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Fatal anthrax infection in a heroin user from southern Germany, June 2012

T Holzmann (thomas.holzmann@klinik.uni-regensburg.de)[1], D Frangoulidis[2], M Simon[1], P Noll[3], S Schmoldt[2], M Hanczaruk[2], G Grass[2], M Pregler[4], A Sing[5], S Hörmansdorfer[5], H Bernard[6], R Grunow[6], R Zimmermann[6], W Schneider-Brachert[1], A Gessner[1], U Reischl[1]

1. Institute of Medical Microbiology and Hygiene, University Hospital of Regensburg, Regensburg, Germany
2. Bundeswehr Institute of Microbiology, Munich, Germany
3. Krankenhaus der Barmherzigen Brüder, Regensburg, Germany
4. District Health Office, Regensburg, Germany
5. Bavarian Health and Food Safety Authority (LGL), Oberschleißheim, Germany
6. Robert-Koch Institute, Berlin, Germany

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Blood cultures from a heroin user who died in June 2012, a few hours after hospital admission, due to acute septic disease, revealed the presence of *Bacillus anthracis*. This report describes the extended diagnosis by MALDI-TOF and real-time PCR and rapid confirmation of the anthrax infection through reference laboratories. Physicians and diagnostic laboratories were informed and alerted efficiently through the reporting channels of German public health institutions, which is essential for the prevention of further cases.

In early June 2012, a case of anthrax infection was identified in an injecting drug user in Germany. Anthrax wasn't suspected initially and the patient died on the day of hospital admission. Two days later anthrax was confirmed and the relevant authorities were informed. This report underlines the importance of considering anthrax as a possible diagnosis in injecting heroin users presenting with fever or sepsis at emergency rooms and of the rapid management of such cases.

Clinical case description

In early June 2012 an injecting drug user in their 50s presented at the emergency department of a hospital in the south of Germany, with a two-day history of worsening swelling and reddening at an injection site, nausea and dyspnoea. The patient had been on oral substitution therapy for two years. Moreover, a history of chronic hepatitis C infection with liver cirrhosis was reported. In the next hours after admission to hospital, the patient developed respiratory failure and was transferred to the intensive care unit (ICU) where they were ventilated mechanically. An elevated white blood cell count (15.9 cells/nL), anaemia (haemoglobin 10.4 g/dL), thrombocytopenia (38 cells/nL), elevated procalcitonin (1.05 ng/mL) and hypokalaemia (2.5 mmol/L) were observed. Elevated liver enzymes, lowered coagulation parameters and extremely high levels of D-dimers (›36,364 ng/mL) were pointing to multi-organ failure. Blood and urine cultures were sent to the Institute of Medical Microbiology and Hygiene, University of Regensburg. The patient's condition worsened and they died on the day of admission due to a septic shock with multi-organ failure and massive disseminated bleeding. At the time, there was no clinical suspicion of anthrax.

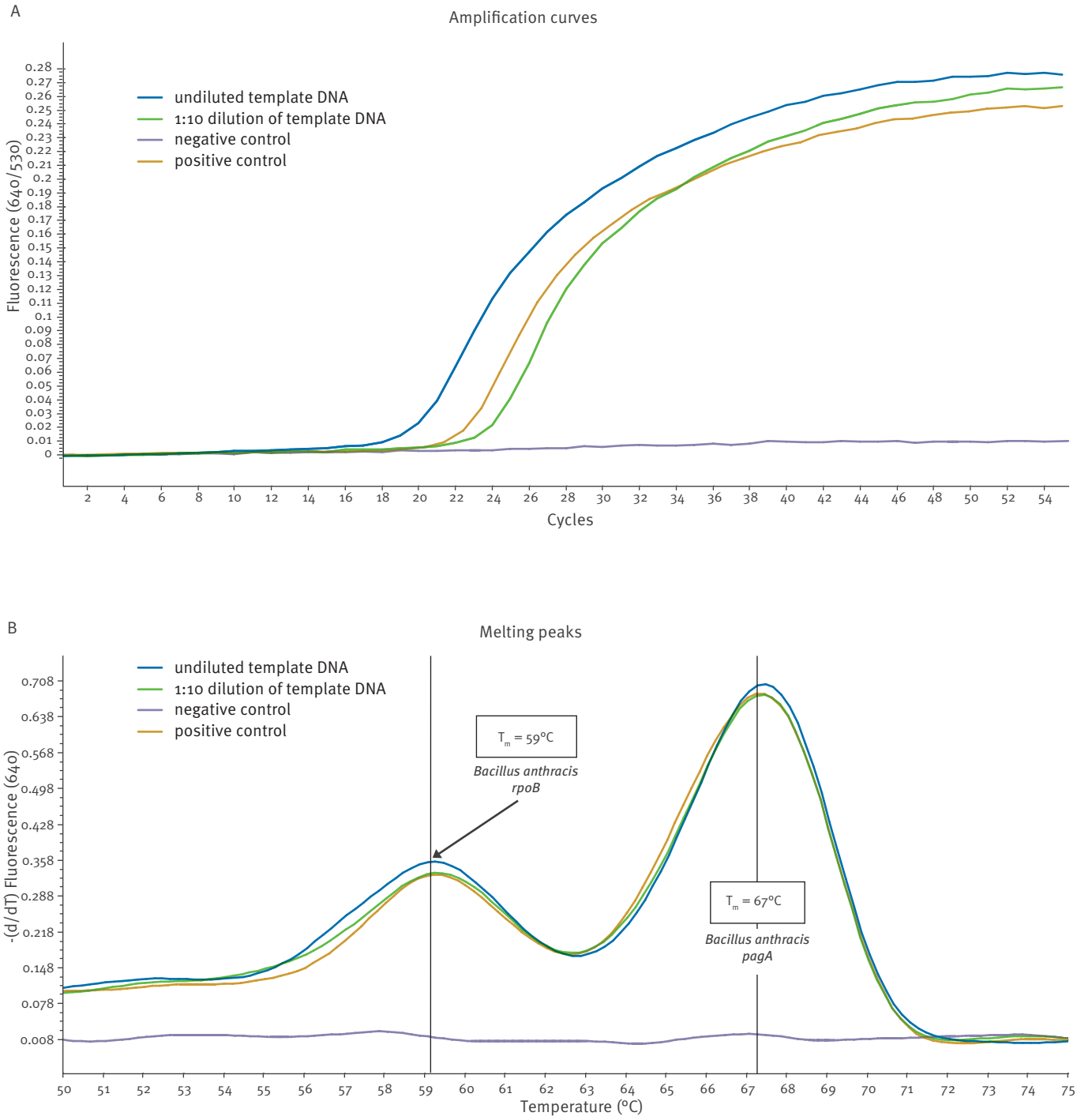
Laboratory analysis

Blood cultures (Becton Dickinson, Heidelberg, Germany) turned positive after 53 minutes of incubation. Gram-stained microscopy showed non-branching Gram-positive bacilli growing in chains. Subcultures presented typical growth of aerobic spore-forming bacilli without haemolysis. Matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF MS) identification revealed *Bacillus cereus* (Bruker Daltonics, Bremen, Germany). The patient's history led to reanalysis with the Bruker 'SR Database' that contains so-called security-relevant organisms, which correctly identified *B. anthracis*.

An initial set of molecular diagnostic tests was performed for confirmation at the Institute of Medical Microbiology and Hygiene, University of Regensburg. Briefly, a loopful of cells was suspended in 500 µL of detergent buffer. The buffer consisted of TE (pH 7.5) containing 0.5% Triton X-100 and 0.25% Tween 20. The suspension was heated at 95°C for 30 minutes with occasional shaking, sonicated for 1 minute, and heated again at 95°C for 30 minutes. After 10 minutes centrifugation at 11,000 × g, the supernatant was passed through a 0.2 µm sterile filtration membrane. Extracting genomic DNA from a boiled bacterial culture proved to be reproducible, easy-to-perform and rapid before [1]. The DNA was directly used as template for a series of real-time PCR assays performed with the Light Cycler PCR system (Roche Diagnostics, Mannheim,

Figure

Real-time PCR amplification plots (A) and melting curve analysis (B), anthrax infection, Germany, June 2012



T_m: melting temperature.

