study will increase knowledge of plasmid epidemiology and help to apply intervention at farms to reduce the antimicrobial resistance determinants presence in food and food-producing animals and thereby in humans.

This project was a joint study between EUPHEM fellows Kyriaki Tryfinopoulou of Greece and Umaer Naseer of Norway, and served to strengthen the collaboration between the fellows. It allowed for the development of scientific skills and built a foundation for future collaborations. The fellow participated in the study design, writing of the protocol, identified appropriate methodology, performed data analysis and contributed to writing of a manuscript for publication.

E. Training modules

29.09.2014 - 17.10.2014 - The EPIET/EUPHEM introductory course: Three weeks of lectures, interactive sessions, case studies, group work, problem based learning (PBL), and writing of a research protocol as training in PHM and intervention epidemiology.

09.02.2015 - 13.02.2015 - Initial management in public health microbiology module: A one week introductory course into different types of personalities, management styles, time management, communication with different authorities and communication in the field.

11.03.2015 - 13.03.2015 - 4th Workshop rapid NGS for clinical, public health, and food microbiology: Three day course in next-generation-sequencing (NGS) technologies rapid development in last years and use in diagnostics and surveillance. Highlighting opportunities and challenges posed by this technology. An introduction to the sequence analyses software SeqSphere+.

23.03.2015 – 27.03.2015 – The multivariable analysis module: An interactive statistic course introducing multivariable analysis, stratification, interactions of variables, how to build logistic regression and binominal regression models (in STATA).

16.11.2015 - 18.11.2015 - The bioinformatics and phylogenetic module: A three day introductory course on basic tools of bioinformatics and phylogenetic analyses.

Educational outcome

The fellow was instrumental in all part of research and acquired training from designing the studies, writing protocols, identifying appropriate methods, implementing new methods, conducting the studies, managing a team of scientists, collecting and analysing the data, interpreting the results, disseminating and communicating the findings and writing reports or a scientific paper. The fellow gained insight into WGS methodologies and statistical modelling tools.

3. Applied public health microbiology and laboratory investigations

Supervisors: Dominique A. Caugant, Martin Steinbakk, Hans Blystad, Ulf Dahle, Lin Brandal, Line Vold, Astrid Wester, Anne Torunn Mengshoel, Vegard Eldholm, Dagny H. Dorenberg, Siri L. Feruglio, Beathe K. Granerud, Kieron Mulroney, Jarrad Hall, Tim JJ Inglis,

A. Epidemiology of invasive group A streptococcal infections in Norway 2010-2014

Streptococcus pyogenes or group A streptococcus (GAS) cause mild to severe infections in humans. Strains *emm1* were responsible for severe invasive GAS (iGAS) disease in the 1980s. Since *emm28* has become the dominant type in the Nordic countries. In this study, we investigated the epidemiology of iGAS infections in Norway from 2010 to 2014 in order to uncover emm-type association with iGAS infections. We retrospectively collected data on antimicrobial susceptibility, multilocus sequence type and emm-type, and linked them with demographic and clinical manifestation data to calculate age and sex distributions, major emm- and sequence types and prevalence ratios (PR) on associations between emm-types and clinical manifestations. We analysed 756 iGAS cases and corresponding isolates, overall incidence 3.0 per 100 000, median age 59 years (range: 0-102), male 56%. Most frequent clinical manifestation was sepsis (49%) followed by necrotizing fasciitis (9%). Fifty-two different emm-

types and sixty-seven sequence types were seen distributed into five evolutionary clusters. The most prevalent strains was *emm1* (ST28) in all years (range: 20-33%) followed by *emm28,* 15% in 2014. All isolates were susceptible to penicillin, 15% resistant to tetracycline and <4% resistant to erythromycin. A PR of 4.5 (95% CI: 2.3-8.9) was calculated for *emm2* and necrotizing fasciitis. All *emm22* isolates were resistant to tetracycline PR 7.5 (95% CI: 5.8-9.9). This study documented the dominance of *emm1*, emergence of *emm89* and probable import of tetracycline resistant *emm112.2* into Norway. Genotypic fluctuations between years suggested a mutual exclusive dominance of evolutionary clades. We recommend studies into the non-invasive GAS infections in Norway to determine the strains in circulation and understand the dynamics of evolutionary clades. With the shifting epidemiology of GAS, and the re-emergence of *emm1*, we recommend European countries to include GAS into their mandatory surveillance systems. The fellow participated in the study design, collected and collated data, performed data analysis, presented data (poster) at ESCAIDE 2015 and at a national public health conference (2015), and wrote the manuscript for publication.

