



EPIET REPORT

Summary of work activities

Tanja Ducombe

European Programme for Intervention
Epidemiology Training (EPIET), 2011 cohort

Background

Pre-fellowship short biography

Tanja Ducombe has extensive experience in medical humanitarian work where she started out as a nurse, field coordinator, and most recently, as advisor for vaccine-preventable diseases at Doctors without Borders, Belgium. She obtained a Master in Control of Infectious Diseases from the London School of Hygiene and Tropical Medicine in 2006.

EPIET assignment

From September 2011 until 2013, she was assigned to the Department for Infectious Disease Epidemiology at Robert Koch-Institute (RKI), Berlin, Germany. Activities developed included the surveillance of a range of infectious diseases, developing and implementing a research project, responding to outbreaks, and participating in RKI training activities.

Fellowship projects

Surveillance projects

The burden of extrapulmonary and meningitis tuberculosis: an investigation of national surveillance data, Germany, 2002–2009¹⁻⁴

Tuberculosis (TB) surveillance commonly focuses on pulmonary TB (PTB), where the main organ affected is the lung. This might lead to underestimate extrapulmonary TB (EPTB) forms, where, in addition to the lung, other sites are affected by TB. In Germany, TB notification data provide the main site and the secondary site of disease.

To gain an overview of all the different EPTB forms, we analysed German TB notification data between 2002 and 2009, using information on both main and secondary disease sites to describe all individual EPTB forms. Further, we assessed factors associated with meningitis, using multivariable logistic regression. Solely analysing the main site of disease lead to one third of EPTB manifestations being overlooked. Case characteristics varied substantially across individual extrapulmonary forms. Of 46 349 TB patients, 422 (0.9%) had meningitis as main or secondary site. Of those, 105 (25%) of the 415 with available information had died. Multivariable analysis showed that meningitis was

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more likely in children younger than five years of age and in those between five and nine years of age (odds ratio (OR): 4.90; 95% confidence interval (CI): 3.40–7.07 and OR: 2.65; 95% CI: 1.40–5.00), in females (OR: 1.42; 95% CI: 1.17–1.73), and in those born in the World Health Organization regions of south-east Asia (OR: 2.38; 95% CI: 1.66–3.43) and the eastern Mediterranean (OR: 1.51; 95% CI: 1.02–2.23). Overall, EPTB manifestations, including meningitis, which is often fatal, were underestimated by routine analysis. We thus recommend using all information on disease manifestation generated by surveillance to monitor severe forms and to transfer the gained knowledge to TB case management, where awareness of EPTB is most important.

Status: Completed

Outbreaks

Investigation of a cluster of gastrointestinal illnesses in a canteen, Berlin, February 2012

Between 9 and 10 of February 2012, an increase of gastrointestinal diseases occurred among clients of an institutional canteen in Berlin. A retrospective cohort study among canteen clients, using a standardised questionnaire to collect information on food consumption from the canteen and gastrointestinal symptoms, was performed to determine the causes of the outbreak.

Of the 100 people participating in the study (participation rate: 40%), 31 reported diarrhoea and/or vomiting between 8 and 13 of February. All cases had eaten lunch in the cafeteria on 9 February 2012. Statistical analysis, using weekdays of the canteen visit as exposure, showed a strong epidemiological link (RR: 69.2; 95% CI 12.4–∞) between the canteen visit on Thursday and the disease. Further subanalyses were limited to subjects who had visited the canteen on Thursday. All cases reported to have eaten chicken fricassee. All cases presented with diarrhoea (and only few vomiting), the onset of symptoms was between 6.5 to 18.5 hours after eating the chicken fricassees. Only one person had eaten the fricassee on Thursday without becoming sick. Multivariable analysis restricted to food items consumed on Thursday confirmed a strong association of chicken fricassee and disease (RR: 9.56; 95% CI 1.2–∞). Further, food safety analysis reported microbiological isolation of toxin-producing *Clostridium perfringens* from a reference sample of the suspected food vehicle (chicken).

The epidemiological study, the described symptoms of the disease, the incubation period and the detection of the pathogen in a food sample indicate that fricassee contaminated with *C. perfringens*, which was offered in the canteen on 9 February 2012, was the point source of this outbreak. Existing food safety regulations regarding preparation and storage of food need to be implemented accordingly in order to avoid food-borne outbreaks linked to improper food hygiene.