LightMix *Bacillus anthracis* PCR Kit (testing 5 µl aliquots of the original and 1:10 diluted template DNA preparations, respectively).

Germany). The real-time assays included an in-house protocol for pan-bacterial 16S rDNA amplification and the LightMix kit *B. anthracis* (Cat. No: 40-0252-16, TIB Molbiol, Berlin, Germany). The kit is designed to detect the *pagA* gene as marker for the plasmid pXO1 and a *B. anthracis*-specific segment of the bacterial *rpoB* gene for species identification, using hybridisation probes. Early crossing points (around cycle 18) and the specific melting points of the respective target genes *pagA* and *rpoB* were observed in the melting curve analysis, indicating the presence of *B. anthracis* carrying at least the virulence plasmid pXO1 (Figure).

To substantiate the initial test results, an aliquot of the DNA preparation was sent to the Bundeswehr Institute of Microbiology in Munich. The initial PCR results were confirmed and extended using PCR assays for the *capC* gene (marker for the second virulence plasmid pXO2) and an additional chromosomal marker highly specific for *B. anthracis* (dhp61) [2]. First results of molecular genotyping of the strain showed close relationship to strains from a large anthrax outbreak among IDUs in Scotland [3].

Control measures

The District Health Office was informed about the suspected case of human *B. anthracis* infection immediately after obtaining the PCR results. Their experts got involved in the management of the case in close contact with the diagnostic institutions, the police authorities and the Task Force Infectiology of the Bavarian Health and Food Safety Authority (LGL). Health officials considered contaminated heroin or cutting agents mixed with the heroin as possible source of the infection. Further investigations by the German police authorities were initiated immediately.

The competent public health authorities at national level were informed immediately about the confirmation of *B. anthracis*. The information on the occurrence of the case was distributed to the public health authorities in all 16 German federal states, at international level through the Early Warning and Response System (EWRS) of the European Commission and via ProMED-mail [4]and according to the International Health Regulations (IHR). In Bavaria, the medical associations were informed. Substance abuse counselling agencies were contacted nationally and at European level through the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) in order to spread the information among drug users. Additional information and materials were published by the public health institutes on their websites.

Identification of the second case

Two weeks after the first case was admitted to hospital, a second case of anthrax was identified in an IDU from the same region as the first case. The patient is stable under antibiotic therapy after surgical debridement [5]. The raised level of awareness created with the first case lead to a much faster workflow in the laboratory analysis in the second case. *B. anthracis* was confirmed three hours after blood cultures turned positive.

Discussion

Injectional anthrax has first been reported 1988 as fourth route of infection besides cutaneous, gastrointestinal and inhalational anthrax infections [6]. The first anthrax case related to injecting drug use was described 2000 from Norway [7]. There were no subsequent reports of injectional anthrax until 10 December 2009 when anthrax was identified in blood cultures from two injecting drug users from Glasgow, Scotland [8]. In the following months an increasing number of cases were identified [9]. By the end of the outbreak in December 2010, there were 47 confirmed cases of injectional anthrax (including 13 deaths), 35 probable cases (including one death) and 37 possible cases in Scotland and five cases including four deaths in England [3]. There were two confirmed cases in Germany related to this outbreak, including one fatal case [10]. The favoured outbreak hypothesis assumed that heroin had been in contact with goat skin contaminated with anthrax spores during transportation to Scotland [3]. Risk factors for infection were longer injection history, receiving opioid substitution therapy, and alcohol consumption [11]. All cases of injectional anthrax reported so far including the case presented here were not associated with the typical black eschar seen in patients with cutaneous anthrax [12].

Box 1

Timeline of events, fatal case of anthrax infection, Germany, June 2012

Day 1	• Patient admitted to the hospital
	• Blood cultures sent to the laboratory
	• Patient dies due to septic shock
	• Blood cultures positive with Gram-positive bacilli (late afternoon)
Day 2	• Growth of *Bacillus* spp. on subcultures
	• MALDI-TOF: *Bacillus cereus*
	• Discussions on anthrax suspicion
	• Different PCRs and 16S sequencing over night
Day 3	• *B. anthracis* confirmed by PCR
	• Information of local health authorities
	• Involvement of regional and national health and police authorities
	• DNA sent to Bundeswehr Institute of Microbiology
Day 4	• *B. anthracis* confirmed using further PCRs
	• Robert Koch Institute promotes further information at national and international level

MALDI-TOF MS: matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry.

Because *B. anthracis* is seen very rarely in Germany and other developed countries, laboratory staff and clinicians should raise their attention when Gram-positive bacilli growing in chains are detected in clinical specimens (Box 2).

B. anthracis cannot be reliably distinguished from *B. cereus* by growth characteristics, bacterial cell morphology or biochemical methods. The applicability of MALDI-TOF-MS for the identification of *B. anthracis* was demonstrated elsewhere [13]. Because of safety regulations, *B. anthracis* and other potential bioterroristic agents are not included in the manufacturer's (Bruker Daltonics) database. As in our case, the isolate is classified as *B. cereus* with the standard databases. Using a special database, containing the missing spectra, *B. anthracis* is identified correctly. The manufacturer discourages the standard use of the *B. anthracis* spectra due to misidentification of members of the *B. cereus* group. Consequently, the result 'B. cereus' in combination with a patient's history of injecting drug use should lead to further diagnostic steps. To differentiate between *B. anthracis* and non-anthracis Bacillus species harbouring anthrax-specific virulence plasmids, PCR targeting a chromosomal marker should be performed in addition to PCR assays covering the virulence plasmids pXO1 and pXO2. Non-pathogenic *B. anthracis* strains not containing plasmids can be identified using this combination as well [2, 14].

Box 2

Recommendations and lessons learnt from the fatal case of anthrax infection, Germany, June 2012

- When growth of *Bacillus cereus* sensu lato is identified by the MALDI species typing database, a sound anamnesis of the underlying clinical case should be performed.
- Suspicious cultures should be transferred to a biosafety level 3 environment and, whenever possible, a spectrum of validated molecular tests should be kept in stock for level 3 pathogens (especially anthrax).
- An agreed case definition and protocol for alerting the authorities should be available and known to all microbiologists and clinicians.
- Appropriate reporting channels should be maintained and exercised by the public health authorities to prevent that similar (or parallel) cases remain undetected.
- Confirmatory PCR testing in a specialised laboratory should be immediately requested. Diagnostic laboratories should know such specialised laboratories in their vicinity for support and check the logistics of sample transport in a situation of emergency (ideally before they encounter their first uncommon strain).
- Clinicians and microbiologists should be trained on a regular basis in the identification of anthrax and other rare infectious diseases that are highly pathogenic.

MALDI: Matrix-assisted laser desorption/ionisation.

Conclusions

Health professionals and diagnostic laboratories should consider anthrax as a possible diagnosis in injecting heroin users presenting with fever or sepsis at the emergency room. The observed re-emergence of drug-related anthrax in Germany supports the hypothesis that heroin may provide a continuing entry route of *B. anthracis* into western Europe.