B. Virulence factors of shiga toxin-producing Escherichia coli and the risk of developing haemolytic uremic syndrome in Norway 1992-2013

Shiga toxin-producing *Escherichia coli* (STEC) may cause haemolytic uremic syndrome (HUS). Young age, presence of *stx2a* and *eae* are reported risk factors for the development of HUS. In this study, we explored the presence of adhesins, toxins and molecular risk assessment (MRA) factors among STEC isolates in Norway from 1992 to 2013, in order to identify novel risk factors for HUS development to improve the STEC surveillance system in Norway. We included non-duplicate isolates of all STEC cases (n=340) reported from 1992-2013 (one isolate per outbreak, 32 HUS cases). Median age of cases were 14 years (range: <1-97), female 56%. Most common STEC were O157:H7 (19%), O103:H2 (14%) and O26:H11 (10%). We screened the isolates by three multiplex PCRs for 31 virulence factors; adhesins (n=12), toxins (n=5), and MRA (n=14), and calculated odds ratios (OR) and adjusted odds ratios (aOR) for associations to HUS development. All STEC isolates from HUS cases were positive for intimin (*eae*) and the long polar fimbriae IpfAO26. Age ≤ 5 years (aOR 13.4, p<0.005) and *stx2a* (aOR 29.3, p<0.005) were identified as independent risk factors for HUS development. Furthermore, O145 (aOR 14.9, p<0.05) and the non-LEE-encoded effector that inhibits apoptosis and phagocytosis, *nleH1-2* (aOR 31.4, p<0.005) were identified as independent risk factors for HUS development. None of the cases between 20-60 years (n=117), O103:H2 isolates (n=47) and isolates producing *stx2b* (n=32) developed HUS. Our study demonstrated that the presence of O145 or *nleH1-2* might be predictors for an elevated risk for HUS development, and conversely *stx2b* or O103:H2 isolates predictors of low-virulent STEC infections. We recommend the national reference laboratory to consider including *nleH1-2* screening into routine STEC surveillance. The fellow participated in the study design, collected and collated data, performed data analysis, presented data at ESCAIDE 2016 (oral), and wrote a manuscript for publication.

C. Prevalence of multidrug resistant, ESBL and AmpC in isolates of notified travel acquired salmonellosis in Norway, 2005-2013

Norway is a low-incidence country of salmonellosis with around 80% of cases imported. In this study, we describe the proportion of antimicrobial resistance among travel acquired *Salmonella* isolates in order to increase knowledge about importation of resistance determinants through travelling. We performed a cross-sectional study including all *Salmonella* notifications in Norway 2005-2013. We described cases by country of acquisition, antimicrobial resistance and serovars. Isolates non-susceptible to third generation cephalosporins, were tested for the presence of ESBLs and AmpC genes. We analysed 13718 cases, 10561 travel acquired (77%). A total of 8.4% of the isolates were multi-drug resistant (MDR; non-susceptible to ≥3 classes of antibiotics), 0.54% ESBLs and 0.24% AmpC. The most frequent serovars were *S. Enteritidis* (51.2%) and *S. Typhimurium* (9.7%). The top three foreign countries for acquisition were Thailand (13.8%), Turkey (13.7%) and Spain (11.2%). From Thailand 11.5% of the isolates were MDR, 1.6% ESBLs and 0.96% AmpC. From Turkey 3.3% of the isolates were MDR, 0.35% ESBLs and none AmpC. From Spain 6.4% of the isolates were MDR, 0.25% ESBLs and one isolate AmpC. Isolates acquired in Thailand showed the highest proportion of MDR, ESBL and AmpC. Our findings underline that the top countries of travel acquisition are also among the most popular holiday destinations for Norwegians. Although proportion of resistant isolates were higher from other countries, it is important to inform all travellers about appropriate hygiene measures, as influx and dissemination of resistant strains in the community will have huge impact on the public health. We recommend sharing this information with clinicians, travel vaccination centres and relevant stakeholders in order to raise the awareness about AMR in travel-associated infections. The fellow participated in the study design, collated data, advised on data analysis and reviewed manuscript for publication.

D. Correlation between culture-based and molecular methods in detection of rifampicin and isoniazid-resistant Mycobacterium tuberculosis strains in Norway, 1997 to 2014

In recent years, Norway has seen an increase in TB notifications. The National Reference Laboratory for Mycobacteria receives all newly diagnosed TB strains for genotyping and drug susceptibility testing. In this study, we aimed to map mutations in *rpoB*, *katG* and *inhA* conferring rifampicin (RIF) and isoniazid (INH) resistance, in order to identify the most common mutations conferring a resistance phenotype. We retrospectively analysed phenotypic and genotypic susceptibility results for rifampicin and isoniazid for all TB isolates tested from 1997 to 2014, and analysed individual- and combination of mutations conferring resistance. We analysed 1316 isolates, 7.1% were phenotypic and 7.3% were genotypic resistant to RIF. Correlation between phenotypic and genotypic RIF resistance was 96.8%. The most common *rpoB* mutation was S531L (n=74). Phenotypic INH resistance was seen in 187 isolates and 62 isolates were genotypic resistant. The most common mutation conferring INH resistance was S515T1 in *katG* (n=48). We confirmed an MDR-TB phenotype in 87 isolates and an MDR-TB genotype in 52 isolates. A combination of S531L and S315T1 mutations in the *rpoB* and *katG* genes respectively, was the cause of most MDR-TB. Mutation in *rpoB* at one of the four specific sites (D516V, H526Y, H526D, S531L) predicted an MDR-TB outcome in 98% (52/53) of the isolates. Our results showed that although most RIF resistant phenotypes may be predicted by mutations covered by conventional methods, *mycobacterium* is evolving new mutation sites that confer RIF resistance. As for the INH resistance, most mutations are still uncharacterised. An early, but also accurate detection and treatment of TB is paramount not only to cease transmission of the disease, but also to avoid increase and spread of resistant bacteria, which requires longer, as well as treatment that is more expensive. We recommend further studies to map mutations responsible for INH resistance in particular. The fellow worked in collaboration with EUPHEM-fellow Natacha Milhano, and contributed to data curation, data analysis and drafting of the final report.