Status: Completed; output: internal report

A hospital outbreak of KPC-2 *K. pneumoniae*, Germany 2010–2012⁵⁻⁸

In May 2012, the Robert Koch Institute was asked to support the local health office in the investigation of a *Klebsiella pneumoniae* carbapenemase-2 *K. pneumoniae* (KPC-2) outbreak in a university hospital. KPC-2 was detected in the primary case, a patient transferred from a Greek hospital, already on 8 July 2010. Although the outbreak seemed to have been contained since March 2011, transmission could not be stopped, and up to three new cases were diagnosed every month.

We aimed to perform an epidemiological description of the outbreak in order to generate a hypothesis on the route of transmission, recommendations on control measures, and thus contribute to the prevention of further spread of KPC-2.

The study includes all cases detected between the start of the outbreak, defined as the admission date of the primary case (28 June 2010) and 31 July 2012. Active case finding was implemented through intensified screening of hospitalised patients using a KPC-2-specific polymerase chain reaction (PCR) and case ascertainment was performed by molecular genotyping (pulsed-field gel electrophoresis). Case information was extracted from patient and hospital administration records.

Between 28 June 2010 and 31 July 2012, 72 cases were identified, 11 of which were detected in June 2012, following intensified screening activities. The median age was 61 years, 41 (57%) were male, 17 (24%) had transplantation, and 21 (29%) malignancy. Infectious manifestations of KPC-2 were observed in 35 (49%) cases, the other 37 (51%) were colonised only. Overall mortality was 47%: 35% among those colonised, and 60% among those with an infectious manifestation. Of a total of 72 cases, 47 (65%) were hospitalised at the same time and in the same ward as other KPC-positive patients before the detection of their KPC infection; 15 (21%) of these 72 cases even shared a room contact with KPC-positive patients. In the time period from 14 days prior to + until the date of the first KPC detection, 28 (39%) of the 72 cases were screened for KPC, defined as testing for KPC-2 in rectal material (swab or stool sample). Among those with at least two follow-up examinations after KPC-2 detection, 14 (48%) of a total of 29 cases had intermittent negative KPC culture test results (positive – negative – positive) of the same examination material. In the described time period, out of a total of 2236 hospitalisation days for KPC-positive patients with available information on isolation status, 1677 (75%) were in (infection control) isolation. Based on the assumption of a monthly ratio of 1:2 (infected:colonised) and a 3-month forward average mean, we estimated an additional

39 cases in addition to the already identified 72 cases. All screening tests were performed on a voluntary basis among hospital staff and on over 1000 environmental examinations – all were KPC-2 negative.

During this outbreak, KPC-2 affected severely ill patients, and mortality was nearly twice as high among those with an infection compared with those who were only colonised. The screening rate among cases prior to KPC-2 detection was low, and nearly half of the cases presented intermittent negative KPC culture test results, probably linked to interrupted excretion. In addition, isolation of KPC-2-positive patients was delayed, especially at the beginning of the outbreak. This may have led to a high number of late and undetected cases acting as 'silent transmitters' that contributed to the prolongation of this outbreak. New cases were steadily reported until April 2013. We recommend intensified screening activities that should begin at the early stages of an outbreak and continued screening among patients with negative results. In addition to early detection, stringent and timely isolation of KPC-positive patients is important to prevent the spread of KPC and thus infection-associated deaths.

Status: completed; output: outbreak report

Participation in two case control studies to investigate a multi-federal state outbreak of gastroenteritis, East Germany, Sep–Oct 2012⁹

Abstract submitted by Dirk Werber to ESCAIDE conference, November 2013:

Large multistate outbreak of norovirus gastroenteritis associated with frozen strawberries, east Germany, 2012

On 27 September 2012, the federal state of Brandenburg informed the Robert Koch-Institute about several outbreaks of gastroenteritis in schools and childcare facilities, with a total of at least 500 cases. The Robert Koch-Institute informed food safety authorities and public health authorities in all federal states, requested information on similar outbreaks, and initiated an outbreak investigation to identify the vehicle of infection and prevent further cases. Norovirus was identified as the causative agent.

Cases had diarrhoea or vomiting from 19 September through 7 October 2012, did not test positive for any pathogen other than norovirus, and attended an affected institution (one with external food supply and which registered ≤ 10 cases in that period). We conducted two case-control studies and two surveys in secondary schools in three of the affected federal states. Product trace-back investigations were performed by the Task Force on Food and Feed Safety.

Overall, 390 institutions in five federal states were identified, with $\sim 11\,000$ patients of gastroenteritis, most of them children in schools and nurseries.