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Healthcare workers' role in keeping MMR vaccination uptake high in Europe: a review of evidence

B Simone[1,2], P Carrillo-Santisteve[1], P L Lopalco (pierluigi.lopalco@ecdc.europa.eu)[1]
1. European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden
2. Institute of Hygiene, Universitá Cattolica del Sacro Cuore, Rome, Italy

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Measles is a highly contagious and potentially fatal disease. Europe is far from the 95% coverage rates necessary for elimination of the disease, although a safe and cost-effective vaccine is available. We reviewed the literature on studies carried out in European countries from January 1991 to September 2011 on knowledge, attitudes and practices of health professionals towards measles vaccination and on how health professionals have an impact on parental vaccination choices. Both quantitative and qualitative studies were considered: a total of 28 eligible articles were retrieved. Healthcare workers are considered by parents as a primary and trustworthy source of information on childhood vaccination. Gaps in knowledge and poor communication from healthcare workers are detrimental to high immunisation rates. Correct and transparent information for parents plays a key role in parental decisions on whether to have their children vaccinated. Healthcare workers' knowledge of and positive attitudes towards measles-mumps-rubella (MMR) vaccination are crucial to meeting the measles elimination goal. An effort should be made to overcome potential communication barriers and to strengthen vaccine education among healthcare professionals.

Introduction

Measles is a highly contagious disease and a leading cause of death among children below five years-old worldwide, although a safe and cost-effective vaccine is available [1]. Although measles usually runs a simple course, serious complications can occur: the most common in industrialised countries are otitis media (in 7–9% of cases), pneumonia (1–6%), diarrhoea (8%), post-infectious encephalitis (1 per 1,000–2,000 cases), subacute sclerosing panencephalitis (SSPE) (1 per 100,000 cases) and death (1–3 per 1,000 cases) [2]. Women who are infected during pregnancy are at greater risk of miscarriage and premature delivery [2]. Individuals at high risk of developing complications are children under 5 years of age, adults and individuals with chronic diseases and impaired immunity [1,3].

The most common way of administration of the measles vaccine is in combination with the mumps and rubella vaccines (the trivalent mumps-measles-rubella (MMR) vaccine), which is a combination of the three live attenuated viruses. Since its introduction in the 1970s, an estimated 500 million doses of MMR vaccine have been administered in over 60 countries worldwide [4]. Some countries have adopted a quadrivalent vaccine (MMRV), which also includes varicella [5].

Before vaccines were available, measles affected most people by adolescence; today, thanks to routine vaccination programmes, the disease is not seen as frequently in Europe. Eliminating measles and congenital rubella syndrome – that is, reducing to zero the incidence of infection [6] – is a goal that all European countries are committed to meet by 2015 [6,7]. In order to eliminate measles, it is necessary to reach and maintain measles vaccination coverage at 95% [1,7]. Currently, however, the vaccination coverage is still far from this level: in fact, a drop in vaccine coverage rates to suboptimal levels has been reported in Europe in recent years [8,9].

In the first eight months of 2011 alone, more than 29,000 cases of measles were reported in Europe. About one third of them required hospitalisation and in the first six months of the year, measles was responsible for eight deaths and 24 cases of acute encephalitis [9].

Currently there is no standard European policy of administration of the MMR vaccine: of 30 European countries, vaccines are administered at the paediatrician's office in 7, in healthcare centres in 12, and in multiple locations in 11 [10, and data from European Centre for Disease Prevention and Control (ECDC) experts for Malta and Romania]. There are also considerable discrepancies in the administration schedules of the MMR vaccine among European Union (EU) countries: although the first dose is always recommended by the age of 18 months in all countries, age at the second dose of MMR vaccine varies widely, from 12

Table 1

System of vaccine delivery and age at first and second measles-mumps-rubella vaccine dose as recommended by national programmes, by EU/EFTA country

Country	System	Age		
		First dose	Second dose	Catch-up vaccination
Austria	Combined	12–24 m	<24 m	7–9 y, 9–17 y
Belgium	Combined	12–13 m	10–13 y	5–7 y, 14–16 y
Bulgaria	GP/FD-based	13 m	12 y	–
Cyprus	Paediatrician-based	12–15 m	4–6 y	11–12 y
Czech Republic	Paediatrician-based	15 m	21–25 m	–
Denmark	GP/FD-based	15 m	12 y	–
Estonia	GP/FD-based	12 m	13 y	–
Finland	GP/FD-based	14–18 m	6 y	–
France	Combined	12–15 m	25 m	<6 y
Germany	Combined	11–14 m	15–23 m	–
Greece	Paediatrician-based	12–15 m	4–6 y	–
Hungary	Combined	15 m	11 y	–
Iceland	Combined	18 m	12 y	–
Ireland	GP/FD-based	12–15 m	4–5 y	11–12 y
Italy	Combined	12–15 m	11–15 y	–
Latvia	GP/FD-based	15 m	7 y	12 y
Lithuania	Combined	15–16 m	6–7 y	12 y
Luxembourg	Combined	15–18 m	5–6 y	–
Malta	Paediatrician-based[a]	13 m	3 y	–
Netherlands	GP/FD-based	14 m	9 y	–
Norway	GP/FD-based	15 m	12–13 y	–
Poland	GP/FD-based	6–7 m	10 y	11–12 y
Portugal	Combined	15 m	5–6 y	–
Romania	GP/FD-based[a]	12–15 m	6–7 y	–
Slovakia	Paediatrician-based	14 m	10 y	–
Slovenia	Paediatrician-based	12–24 m	5–6 y	–
Spain	Paediatrician-based	12–15 m	3–6 y	–
Sweden	GP/FD-based	18 m	12 y	–
Switzerland	Combined	12 m[a]	15–24 m[a]	–
United Kingdom	GP/FD-based	13 m	40 m	–

Combined: both general practitioners/family doctors and paediatricians; EFTA: European Free Trade Association; EU: European Union; GP/FD: general practitioner/family doctor; m: months; y: years.

[a] Data from European Centre for Disease Prevention and Control (ECDC) experts.

Source: unless otherwise indicated, data adapted from the EUVACnet vaccination schedules [5], Van Esso et al. [10] and VENICE report [11]).

months to 15 years [11]. Some EU countries have also implemented catch-up vaccination programmes, which are very heterogeneous in terms of age of those eligible (Table 1).

In spite of the solid evidence base on the efficacy and safety of measles vaccination [2], attitudes and practices of healthcare workers in Europe appear at times erratic: the misconception that measles is not a serious threat to health persists, not only among the parents of young children, but also among healthcare providers [12]. In this sense, there is complacency towards measles that is not present with regard to other vaccine-preventable diseases such as polio, tetanus or bacterial meningitis, which are generally perceived as extremely serious threats to health [12]. Memory of diseases and their severity fades quickly: because of routine vaccination programmes, there are generations of doctors, nurses and parents who have never seen measles or complications caused by measles.

Especially after a British study linked the MMR vaccine to increased incidence of autism, Crohn disease and other disorders [13], coverage in some European countries dropped, resulting in measles outbreaks and consistent burden of disease and costs [12]. Although the vaccine–autism controversy was dismissed and the article retracted by the journal editors [14] and

although all possible associations were repeatedly disproven [15-17], the misconception that the vaccine risks outweigh those related to acquiring natural measles immunity is still widespread among parents [16]. Practices such as measles parties are said to have made a comeback in recent years [18] and anti-vaccination groups are common and active, especially on the Internet. Furthermore, the ever-increasing recourse to alternative practices such as homeopathy has been associated with higher rates of rejection of vaccines [19,20].

The objectives of our study were: (i) to review the literature produced in European countries on the knowledge, attitudes and practices of health professionals towards measles vaccination and (ii) to assess how health professionals have an impact on parental vaccination choices.

Methods

Eligibility criteria

Study types

Studies reporting the knowledge, attitudes and practices of healthcare workers (general practitioners, paediatricians, other doctors, nurses, midwives) towards measles or MMR vaccination, as well as those reporting the influence of healthcare workers' attitudes on parental vaccination choices for their children, were eligible for inclusion. Both quantitative (surveys) and qualitative studies (focus groups) and reviews of literature focusing on one or more EU/European Economic Area (EEA) countries were searched.