E. Validation of a new Ebola Zaire detection assay, Norway 2015

The Division of Infectious Disease Control at the NIPH is in need of a rapid, easy to handle and first hand screening test for Ebola Zaire virus during an outbreak situation. Presently, Ebola diagnostic is dependent upon real time PCR performed on inactivated samples using a commercial assay (A) and an in-house Ebola PCR test. Current methodologies are labour intensive, require the presence of high copy number RNA per reaction and have considerably lengthy hands-on time for Ebola. In this study, we aimed to validate a new PCR based integrated Ebola Zaire assay (B) for use in Ebola diagnostics in order to assess its robustness in terms of reproducibility, repeatability and concentration limit of detection (cLOD). As sample, we used inactivated whole blood from an Ebola infected patient (680 RNA copies/µl). We performed the assay B on its provided instrument. Setup involved, injecting hydration solution and injecting the whole blood sample after adding a protease mixture to provided pouch. The pouch was run on the instrument for four hours. We confirmed test repeatability and reproducibility for all tested sample dilutions. Minimum repeatable detection was established at 600x dilution. Concentration was estimated to 83.3 RNA copies/reaction equivalents to 0.14 copies/µl. Our study showed that the assay B was well suited for detection of Ebola Zaire in blood concentrations above 0.14 RNA copies/µl. The assay was more sensitive than assay A (2.23 RNA copies/µl), easier to perform, more rapid and had required less hands-on time. Assay B was evaluated as satisfactory both for use in preparedness and during an outbreak. We recommend NIPH to include assay B among their methodologies for rapid, reliable and safe Ebola screening in the future. The fellow contributed to study design, performed the laboratory experiments, interpretation of the results and drafting the final validation report.

F. Molecular characterization of pharyngeal Streptococcus pyogenes in Norway

S. pyogenes (GAS) is responsible for around 600 million pharyngitis cases reported globally each year. It causes a diverse range of diseases, from relatively mild to life threatening infections. The aim of this study was to describe the molecular epidemiology and antimicrobial susceptibility of non-invasive GAS (non-iGAS) isolates in Norway, in 2010 and 2012, in order to compare with invasive GAS (iGAS) isolates from the same period to understand the population dynamics of GAS. We found that the most prevalent emm-types were *emm1* (18%), *emm4* (10%), *emm12* (25%), *emm28* (7%), and *emm89* (13%), with sequence types, ST28, ST39, ST36, ST52, ST101, respectively. We found antimicrobial resistance to tetracycline in 7.1% of the isolates, erythromycin (1.5%), clindamycin (1.3%), and trimethoprim sulfamethoxazole (0.3%). The comparison between non-iGAS and iGAS isolates showed common emm-types and similar increasing or decreasing trends of *emm1* and *emm89* from 2010 to 2012. This study indicates that the circulation of GAS strains among the non-invasive and invasive infections are similar, and that surveillance of the non-invasive strains may serve as indicators of the epidemiological patterns of

invasive GAS infections. We recommend studies to explore independent risk factors associated with invasive GAS infections. The fellow contributed to interpretation of results and reviewing of scientific manuscript.

G. Realtime antimicrobial susceptibility profiling of carbapenem-resistant Klebsiella pneumoniae.

The expanding distribution of multi-resistant *Klebsiella pneumoniae* highlights a need for faster antimicrobial susceptibility tests. Clinical laboratory methods rely on extended culture to differentiate between resistance and sensitivity after initial isolation of bacteria from a clinical specimen. In this study, we described a bacterial flow cytometry workflow for rapid determination of *Klebsiella* carbapenem susceptibility phenotype that predicts both the breakpoint and the Minimum Inhibitory Concentration (MIC) in order to allow for evidence based empirical therapy. We assembled an internationally representative panel of *K. pneumoniae* isolates resistant to carbapenems covering a susceptibility range from sensitive to highly resistant and various beta-lactams. The MIC to meropenem for the isolates was determined by the flow cytometry-assisted susceptibility test (FAST) method and by broth microdilution for reference. We estimated a FAST breakpoint sensitivity of 1.000, a specificity of 0.954 and the FAST MIC correlation with broth microdilution MIC of 0.899. We demonstrated that real-time antimicrobial susceptibility profiling by acoustic flow cytometer predicts both qualitative and quantitative MIC. Fast and accurate susceptibility testing will have an immediate implication on the individual and public health, through avoiding delay in appropriate treatment and reducing the selection pressure on antimicrobial resistance and its spread. We recommend further development of the FAST protocol to adapt for use in multiple bacteria and for various resistance mechanisms. This project is a joint international study. The fellow contributed to the Norwegian participation with management and writing grant application, performing laboratory experiments in Perth Australia as visiting scientist, interpreting the results, presenting results at NIPH, establishing FAST at NIPH, and reviewing of the scientific manuscript.