All studies identified strawberries, contained in various dishes, as the most likely vehicle in this outbreak, with odds ratios ranging from 2.6 to 45.4. Strong epidemiological evidence was available within a week after outbreak detection. The strawberry-containing dishes had been prepared in regional kitchens of a large catering company and were served two days before to the respective outbreak peaks. Trace-back investigations revealed that the strawberries were imported frozen from mainland China.

This largest food-borne outbreak in Germany exemplifies infection risks in the era of global food trade and underlines the importance of timely surveillance of local outbreaks and the role of epidemiological outbreak investigations for food safety.

Status: completed

Research

Investigation on possible transmission of the new Schmallenberg virus to humans, Germany, 2012¹⁰⁻¹³

Since the second half of 2011, a novel vector-borne *Orthobunyavirus*, Schmallenberg virus (SBV), has been infecting ruminants, especially sheep, throughout Europe. Transplacental transmission leads to severe congenital malformations and high viral loads in animals, especially their birth products. Phylogenetically related viruses (e.g. *Oropouche* virus) have proven zoonotic transmissibility. We conducted a seroprevalence survey among shepherds in the most affected area in Germany (North Rhine-Westphalia) to investigate possible transmission to humans and assess potential exposure and symptoms.

During an SBV information meeting, we asked shepherds from an SBV epizootic area to complete a questionnaire on demographics, exposure to infected animals, insect bites, and personal health since, going back to late summer 2011. We tested a serum specimen from each participant with real-time reverse-transcription quantitative polymerase chain reaction (qRT-PCR) for SBV and via indirect fluorescent antibody test (IFAT) for SBV-specific antibodies. For confirmation of indeterminate and positive results, we used a serum neutralisation test (SNT).

Of the 60 participating shepherds, 48 (89%) reported contact with malformed lambs or respective birth products, 36 (60%) reported SBV isolation in their respective livestock, and 22 of 56 (39%) frequent insect bites. Nine shepherds self-reported unexplained symptoms (fever, headache, myalgia/arthralgia, respiratory symptoms, skin rash), without relevant differences between exposure groups. All sera tested negative by RT-qPCR. Eight samples showed indeterminate fluorescent signals in the IFAT at 1:20 serum dilution but were non-reactive at a 1:80 dilution. Re-testing by SNT showed no antibodies.

We did not find molecular or serological evidence for SBV infection among a highly exposed population. Reported symptoms were compatible with illnesses commonly experienced during winter months. We conclude that it is very unlikely that the novel virus may pose a threat to humans.

Status: completed

Scientific communication

- Four scientific papers in peer reviewed journals; two published as first author, two published as co-author, and one article submitted as first author.
- Three oral communications; ESCAIDE and Wolfheze Workshops.
- Two poster presentations, ESACIDE and Conference of the Tuberculosis Union, European Region.

Teaching experience

- June 2012, Germany. Training title: Outbreak investigation for health officers in Germany (ÖGD-Kurs)
- Subject of the training experience: the epidemic curve. Duration of the lecture: 1 hour
- 2012, Germany. Presentation of the German Tuberculosis Surveillance System to a delegation of Chinese representatives of the national tuberculosis programme.

Miscellaneous

Peer review for journals (under the supervision of EPIET coordinators): two articles for the National Medical Journal of India and Epidemiology and Infection.

Supervisor's conclusions

Tanja Ducombe was involved in a wide range of activities during her two-year fellowship, covering all core competencies of the EPIET programme. She was involved in complex outbreaks and research projects on emerging infectious disease as well as in the analysis of routine surveillance data. She is a team player who gets along well with her peers. At the same time, she is a dedicated and open-minded colleague with a positive attitude and a pleasant sense of humour which helps to keep team meetings interesting. She executed her tasks and projects with a high degree of independence and diligence, reaching high scientific standards as documented by her publications in several highly reputed journals. Based on her personal and professional skills, I can highly recommend Tanja Ducombe for any work in the field of public health.

Next steps

- Following the EPIET programme, Tanja Ducombe will work for six months in the Unit for Healthcare-associated Infections, Surveillance of Antimicrobial Resistance and Consumption, at Robert Koch-Institute, Berlin, on a project on the burden of communicable diseases of nosocomial infections. She will also work on a manuscript on the hospital outbreak of KPC-2 *K. pneumoniae* in Germany 2010–2012.
- Tanja has a strong interest in emerging and neglected infectious diseases as well as in healthcare-associated infections. She especially enjoys outbreak investigations. In the future, she would like to conduct epidemiological work in Europe as well as in developing countries.

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