Types of data

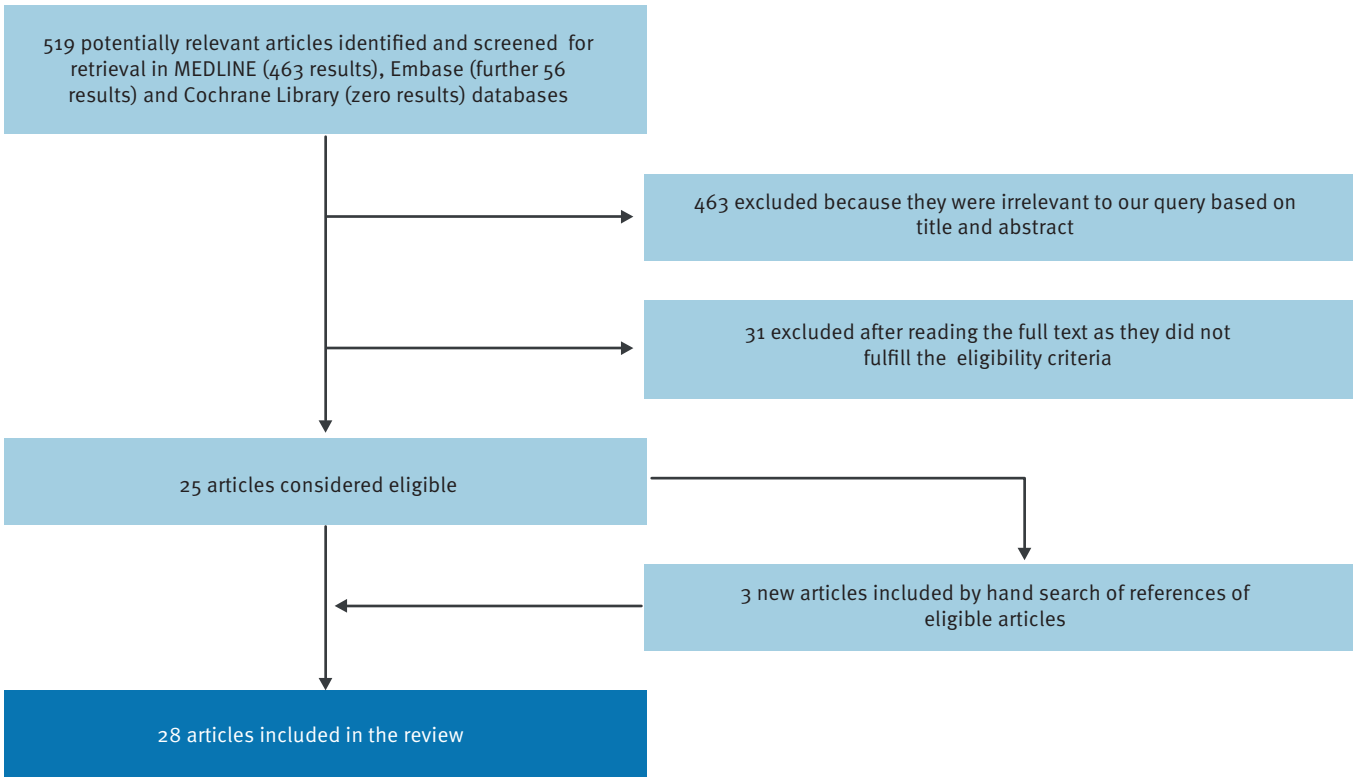
The types of data collected were: prevalence and characteristics (demographics, profession, practice/training in alternative medicine) of healthcare workers partially or entirely unfavourable to measles/MMR vaccination; common reasons for advising against vaccination; prevalence of unvaccinated children attributable to healthcare workers' knowledge, attitudes and practices; opinions of parents towards healthcare workers as a reliable source of information on MMR vaccine efficacy and safety; and common reasons for parental distrust towards healthcare workers.

Data sources and search methods for identification of studies

We searched MEDLINE and Embase. All records with the following terms were retrieved: attitude to health; health personnel OR parents; vaccine OR immunisation; Europe OR EU OR *[list of EU and EEA/European*

Figure

Search strategy for review of studies reporting knowledge, attitudes and practices of healthcare workers towards measles or MMR vaccination and those reporting the influence of healthcare workers' attitudes on parental vaccination choices



MMR: measles-mumps-rubella.

Table 2

Relevant studies reporting knowledge, attitudes and practices of healthcare workers towards measles or MMR vaccination and those reporting the influence of healthcare workers' attitudes on parental vaccination choices (n=28)

Study	Setting	Type of study	Study population
Anastasi et al. [21]	Nine randomly selected boards of physicians, Italy	Questionnaire survey	500 randomly selected paediatricians
Angelillo et al. [22]	Randomly selected kindergartens in Cassino (Frosinone) and Crotone, Italy	Questionnaire survey	841 mothers of infants
Commité français d'éducation pour la santé [23]	France	Questionnaire survey	2,000 general practitioners
Hak et al. [24]	Day-care centres associated with a large organisation, the Netherlands	Focus group and questionnaire survey	283 parents of 3-month to 5-year-old children
Petrovic et al. [25]	North Wales Health Authority Area, UK	Questionnaire survey	148 health visitors, 239 practice nurses and 206 general practitioners
Smith et al. [26]	Salford and Trafford Health Authority Area, UK	Questionnaire survey	136 general practitioners, 78 practice nurses, 40 health visitors
Cotter et al. [27]	Counties Cork and Kerry, Ireland	Focus group	47 parents, 23 public health nurses, 14 midwives, 12 practice nurses
Rotily et al. [28]	12 counties, France	Interview survey	7,382 parents of 3 year-old children
Theeten et al. [29]	125 randomly selected clusters in 107 municipalities, Flanders, Belgium	Interview survey	Parents of 1,354 children aged 18 to 24 months
Posfay-Barbe et al. [30]	Switzerland	Questionnaire survey	2,070 physicians subscribers to Infovac.net
Trier [31]	97 general practices in the county of Vestsjellænd, Denmark	Questionnaire survey	171 general practitioners
Ernst [32,33]	Exeter, UK	Questionnaire survey	45 homeopaths
Schmidt et al. [34]	UK	Questionnaire survey	104 homeopaths and 22 chiropractors registered on three websites
Lehrke et al. [35]	Germany	Questionnaire survey	219 medically qualified homoeopathic and 281 non-homoeopathic physicians
McMurray et al. [36]	Five general practices in the Leeds area, UK	Interview survey (qualitative)	69 parents of children aged between 4 and 5 years; 12 healthcare workers
Ramsay et al. [37]	UK	Cross-sectional interview surveys	1,016 mothers of children aged ≤3 years
Pareek et al. [38]	Birmingham, UK	Questionnaire survey	300 mothers of children approaching a routine MMR vaccination
Coniglio et al. [39]	8 randomly selected day-care centres in Catania, Sicily, Italy	Questionnaire survey	Parents of 1,500 children aged 3–5 years
Impicciatore et al. [40]	6 geographically dispersed centres in Italy	Questionnaire survey	1,035 mothers of children 6 years-old or younger
Heininger [41]	Germany	Questionnaire survey	6,025 participants
Dannetun et al. [42]	County of Östergötland, Sweden	Interview survey	203 parents of children who had no date registered for MMR vaccination at a child health centre
Stefanoff et al. [43]	England, Norway, Poland, Spain, Sweden	Questionnaire and interview surveys	6,611 parents of children aged 0–2 years (England, Norway, Poland, Sweden) and 0–3 years (Spain)
Swennen et al. [44]	Belgium	Interview survey	Parents of 1,110 children from Flanders and 1,088 from Wallonia
Smith et al. [45]	UK	Interview survey	1,016 mothers of children aged ≤3 years
Brown et al. [46]	Papers published in English between 1987 and 2008	Review	31 studies (23 from Europe)
Hilton et al. [47]	Central Scotland, UK	Focus group	72 parents
Casiday et al. [48]	A primary care trust in north-east England, UK	Questionnaire survey	Parents of 996 children born from 1 Oct 2000 to 30 Sep 2002
Ciofi degli Atti et al. [49]	Italy	Interview survey	Parents of 4,602 children aged 2 years

MMR: measles-mumps-rubella; UK: United Kingdom.