H. Training modules

29.09.2014 - 17.10.2014 - The EPIET/EUPHEM introductory course: Three weeks of lectures, interactive sessions, case studies, group work, problem based learning (PBL), and writing of a research protocol as training in PHM and intervention epidemiology.

09.02.2015 - 13.02.2015 - Initial management in public health microbiology module: A one week introductory course into different types of personalities, management styles, time management, communication with different authorities and communication in the field.

16.02.2015 - 20.02.2015 - Biorisk and quality management module: A one week course in biorisk and quality control management. Included in the module are elements related to identification and mitigation of biorisks and shipment protocols for infectious substances, and applied methodologies for quantitative and qualitative test controls.

23.03.2015 – 27.03.2015 – The multivariable analysis module: An interactive statistic course introducing multivariable analysis, stratification, interactions of variables, how to build logistic regression and binominal regression models (in STATA).

Educational outcome

The fellow developed understanding of the basis and limitations of laboratory methods and application of these methods in a public health setting, including general microbiology, laboratory investigation, laboratory methods validation, development of novel methodology and data analysis.

4. Biorisk management

Supervisor: Siri L. Feruglio, Beathe K. Granerud

A. Biorisk and quality management module, ECDC, Sweden

Biorisk and quality management module in biomedical laboratories, is a five-day module providing an introduction to; i) principles and practices of biosafety according to those outlined by WHO & EU Directives ii) requirements of personal protective equipment (PPE), iii) principles of decontamination and waste control strategies, and iv) processes associated with BSL3 and BSL4 laboratories.

The fellow participated in the Biorisk and quality management module

B. Preparedness laboratory training – NIPH, Norway

The national preparedness laboratory at the NIPH holds a training course of all personnel that are involved with pathogens during an emergency requiring BSL3. The course duration is 24 hours, distributed over 6 days over a period of 2 weeks. The training focuses on the biosafety while working in a BSL3-Laboratory. Training includes culture and molecular methods when working with the pathogens; *Bacillus anthracis, Brucella spesis, Burkholderia mallei, Francisella tularensis, Yersinia pestis, Coxiella burnetii*. The fellow participated and completed the BSL-3 laboratory-training programme.

C. Certifications

- Certificate of Achievement: Basic Security in The Field II (UNDSS)
- Certificate of Achievement: Advanced Security in The Field (UNDSS)
- Certificate of Participation: The BSL-3 Laboratory Basic Training Course (NIPH)
- International Transport of Infectious Substances (WHO)

D. Training modules

16.02.2015 - 20.02.2015 - Biorisk and quality management module: A one week course in biorisk and quality control management. Included in the module are elements related to identification and mitigation of biorisks and shipment protocols for infectious substances, and applied methodologies for quantitative and qualitative test controls.

Educational outcome

The fellow developed understanding of the importance of biorisk management, and the requirements necessary to control risks associated with the handling, storage and disposal of biological agents and toxins in laboratories and facilities.

5. Quality management

Supervisor: Susanne G Dudman, Ulf R. Dahle

A. Norwegian accreditation visit to the department of virology at NIPH, 2015

The Division of Communicable Diseases at the NIPH hosts an annual visit from the Norwegian body for accreditation (NA). NA is the Norwegian signatory to the EA multilateral agreements on accreditation (MLA), which provides accreditation to establish confidence in the quality of products and services worldwide. NA uses the ISO/IEC 17025 standards for testing and for the calibration of laboratories in Norway including the laboratories at NIPH. ISO/IEC 17025 specifies requirements for the competence to carry out tests and/or calibrations, including sampling. It covers testing and calibrations performed using standard methods, non-standard methods, and laboratory-developed methods. The aim of this project was to follow the NA visit at the Department of Virology (SMVI) at NIPH overseeing their procedures of external quality assessment and working in developing action plans for corrective actions of nonconformities. With the NA-team, we performed laboratory visits, interviewing technicians and going through protocols and methods descriptions and workflows in the laboratories. We had meetings to discuss non-conformities and corrective actions. NA uncovered four significant and two minor nonconformities among the 20 accredited methods at SMVI. The nonconformities included lack of adequate description, reference to latest methodological documents and maintenance of competence. Corrective actions, including updating description and references in protocols, and providing training to maintain competency was initiated by SMVI. NA completed its visit to SMVI yielding an overall satisfactory result. No serious nonconformities were detected, and plans and work for corrective actions of significant and minor nonconformities were started. The NA visit confirmed the reliability of results generated at SMVI laboratories. The fellow joined a team from NA-investigators in their laboratory visits, interviewing technicians and going through protocols and methods descriptions and workflows in the laboratories, and the fellow was involved in devising corrective actions plans to non-conformities and writing an internal report.