Free Trade Association (EFTA) countries]. The Cochrane Library was also consulted. The search covered articles published from 1 January 1991 to 27 September 2011, the date of the search. No language restriction was applied in the search. Two researchers (PCS and BS) reviewed the records independently, then discussed and agreed on the eligibility of each study. All references of eligible articles were hand searched and evaluated.

Data extraction and analyses

The following information was extracted for each study: references, country/countries involved, setting and characteristics of the healthcare workers interviewed, including details of their professions, and summary of the relevant data.

Results

The MEDLINE search yielded 463 results and a further 56 results were obtained through Embase. No systematic review of measles/MMR was found in the search of the Cochrane Library. Of the 519 overall articles retrieved, 463 were discarded as the title and abstract were not relevant and 31 after reading the full text as they did not meet the eligibility criteria. A further three articles were retrieved through hand search of references from the eligible articles. A total of 28 articles overall were included, as shown in the Figure and Table 2.

Knowledge, attitudes and practices of healthcare workers towards measles/MMR vaccination

A 2009 survey conducted among 156 Italian paediatricians [21] reported that only 88% knew that measles vaccination was recommended in the country, and only 35% knew the vaccination calendar. As for perceptions of the utility of recommended vaccinations (including MMR), paediatricians were asked to assign a score on a scale from 1 to 10: only 10% of those sampled resulted very favourable (scores of 9 or 10), although this percentage was significantly higher among those who administered recommended vaccinations for infants (odds ratio (OR):3.3; 95% confidence interval (CI): 1.1–9.9). Only a quarter of respondents administered the recommended vaccinations (which include measles) (26%), whereas among paediatricians who did not normally administer vaccines, 81% still advised parents to have their children immunised for recommended vaccinations. A total of 83% of the paediatricians sampled routinely provided information about recommended vaccinations to their patients, whereas a lower percentage (78%) informed them about benefits and risks.

An article published in 1999 in the *Bulletin of the World Health Organization* [22] reported that around 10% of 841 mothers of kindergarten children sampled from two Italian towns declined MMR vaccination because they were advised against it by healthcare professionals before deciding.

A French survey from 2001 from the French Committee for Health Education (Commité français d'éducation pour la santé) [23] categorised the attitudes of 2 000 general practitioners towards MMR vaccination into those who were: (i) very favourable, i.e. those who vaccinated systematically following the vaccination calendar (41%); (ii) favourable, i.e. those who vaccinated depending on the situation and did not follow the vaccination calendar systematically (56%); and (iii) unfavourable, i.e. those who disregarded the vaccination calendar (3%). Overall, 6% of those sampled were very or rather unfavourable to MMR vaccination. Those who were unfavourable were mostly practitioners who practiced homeopathy and/or alternative medicine and who worked with higher social/educated classes. The vaccination practices of practitioners who were favourable to the vaccination were also likely to improve after further training on vaccination.

A survey performed in the Netherlands in 2005 [24], among 283 parents of children attending day-care centres, showed that a negative attitude towards future vaccinations was significantly more common among healthcare workers (OR: 4.2; 95% CI: 1.4–12.6) and highly educated parents (OR: 3.3; 95% CI: 1.3–8.6) than among other parents.

Following the MMR–autism controversy, several studies were carried out on practitioners' attitudes towards MMR vaccination in the United Kingdom (UK) and Ireland. In north Wales, Petrovik et al. [25] found in 2001 that knowledge and practice among 593 healthcare professionals regarding the second MMR dose varied widely: 48% of healthcare professionals had reservations about the policy of giving the second MMR dose and 3% disagreed with it.

From a UK survey from Smith et al. [26], 40% of the 136 responding physicians were unsure of the need for the second dose and around 10% thought it unnecessary.

In Ireland, a survey in 2001 among 86 general practitioners, nurses and parents [27] showed a negative impact on vaccination uptake due to health professionals' ambivalence about vaccinations, inability or unwillingness to answer parents' questions or lack of empathy with parents concerned about the alleged side effects of the vaccines.

A French telephone survey published in 2001 [28], among 7,382 parents, showed that the coverage was significantly higher among children attended by a paediatrician compared with children not attended by a paediatrician (90.9% vs 85.4%, $p<0.001$).

A survey conducted in Flanders, Belgium, in 2004 [29] found that having completed the schedule for the MMR vaccine depended on the vaccinating physician: children mainly vaccinated by a general practitioner were less likely to be completely vaccinated (adjusted OR: 0.3; 95% CI: 0.1–0.7) than children mainly vaccinated

by a paediatrician (reference group) and children vaccinated in a baby clinic or day-care centre were more likely to have received a valid schedule (OR: 2.3; 95% CI: 1.8–5.1).

A survey conducted in Switzerland among physicians [30] showed that 93% of the 2,070 surveyed physicians agreed with current official vaccination recommendations and would apply them to their own children. As for MMR vaccine, however, more paediatricians had their children vaccinated with the vaccine according to the recommended schedule than the other physicians (OR: 2.8; 95% CI: 1.6–4.7). A statistically significant number of non-paediatricians (4.8%) did not have their own children vaccinated.

A total of 171 practitioners were interviewed in Denmark in a 1991 survey on their attitude with regard to the usefulness of MMR vaccination: all expressed a positive attitude, but only 56% of respondents expressed a wholeheartedly positive attitude. Average vaccination rates were connected with such attitudes, being 85% in practices with unreservedly positive attitudes and 69% in practices with more guarded attitudes [31].

Providers of complementary medicine and homeopaths

Providers of complementary medicine are sometimes reported as having a negative attitude towards immunisation in general, including MMR [32]. Some studies have shown that homoeopathic physicians do not recommend or apply vaccinations as frequently as their allopathic colleagues [32-34].

A small study from Ernst et al. [33] in the UK (n=23) on homeopaths' attitudes towards vaccination showed that all non-medically qualified homoeopaths refused vaccinations (13/13) but only 3 of the 10 medically qualified homoeopathic physicians did so.

In a 2002 UK study [34], Schmidt and Ernst evaluated and compared the response of professional homoeopaths, chiropractors and general practitioners to an inquiry about MMR vaccination. Of 104 homeopaths who responded to the survey, 40 advised explicitly against immunisation; another 26 withdrew their answer after being told that the query was, in fact, part of a research project. Out of 63 chiropractors, 3 advised against immunisation and 27 withdrew their answers.

Lehrke et al. [35] performed a study in 2001 among medically qualified homeopathic practitioners and non-homeopathic physicians (both generalists and paediatricians) in Germany about the administration and recommendation of 17 different vaccinations in their practices. The study showed that the responding homoeopathic physicians (n=219) did not generally refuse vaccines but rather viewed them with a specific hierarchy: the 'classical' vaccines against tetanus, diphtheria and poliomyelitis were applied to nearly the same degree as by their non-homoeopathic colleagues (n=281); however, vaccines against childhood diseases, including measles, were judged as ineffective and accepted with more restraint by homoeopathic physicians.

A 2001 French survey [28] involving 7,382 parents showed that coverage rates were significantly lower among children whose parents exclusively or sought advice from a homeopath (70%), as compared with children whose parents never (92.1%) or sometimes (90.1%) did.

Impact of healthcare workers knowledge, attitudes and practice on parental vaccination choices for their children

Primary care providers have a central role in educating their patients on the safety and effectiveness of the MMR vaccine and can influence the rates of MMR immunisation just by answering parents' questions and addressing common misconceptions [36].

Several studies across Europe report that parents consider healthcare workers to be the most important source of information when deciding whether their children should be immunised with the MMR vaccine: 74% of mothers from a nationally representative sample of over 1,000 in a 2002 survey conducted in England reported seeking advice from health professionals before having their children immunised with the vaccine [37]. Information provided by healthcare workers was considered as the most influential and reliable by 77–78% of the respondents in a 2000 UK survey involving 300 mothers [38].

In a 2011 study [39] conducted in Sicily, one of the Italian regions with relatively high MMR vaccine coverage rates (87%), the great majority of parents interviewed (74%) singled out family paediatricians as the most important source of information. A total of 63% of mothers interviewed in a 2000 study [40] conducted in Italy also reported paediatricians to be their most important information source.

In Germany, 95% of respondents considered their paediatrician as the most important source of information in a 2006 online survey [41]; doctors and nurses from Child Health Centres were trusted as the most important source by 77% of interviewed parents in Sweden in 2005 [42].

The first results from the European *Vaccine Safety, Attitudes, Training and Communication* (VACSATC) project of 2010 [43] – comparing five cross-sectional surveys of parents with children less than three years of age in England, Norway, Poland, Spain and Sweden (6,611 respondents) – showed that healthcare providers ranked first among most used and most trusted sources of information on vaccines. Health professionals were

the most trusted by 92% of respondents in England; in Norway, the public health nurse was the most used source (49%) and the public health doctor the most trusted (67%); in Poland and Spain, the primary care physician was both the most used (79% and 85%, respectively) and most trusted (82% and 87%, respectively) source; in Sweden the public health nurse was used as main source of information by 82% of respondents and was the most trusted by 87%.

The attitude of the physician was mentioned as being very influential in the decision to vaccinate a child in the French-speaking community in Belgium [44].

In contrast, another survey conducted in the UK in 2007 showed a sharp drop in the level of trust in health professionals [45]. However, a 2010 systematic review by Brown et al. showed that parents are more likely to trust the information given to them by their general practitioners, health visitor or practice nurse than by the government: this relationship was observed in all five studies on the topic ($p<0.05$ in three of the five) [46].

As seen in several studies, trust in individual health professionals and vaccine policymakers can be compromised by perceived conflicting interests (such as 'toeing the party line', meeting targets and giving financial compensation to doctors who reach high vaccine coverage rates) [36,47]. Health providers who were too resolute about the safety of the MMR vaccine led to parents questioning the providers' motives and knowledge; conversely, when the healthcare providers sounded vague, some parents interpreted this as concern that the vaccine was unsafe [47]. Such perceptions can be counteracted to some degree by trust in professional expertise and by healthcare workers sharing their personal experience (for example, confirming that they have vaccinated their own children) [36].

One of the most recurrently reported reasons for low vaccine acceptance rates is dissatisfaction with the adequacy of information provided to parents: a survey conducted in 2005 in the UK showed that 53% of respondents felt that doctors were too dismissive of parents' concerns about vaccine side effects. This figure rose to 89% among those who declined vaccination for their children [48].

A national survey conducted in Italy in 2003 showed that lack of appropriate information accounted for 22% of the missed or delayed MMR/measles vaccinations and intercurrent illness for 29% [49].

Discussion

Measles is a serious threat to public health: elimination of the disease in the EU is not only feasible, but necessary. Europe failed to meet the goal of eliminating measles by 2010, because of lower-than-required vaccination coverage. The commitment has been renewed, to eliminate measles by 2015 [50]. However, instead of a progressive reduction of the disease in Europe, incidence and the number of outbreaks increased dramatically over the past 15 years, with unacceptable consequences in terms of mortality, morbidity and costs.

From our review, it is quite clear that doctors and other healthcare providers are regarded as the most reliable sources of information from parents. Healthcare workers are generally trusted and consulted on whether children should be vaccinated and they are in a good position to empower parents to take an informed decision about MMR vaccination for their children. If this is a reassuring thought, it has to be noted that trust towards healthcare workers on motives to vaccinate and safety and efficacy of the vaccine can be compromised if inadequate or vague information is provided or a conflict of interest perceived. For example, a history of safety issues cannot be denied but have to be explained in a clear and transparent manner. Parents need to be educated to make an informed choice.

Although a small percentage of practitioners, especially providers of complementary medicine, are against vaccines on principle, we found that the main problem among healthcare providers was lack of knowledge. In most cases, suboptimal vaccination rates resulted from inadequate knowledge among healthcare providers of vaccination schedules, as well as the benefits and side effects. In some cases, healthcare providers were even found to have misleading beliefs about immunisation and sent unclear or untrue messages to parents. Whenever healthcare workers' knowledge was found to be inadequate, vaccination coverage in the general population decreased. The same happened when healthcare workers were reported to have a relaxed attitude towards measles, which is itself a consequence of lack of knowledge of the disease infectivity and morbidity.

Even among providers of complementary medicine, medically qualified homeopaths tended to have a less negative attitude towards immunisation as compared with non-medically qualified practitioners [33].

A limitation of our study is related to the search strategy. Studies published in journals that are not indexed in MEDLINE and/or Embase (or cited in their references) were not included in the review: this might have caused us to overlook some evidence produced and published at a national level, especially in languages other than English. We know of at least one paper, published in the German *Epidemiologisches Bulletin* in 2008 [51], that was not included in the review for this reason, although the topic was relevant to our query. The authors surveyed attitudes and knowledge of childhood vaccination among 549 German midwives: about a quarter of the midwives interviewed did not support the administration of the MMR vaccine to children and over 40% considered diseases such as measles important for the personal development of the child. The survey also reported that over 10% of the sample

disagreed with the statement 'measles infection can be fatal'. The survey showed a significantly lower support for MMR vaccination among midwives trained in alternative medicine (p=0.025); furthermore, midwives who declared that they were against the administration of the vaccine were less likely to inform parents about the availability of the vaccine (p=0.009).

Another potential limitation of this review is that all the studies considered were produced in western Europe (Table 2). This might warrant caution in the interpretation of the results. Attitudes and knowledge of immunisation among healthcare providers might not be the biggest problem in lower-resource countries, as in some Central and Eastern European countries, where low coverage rates might also be due to logistic and organisational issues in vaccine delivery. However, it should be noted that, with the exception of Romania (4,015 confirmed cases), the major outbreaks of measles in 2011 were reported in western European countries: France (15,206 confirmed cases), Italy (5,181 confirmed cases) and Spain (1,986 confirmed cases) [52]. For these countries, low vaccination coverage rates, and thus the high incidence of measles, are unarguably, at least in part, a consequence of a general complacency towards the disease and of loose strategies for vaccination coverage. This is partly due to false myths and anti-vaccine propaganda and partly to the fact that vaccination has made measles an uncommon disease, diluting perceptions and memories of how threatening it can be.

In order to improve vaccination coverage, therefore, it is fundamental to raise awareness about the disease and fill any knowledge gaps of healthcare workers, providing them with evidence-based information on vaccines and educating them to communicate effectively with patients and parents; this could be attained through dedicated websites and by emphasising vaccine education in the medical and nursing curricula. The Council of the European Union [53] has invited Member States to make efforts along these lines.

Similar to the situation for healthcare workers, we found that there was a small proportion of parents who were very reluctant to have their children vaccinated with the MMR vaccine, regardless of proof of its efficacy and safety. However, most vaccine-decliners are simply under-informed or received misconceived information [24,28,36,37,43,48]. Better informed and trained health professionals could have a substantial impact on the vaccination choices of those parents. For example, the results of Ciofi degli Atti et al. are indicative of the fact that that more efforts are needed to educate mothers (as well as physicians) regarding the risks associated with measles, as well as the fact that intercurrent illness is rarely a contraindication to immunisation [49].

Reaching 95% vaccine coverage is a priority for Europe. Measles was eliminated in 2002 in the Americas through universal coverage and active case surveillance [54]. One of the reasons behind this successful story in the Americas was good coordination among a consortium of countries. The Pan American Health Organization developed an enhanced and, most importantly, integrated disease elimination strategy [55].

The successful experience in the Americas shows the added value of addressing measles elimination at the European level. No country in Europe can attain it individually: only a joint effort will succeed.