B. Internal audit of the national reference laboratory for enteropathogenic bacteria – the DNA unit, 2015

Internal audit of the national reference laboratory for enteropathogenic bacteria was performed as an assignment post biorisk and quality management module. The audit inspected process management and quality control indicators as well as documentation. The audit yielded a general indicator percentage of 93%, with lowest scores for technical records (63%) and control documentation of nonconformities (50%). The laboratory was advised to complete their technical documentation records and keep records of nonconformities and corrective actions taken.

The fellow completed the audit by interviewing laboratory technicians, going through protocols and methods descriptions and workflows in the laboratories.

C. Global microbial identifier proficiency test at the national reference laboratory for enteropathogenic bacteria, 2015

Global microbial identifier (GMI) is a proficiency test initiated by scientists and stakeholders applying novel genomic technologies and bioinformatic tools to improve global patient diagnostics, surveillance and research. The GMI proficiency test of 2015 was supported by the collaborative management platform for detection and analyses of (re-) emerging and foodborne outbreaks in Europe (COMPARE), which received funding from the European Union's Horizon 2020 research and innovation programme. The inter-laboratory performance test is provided to facilitate harmonization and standardization in whole genome sequencing and data analysis, with the aim to produce comparable data for the GMI initiative. The National Reference Laboratory for Enteropathogenic Bacteria at NIPH signed up for the GMI test for *Salmonella* and *E. coli*. The proficiency tests included quality assessment of DNA extraction, purification and library preparation methodologies from bacterial culture and provided DNAs-samples. In addition, the proficiency test evaluated phylogenetic analyses based on provided sequence data sets. We received i) extracted DNA of two *E. coli* and two *Salmonella* isolates, ii) sequenced datasets of two *E. coli* and two *Salmonella* , and iii) two *E.coli* and two *Salmonella* cultures. We performed all steps from DNA extraction to sequence analyses and uploaded our results to GMI server. Our result scores were >90% for mapped reads to reference genome and >99.9% for chromosome coverage. More than 80% of our contigs were >200bp long and N50 scores were above 150 000, which is indicative of good quality sequence. All methodological steps in the sequencing process yielded satisfactory results, and our sequencing results are reliable for use in both surveillance and research. The fellow communicated with the GMI team, supervised laboratory methodologies, participated in data analysis and submitted results to the GMI server.

D. Training modules

16.02.2015 - 20.02.2015 - Biorisk and quality management module: A one week course in biorisk and quality control management. Included in the module are elements related to identification and mitigation of biorisks and shipment protocols for infectious substances, and applied methodologies for quantitative and qualitative test controls.

Educational outcome

The fellow was involved in both internal and external quality controls and developed understanding of the importance of laboratory quality management programmes to ensure day-to-day laboratory consistency and to be able to produce accurate and reliable results for use in diagnostics, surveillance and research. The fellow was instrumental in providing these standards for the newly established whole genome sequencing protocols, and through audit and accreditation getting an insight into how standards are maintained.

6. Teaching and pedagogy

A. Lecturing

- Two hour lecture on molecular typing and antimicrobial resistance to Ullern upper secondary class site visit of NIPH.(Completed 15.04.2015)
- Two hour lecture on molecular typing and antimicrobial resistance to Ullern upper secondary class site visit of NIPH. (Completed 04.04.2016)

- Four hour lecturing on antimicrobial resistance at the International Summer School 2015 – ISSMF4205 International Community Health, Institute of Health and Society, University of Oslo. (Completed 02.07.2015)
- Four hour lecturing on antimicrobial resistance at the International Summer School 2016 – ISSMF4205 International Community Health, Institute of Health and Society, University of Oslo. (Completed 02.07.2015)

B. Supervising

- PhD fellow – Co-supervisor, thesis; *Extended-spectrum β-lactamase (ESBL) producing Klebsiella pneumoniae: An outbreak in a neonatal intensive care unit, duration of colonization in children, intra-household transmission and ESBL-plasmid properties(defended 19.12.2014)*
- PhD fellow – Main supervisor, thesis; *Extended-spectrum Beta-lactamases and carbapenemases in clinical isolates of Enterobacteriaceae in Norway (defended 16.04.2015)*
- EUPHEM fellow – Project supervisor, title: *"Characterization and sequencing of ESBL and AmpC encoding plasmids isolated from human and poultry Salmonella entérica and Escherichia coli isolates in Greece from 2008 to 2014" (ongoing)*

C. Organising

- One day seminar; *"Challenges of faecal diagnostic".* Organisation of a seminar for all diagnostic microbiological laboratories in Norway to share methodological experience and increase awareness for culture-independent diagnostics and discuss future of reporting and sample submission. (Completed 22.01.2015).