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Infectious diseases among travellers and migrants in Europe, EuroTravNet 2010

P Gautret[1], J P Cramer[2], V Field[3], E Caumes[4], M Jensenius[5], E Gkrania-Klotsas[6], P J de Vries[7], M P Grobusch[7], R Lopez-Velez[8], F Castelli[9], P Schlagenhauf[10], H Hervius Askling[11], F von Sonnenburg[12], D G Lalloo[13], L Loutan[14], C Rapp[15], F Basto[16], F Santos O'Connor[17], L Weld[18], P Parola (philippe.parola@univ-amu.fr)[1], for the EuroTravNet Network[19]

1. University Hospital Institute for Infectious and Tropical Diseases, Marseille, France
2. University Medical Center Hamburg-Eppendorf, Department of Tropical Medicine and Infectious Diseases, Bernhard Nocht Clinic, Hamburg, Germany
3. InterHealth and National Travel Health Network and Centre (NaTHNaC), London, United Kingdom
4. Service des Maladies Infectieuses et Tropicales (Department of Infectious and Tropical Diseases), Hôpital Pitié-Salpétrière, Paris, France
5. Department of Infectious Diseases, Oslo University Hospital, Oslo, Norway
6. Department of Infectious Diseases, Addenbrooke's Hospital, Cambridge, United Kingdom
7. Center for Tropical Medicine and Travel Medicine, Department of Infectious Diseases, Academic Medical Center, Amsterdam, the Netherlands
8. Tropical Medicine and Clinical Parasitology, Infectious Diseases Department, Ramón y Cajal Hospital, Madrid, Spain
9. University Division of Infectious and Tropical Diseases, University of Brescia and Brescia Spedali Civili General Hospital, Brescia, Italy
10. Centre for Travel Medicine, University of Zürich, Zürich, Switzerland
11. Department of Medicine/Solna, Unit for Infectious Diseases, Karolinska Institute, Stockholm, Sweden
12. Department of Infectious Diseases and Tropical Medicine, Ludwig-Maximilian's University of Munich, Munich, Germany
13. Liverpool School of Tropical Medicine, Liverpool, United Kingdom
14. Division of International and Humanitarian Health, Geneva University Hospitals, Geneva, Switzerland
15. Department of Infectious and Tropical Diseases, Bégin Military Hospital, Saint-Mandé, France
16. Centro Hospitalar São João (Hospital Centre São João), International Health Unit, Porto, Portugal
17. European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden
18. ISTM/Geosentinel Statistician Consultant, Victoria, Canada
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To investigate trends in travel-associated morbidity with particular emphasis on emerging infections with the potential for introduction into Europe, diagnoses of 7,408 returning travellers presenting to 16 EuroTravNet sites in 2010 were compared with 2008 and 2009. A significant increase in reported *Plasmodium falciparum* malaria (n=393 (6% of all travel-related morbidity) vs. n=267 (4%) and 296 (5%); p<0.001), *P. vivax* malaria (n=53 (1%) vs. n=31 (0.5%) and 39 (1%); p=0.038) and dengue fever (n=327 (5%) vs. n=131 (2%) and 172 (2%); p<0.001) was observed. *Giardia lamblia* was identified in 16% of patients with acute diarrhoea, with no significant annual variation. The proportion of acute diarrhoea due to *Campylobacter* increased from 7% in 2008 to 12% in 2010 (p=0.002). We recorded 121 patients with pulmonary tuberculosis in 2010, a three-fold increase in the proportionate morbidity from 2008 to 2010. In 2010, 60 (0.8%) cases of chronic Chagas disease, 151 (2%) cases of schistosomiasis and 112 (2%) cases of cutaneous larva migrans were reported. Illness patterns in sentinel travellers, captured by EuroTravnet, continue to highlight the potential role of travellers in the emergence of infectious diseases of public health concern in Europe and the relevance of offering medical travel advice and enforcing specific and adequate prophylaxis.*

Introduction

EuroTravNet (www.eurotravnet.eu), a network of clinicians who are specialists in tropical and travel medicine, was founded in 2008. It includes 16 EuroTravNet sites staffed by clinicians that have demonstrated training, experience, and/or significant publications in travel or tropical medicine. Sites in France, Germany, Italy, the Netherlands, Norway, Portugal, Spain, Sweden, Switzerland and the United Kingdom, participate in surveillance and monitoring of travel-related illnesses by collecting epidemiological data on returning ill travellers using the GeoSentinel technology platform (www.geosentinel.org) [1-3]. Network-based surveillance data allow for patient diagnoses, chronology of travel, and standardised exposure details to be collected for detailed analysis of travel-related morbidity. In addition, such networks can detect disease outbreaks through sentinel travellers, enhance surveillance, and facilitate rapid communication, response and dissemination of information among healthcare providers and public health partners. A good example of efficient detection of outbreaks among travellers was the recent report of a cluster of travellers returning from Tioman Island, Malaysia with muscular sarcocystosis [4].

This report describes the spectrum of selected infectious diseases in European travellers in 2010, and compares these numbers with the data sets from 2008 and 2009. Thanks to the multi-centre nature of EuroTravNet, which provided a large number of ill travellers from many countries with different reasons for travelling, we were able to capture statistically significant trends in imported infectious diseases over a relatively short period of three years.

Methods

The detailed methods for patient recruitment, inclusion criteria, and limitations of the GeoSentinel database have been described elsewhere [1-3,5]. In brief, patients must have crossed an international border, including borders within Europe, before the clinic visit and must have sought medical advice for a presumed travel-related illness or for screening for asymptomatic infection. All returned travellers presenting to EuroTravNet sites are systematically and prospectively included in the GeoSentinel database provided the diagnosis is clinically or laboratory-confirmed and that the causality of travel is confirmed. Travellers undergoing screening for asymptomatic infections or clinically cured travellers looking for a confirmation of the diagnosis established elsewhere are however also included in the database, with "healthy" as a diagnosis when the screening remains negative. Patients included in the study may be symptomatic or not. For example, patients with chronic infection such as Chagas disease, schistosomiasis, tuberculosis, hepatitis B, were included whether or not they had clinical symptoms at the time they presented*. Anonymous, almost real-time, surveillance data that cannot be linked to individual patients are entered into the GeoSentinel database. Final diagnoses are assigned by the treating clinician from an internal standardised GeoSentinel list of more than 500 possible individually coded diagnoses [5]. Patients can be assigned as many diagnostic codes as applicable. All sites use the best available reference diagnostic tests and clinical protocols in their respective countries. Travellers who presented between 1 January 2010 and 31 December 2010 to a EuroTravNet site during or after travel were included in this analysis and were compared with travellers who presented in EuroTravNet sites between 1 January and 31 December in 2008 and 2009. Sites see two distinct groups of patients. The first group represents travellers on short trips, including mainly tourists, business travellers and non-recent migrants or their descendants visiting friends and relatives in their origin countries (VFRs), but also missionaries, volunteer workers, aid workers and researchers, students travelling for field work, military personnel on missions, and individuals travelling to seek medical care (medical tourism). The second group represents travellers with long-time exposure abroad including mainly recent immigrants, usually seen for screening when they first enter the migration country, and long-term exposed expatriates (missionaries, volunteers, aid workers and researchers as well as people staying abroad for business).

Data were analysed using SPSS, v16.0 (SPSS Inc, Chicago). We calculated proportionate morbidities by comparing the number of cases of a specific diagnosis (or of a group of specific diagnoses within a syndrome group) with all cases of returning ill travellers seen during the same time period (or to sub-groups of travellers). This allowed us to make comparisons over time and between subgroups. Differences in proportions between sub-groups of returning ill travellers seen at EuroTravNet sites were tested using Pearson's Chi-square or Fisher's exact tests. A p value of under 0.01 was chosen as significant to take into account the large number of statistical tests performed. One new site had joined EuroTravNet in late 2008, and four new sites had joined EuroTravNet in 2010, contributing together 10% of cases in 2009 and 16% in 2010. To allow a reliable comparison by year, cases reported by sites that joined after mid-2008 were excluded for trend analysis.