E. Educational outcome

As supervisor for two PhD candidates and project supervisor for specific projects, the fellow was involved in defining projects, describing objectives and strategies to reach appointed targets. The fellow has given lectures to international public health professionals, developed and moderated a case study, and used various pedagogical techniques to stimulate learning. Through organisation of a seminar, the fellow gained experience in organisation, design and logistical requirements for such conferences.

7. Public health microbiology management

General public health microbiology management was an integral component of all projects and activities during the fellowship. For all projects, the fellow described the benefit to PHM and was engaged in scientific communication to peers and stakeholders. During the outbreak investigation and the syndromic surveillance study, the fellow was involved in planning an outbreak response, planning infection control measures, identifying basic laboratory requirements in the field and applying rapid assessment techniques. The fellow acquired team building and negotiation skills by working as a team member during the outbreak investigation, while setting up the surveillance systems, during all national projects working alongside epidemiologist and microbiologist from different departments at NIPH, and during international project collaborations with EUPHEM fellow Kyriaki Tryfinopoulou in Athens and with scientists in Perth. The fellow acquired laboratory management skills such as identifying best laboratory techniques, sample transportation and designing protocols during setup of a laboratory based surveillance system for Rotavirus and during all projects of applied public health microbiology and laboratory research and laboratory investigations. In particular, during the WGS study on listeria, the fellow was responsible for developing experimental and analytical pipelines, through management of laboratory personnel. During the real-time antimicrobial susceptibility-profiling project, the fellow enhanced his managerial skills through contributions to writing a grant application and establishing the FAST protocol at NIPH. The fellows' communication output in terms of manuscripts, reports and presentations are listed in section 8.

B. A common platform for whole genome sequencing, SSI, Denmark

The fellow participated at a whole genome sequencing (WGS) meeting held at SSI in Copenhagen Denmark January 2015 to discuss methods and challenges of WGS for surveillance of food-borne pathogens. As representative from the NIPH, the fellow was engaged in discussing and negotiating with peers from different

public health institutes in Europe to create guidelines for the WGS experimental and analytical workflows, and nomenclature for inter-laboratory communication, in order to improve WGS typing and communication in Europe.

C. Initial management in public health microbiology, ECDC, Sweden

As part of the EUPHEM training, a one-week module focusing on understanding roles and responsibilities in public health management. Topics included the identification of different management styles, team roles and team evolution, the delegation of tasks and the provision of structured feedback.

8. Communication

A. Publications

1. Naseer U, Steinbakk M, Blystad H, Caugant DA. Epidemiology of invasive group A streptococcal infections in Norway 2010-2014: A retrospective cohort study. European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology. 2016.
2. Solheim M, Bohlin J, Ulstad CR, Schau Slettemeas J, Naseer U, Dahle UR, et al. Plasmid-mediated colistin-resistant Escherichia coli detected from 2014 in Norway. International journal of antimicrobial agents. 2016;48(2):227-8.
3. Naseer U, Bohlin J, Bruvik T, Dahle UR, Brandal LT. Whole genome sequencing of the major Listeria MLVA-cluster in Norway 2005-2015. (submitted Eurosurveillance)
4. Naseer U, Løbersli I, Hindrum M, Dahle UR., Brandal LT. Virulence factors of Shiga toxin-producing Escherichia coli and the risk of developing Haemolytic uremic syndrome in Norway 1992-2013. (in preparation)
5. Einöder-Moreno M, Naseer U, Wester AL, Borgen K, Nygård K. Prevalence of multidrug resistant, ESBL and Amp C in isolates of notified travel acquired salmonellosis in Norway 2005-2013. (in preparation)
6. Milhano N, Naseer U, Steinbakk M, Sandnes R, Nilsen E, Opland GS, Noraas S, Caugant DA. Molecular epidemiology and antimicrobial susceptibility of clinical isolates of Streptococcus pyogenes in Norway, 2010 and 2012. (in preparation)
7. Mulroney KT , Hall JM, Inglis TJJ, Huang X, Turnbull EI, Bzdylb NM, Chakeraa A, Naseer U, Coreag EM, Ellingtone M, Hopkins K, Wester AL, Ekelund O, Woodford N. Realtime antimicrobial susceptibility profiling of carbapenem-resistant Klebsiella pneumoniae. (Submitted)
8. Tryfinopoulou K, Naseer U, et al. Characterization and sequencing of ESBL and AmpC encoding plasmids isolated from human and poultry *Salmonella entérica* and *Escherichia coli* isolates in Greece from 2008 to 2014 (in preparation)

B. Reports

1. Naseer U, Guzman B, MacDonald E, Nygård K, Borgen K, Vold L. Outbreak of gastroenteritis at the Radisson Blu Hotel Gardermoen, Oslo 2014.
2. Naseer U, Vanio K, Haltbakk I, Gibory M, Dudman SG. Laboratory-based surveillance system for rotavirus infections in Norway, Norwegian Institute of Public Health, 2015
3. Naseer U, Vanio K, Haltbakk I, Gibory M, Dudman SG. Laboratory-based surveillance system for rotavirus infections in Norway – Results 2015
4. Naseer U, Meijerink H, Milhano N, Veneti L, Borgen K. Setting up a syndromic surveillance system at Råde immigration centre, Norway 2015
5. Milhano N, Naseer U, Mengshoel AT. Correlation between culture-based and molecular methods in detection of rifampicin and isoniazid-resistant Mycobacterium tuberculosis strains in Norway, 1997 to 2014
6. Naseer U, Basset C. Validation of a new Ebola Zaire detection assay, Norway 2015
7. Naseer U. Norwegian accreditation visit to The Department of Virology at NIPH, 2015
8. Naseer U, Blystad H, Kløvstad H, Nilsen ØJ. Estimating the incidence of HIV in Norway, NIPH 2015

C. Conference presentations

1. Einöder-Moreno M, Naseer U, Wester AL, Borgen K, Nygård K. Prevalence of multidrug resistant, ESBL and Amp C in isolates of notified travel acquired salmonellosis in Norway 2005-2013 (Poster ESCAIDE 2015)
2. Einöder-Moreno M, Naseer U, Wester AL, Borgen K, Nygård K. Prevalence of multidrug resistant, ESBL and Amp C in isolates of notified travel acquired salmonellosis in Norway 2005-2013 (Poster NIPH Conference 2015)
3. Naseer U, Steinbakk M, Blystad H, Caugant DA. Epidemiology of invasive group A streptococcal infections in Norway 2010–2014: A Change in Epidemiology (Poster ESCAIDE 2015)
4. Naseer U, Steinbakk M, Blystad H, Caugant DA. Epidemiology of invasive group A streptococcal infections in Norway 2010–2014: A Change in Epidemiology (Poster NIPH Conference 2015)

5. Naseer U. Meijerink H, Milhano N, Veneti L. Setting up a syndromic surveillance system at Råde immigration centre, Norway 2015 (Oral NIPH Conference 2015)
6. Naseer U, Bohlin J, Bruvik T, Brandal L, Dahle, U. Whole genome sequencing of the major listeria MLVA-cluster in Norway 2005-2015 (Oral NIPH Conference 2015)
7. Naseer U, Bohlin J, Bruvik T, Brandal L, Dahle, U. Whole genome sequencing of the major listeria MLVA-cluster in Norway 2005-2015 (Oral ESCAIDE 2016)
8. Naseer U, Løbersli I, Hindrum M, Dahle U, Brandal L. Virulence factors of Shiga toxin-producing *Escherichia coli* and the risk of developing Haemolytic uremic syndrome in Norway 1992-2013 (Oral ESCAIDE 2016)

D. Selected other oral presentations

1. Naseer. U, Vinio K, Haltbakk I, Giboy M, Dudman S. Laboratory-based surveillance system for rotavirus infections in Norway (NIPH Scientific Forum)
2. Naseer U, Løbersli I, Hindrum M, Dahle U, Brandal L. Virulence factors of Shiga toxin-producing *Escherichia coli* and the risk of developing Haemolytic uremic syndrome in Norway 1992-2013 (NIPH Scientific Forum)
3. Naseer. U. Rapid Determination of Bacterial Physiology by Acoustic Flow Cytometry and Determining Antimicrobial Susceptibility (NIPH Scientific Forum)
4. Naseer U, Einöder-Moreno M, Meijerink H, Milhano N. Ebola preparedness plan of Norway (ECDC, IMPHM Module)
5. Naseer U, Ákos Tóth. Vaccines against malaria (EUPHEM PBL, Vaccinology module)

9. EPIET/EUPHEM modules attended

1. EPIET/EUPHEM introductory course, Spetses, Greece (three weeks, Sep-Oct 2014)
2. Outbreak module, Robert Koch Institute, Berlin, Germany (one week, December 2014)
3. Initial management in public health microbiology, ECDC, Stockholm, Sweden (one week, February 2015)
4. Biorisk and quality management module, ECDC, Stockholm, Sweden (one week, February 2015)
5. Multivariable analysis module, Vienna, Austria (one week, March 2015)
6. Mini project review, SSI, Copenhagen, Denmark (two days, April 2015)
7. Vaccinology, Krakow, Poland (one week, April 2015)
8. Rapid assessment and survey methods module, Athens, Greece (one week, June 2015)
9. Project review module, Lisbon, Portugal (one week, August 2015)
10. Bioinformatics and phylogenetic module (three days, November 2015)
11. Mini project review, Stockholm, Sweden (two days, April 2016)
12. Project review module, Lisbon, Portugal (one week, August 2016)

10. Other training

1. 4th Workshop Rapid NGS for Clinical, Public Health, and Food Microbiology: Three day course in Next-Generation-Sequencing (NGS) technology rapid development in last years and use in diagnostics and surveillance. Highlighting opportunities and challenges posed by this technology. An introduction to the sequence analyses software SeqSphere+.
2. Better Training for Safer Food (BTSF): An European Commission initiative aimed at organising a training strategy in the areas of food law, feed law, animal health and animal welfare rules, as well as plant health rules. The course provides training into investigation of food-borne outbreaks aimed at improved cooperation, communication, collaboration and data control management between veterinarians, food protection agencies and the public health institutes. Organised by; Consumers, Health, Agriculture and Food Executive Agency (CHAFEA).
3. Nordic mini project review: Module with feedback from Nordic expert on scientific projects in order to meet EPIET / EUPHEM standards.
4. Nordic mini project review: Module with feedback from Nordic expert on scientific projects in order to meet EPIET / EUPHEM standards.

Discussion

Coordinator's conclusions

During his EUPHEM fellowship we had several opportunities to assess Umaer's great capacity for hard work coupled with willingness to exploit his keen interest in molecular methodologies on the various disease groups and public health issues. With his enthusiasm and capacity to take on different tasks he has significantly contributed to setting up, implement and evaluation of the surveillance system for Rotavirus infection in Norway. His comprehension of the complexity of the Public health world has deepened during his fellowship as is testified by the numerous projects he has undertaken and brought to success. For example he has contributed setting up of a new method for the antibiotic resistance profile of carbapenem resistant Klebsiella *pneumonia.* For this specific project, he had to confront with international cooperation where he succeeded to bring his expertise and team working capability to a very high level. All Umaer's Projects had a clear outcome, with results communicated in scientific journals and at conferences. The contributions made by this EUPHEM fellow to the Norwegian public health indicates 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 his tasks to a high standard and with a professional attitude, which indicates his development in leadership. We wish the fellow every success in his future career as a public health microbiologist.

Supervisor's conclusions

During his EUPHEM training, Umaer has further strengthened his skills as an expert public health microbiologist. He has gained comprehensive practical and theoretical knowledge in various fields of microbiology and epidemiology. His project matrix and high quality scientific work during the two-year period, clearly testifies to his motivation and ability to assimilate new knowledge in excellent manners. Umaer has contributed to strengthening the collaboration between the EPIET and EUPHEM fellows at NIPH. In particular, he has explained and applied advanced laboratory methods of PHM into the field of epidemiology. This has been of great importance for future work in prevention of communicable diseases at NIPH. Umaer has independently planned and implemented analytical and epidemiological studies. He represents a valuable co-worker that helps ensure interdisciplinary communication, scientific collaboration, and the success of our organization's work. Tutoring and support of Umaer and his work have been a joyful task, as he is also a solid team player, with unsurpassed collaborative abilities, and he has thus been welcomed in every laboratory he has visited.

Personal conclusions of fellow

The EUPHEM programme presented me with the unique opportunity to work on diverse projects within various areas of public health, allowing me to increase and expand my knowledge into new and exciting areas. Through the fellowship, I was able to interact with scientists and experts in various fields at different locations, to form lasting bonds of friendship extending beyond science. One of the major achievements of the fellowship has been bridging the gap between microbiology and epidemiology, paving the way for communication, networking and close collaborations between the two. The fellowship has instilled confidence in my competencies, which will undoubtedly result in better microbiology practice in the years to come. As a fellow positioned at the NIPH, I was provided with all the support, opportunity and guidance required to complete my fellowship. The EUPHEM milieu at NIPH has been very conducive for teambuilding, and encouraged reflection and scientific growth. I believe we can do best service to public health by combining the best practices on all disciplinary levels, and the EUPHEM programme ensures that the public health microbiologist is equipped with knowledge and skills to confidently take its share.

Acknowledgements of fellow

I would like to thank my local EUPHEM supervisors, Ingeborg S. Aaberge and Ulf R. Dahle, for their supervision and kind engagement in all my activities. A special recognition must go to Ulf for introducing me to the EUPHEM-programme and allowing me to apply. His encouragement, facilitation and understanding during stressful times cannot be valued enough. Many appreciations also go to Katrine Borgen for her coordinator role and for sharing her insight into the world of epidemiology, her ever-positive attitude and efforts in keeping the EUPHEMs and EPIETs as one big happy family at NIPH. Thanks also to the countless numbers of supervisors on the different projects for sharing their knowledge and for their guidance.

I will forever be grateful to my EUPHEM coordinators Aftab Jasir, Loredana Ingrosso, and Silvia Herrera Leon. Their guidance, patients and understanding during all my projects and work has been excellent. A special recognition must go to Aftab, who was my lone coordinator for the first year. Especially for her warm and openhearted welcome of me to the EUPHEM-family, and her forever encouragement and support of all my works. I am also thankful to my wonderful EUPHEM and EPIET cohort 2014, and especially all the active fellows at NIPH I had the fortune to interact with and learn from during my fellowship, especially Hinta Meijerink and Natacha Milhano.

Lastly, I cannot forget and will forever be in-debt to my dear family who held out the two years with and without me.