Table 1

Number and percentage of travellers seen at the 16 EuroTravNet sites, 2008–2010 (n=20,757)

Sites	2008	2009	2010
Number (%)	**6,957 (100)**	**6,392 (100)**	**7,408 (100)**
France (3 sites)			
Marseille	351 (5)	496 (8)	395 (5)
Paris	548 (8)	580 (9)	564 (8)
Saint Mandé	–	–	201 (3)
Germany (2 sites)			
Hamburg	1,480 (21)	806 (13)	1,050 (14)
Munich	1,547 (22)	1,441 (23)	1,365 (18)
Italy (1 site)			
Brescia	136 (2)	246 (4)	237 (3)
Norway (1 site)			
Oslo	498 (7)	476 (7)	588 (8)
Portugal (1 site)			
Porto	–	–	8 (<1)
Sweden (1 site)			
Stockholm	–	–	416 (6)
Switzerland (2 sites)			
Geneva	417 (6)	293 (5)	385 (5)
Zurich	225 (3)	132 (2)	245 (3)
Spain (1 site)			
Madrid	456 (7)	217 (3)	225 (3)
The Netherland (1 site)			
Amsterdam	41 (1)	670 (11)	507 (7)
United Kingdom (3 sites)			
Cambridge	126 (2)	125 (2)	152 (2)
Liverpool	–	–	52 (1)
London	1,132 (16)	910 (14)	1,018 (14)

Results

In 2010, data from 7,408 ill travellers were collected. There were no significant changes from 2008 to 2010 in the number of patients seen at each site (Table 1), nor in the age and sex distribution of patients. More non-VFR short-term travellers were hospitalised in 2009 and 2010 than in 2008, and fewer patients were known to have received a pre-travel consultation (Tables 2 and 3). The results remained the same when the new sites were excluded.

Mortality observed in imported diseases

Five deaths were recorded in 2010. A French tourist in their 30s died in Switzerland of melioidosis with septic shock, multi-organ failure and acute respiratory distress syndrome after a trip to Martinique [6]. A migrant from India in their 30s died in Brescia with a diagnosis of pyogenic liver abscesses and diabetes mellitus. A Swiss in their 50s tourist died of disseminated *Salmonella enterica* serovar Weltevreden infection after returning to Switzerland from Puerto Rico. A Norwegian tourist in their 60s died of Legionnaires' disease after a returning from the Czech Republic. A Portuguese

Table 2

Demographic characteristics of immigrants and expatriates (long-term exposure) seen at the 16 EuroTravNet sites, 2008–2010 (n=3,494)

	Immigrants			Expatriates		
Year	**2008**	**2009**	**2010**	**2008**	**2009**	**2010**
Number	**656**	**489**	**639**	**479**	**548**	**683**
Sex (%) Female	311 (47)	215 (44)	298 (47)	230 (48)	292 (53)	341 (50)
Age (years)						
Mean	32.6	31.6	32.9	40.2	37	36.8
25th percentile	26	24	25	30	29	28
Median	32	30	32	40	38	38
75th percentile	39	38	39	53	48	50
Travel reason (%)						
Business	–	–	–	123 (26)	105 (19)	150 (22)
Immigration	656 (100)	489 (100)	639 (100)	–	–	–
Medical tourism	–	–	–	0 (0)	0 (0)	0 (0)
Military	–	–	–	0 (0)	0 (0)	0 (0)
M/V/AW/R	–	–	–	348 (73)	442 (81)	533 (78)
Student	–	–	–	0 (0)	1 (0)	0 (0)
Tourism	–	–	–	6 (1)	0 (0)	0 (0)
Risk level (%)						
Expatriate	–	–	–	479 (100)	548 (100)	683 (100)
Pre-arranged or organised travel	–	–	–	–	–	–
Risk travel[a]	656 (100)	489 (100)	639 (100)	–	–	–
Clinical setting (%)						
Immigration only	656 (100)	489 (100)	639 (100)	–	–	–
Seen after travel	–	–	–	272 (57)	320 (58)	367 (54)
Seen during travel	–	–	–	207 (43)	228 (42)	316 (46)
Inpatient (%)	106 (16)	166 (34)	243 (38)	23 (5)	15 (3)	29 (4)
Pre-travel consultation (%)						
Yes	9 (1)	6 (1)	4 (1)	301 (63)	365 (66)	434 (64)
No	60 (9)	130 (27)	144 (23)	54 (11)	41 (8)	76 (11)
Do not know	587 (90)	353 (72)	491 (77)	124 (26)	143 (26)	173 (25)
Live in Europe (%)						
Yes	654 (100)	489 (100)	639 (100)	244 (51)	318 (58)	396 (58)
Born in Europe (%)						
Yes	28 (4)	26 (5)	62 (10)	423 (88)	474 (87)	568 (83)

AW: aid worker; M: missionary; R: researcher; V: volunteer; VFR: visiting friends and relatives.

[a] Risk travel: intended to identify travellers who will, by their behaviour, encounter a substantial number of the risks faced by the local population. This classification would generally include travelling without pre-booking accommodation for most or all nights, using accommodation specific to budget travellers and/or staying in local residents' homes.

business traveller in their 50s died with a *Plasmodium falciparum* infection and acute respiratory distress syndrome after a four-month stay in Angola. This patient had not taken anti-malarial prophylaxis. The overall mortality rate was 0.7 per 1,000 ill travellers in 2010, compared with 0.3 per 1,000 in 2009 (two deaths due to visceral leishmaniasis, and Acinetobacter sp. pneumonia) and with 0.4 per 1,000 in 2008 (three deaths due to *P. falciparum* cerebral malaria, dengue shock syndrome and *E. coli* pyelonephritis) [2,3]. The mortality rate associated with malaria was 1.7 per 1,000 malaria cases in 2010, compared with 0 per 1,000 in 2009 and 2.7 per 1,000 in 2008.

Spectrum of imported diseases

Among diagnoses with an identified pathogen (Tables 4 and 5), malaria and dengue fever accounted for most cases of febrile systemic illnesses. *Giardia lamblia* was the most common pathogen identified in acute diarrhoea, followed by *Campylobacter* and *Salmonella* spp. Other common parasitic infections included

Table 3

Demographic characteristics of patients visiting friends and relatives and other short-term travellers seen at the 16 EuroTravNet sites, 2008–2010 (n=17,263)

	VFRs			Other short-term travellers		
Year	**2008**	**2009**	**2010**	**2008**	**2009**	**2010**
Number	**831**	**800**	**942**	**4,991**	**4,555**	**5,144**
Sex (%) Female	347 (42)	350 (44)	403 (43)	2,510 (50)	2,355 (52)	2,561 (50)
Age (years)						
Mean	33.3	34.7	36.7	38.5	37.9	38.7
25th percentile	23	25	28	28	27	27
Median	34	35	37	36	35	36
75th percentile	45	45	46	49	48	49
Travel reason (%)						
Business	–	–	–	606 (12)	600 (13)	741 (14)
Immigration	–	–	–	–	–	–
Medical tourism	–	–	–	10 (0)	24 (1)	27 (1)
Military	–	–	–	40 (1)	61 (1)	73 (1)
M/V/AW/R	–	–	–	1,221 (25)	838 (18)	996 (19)
Student	–	–	–	91 (2)	157 (3)	131 (3)
Tourism	–	–	–	3,023 (61)	2,875 (63)	3,176 (62)
VFRs	831 (100)	800 (100)	942 (100)	–	–	–
Risk level (%)						
Expatriate	–	–	–	–	–	–
Pre-arranged or organised travel	–	–	–	1,570 (32)	1,698 (37)	2,015 (39)
Risk travel[a]	831 (100)	800 (100)	942 (100)	3,367 (68)	2,780 (61)	3,074 (60)
Missing information	–	–	–	54 (1)	77 (2)	55 (1)
Clinical setting (%)						
Immigration only	–	–	–	–	–	–
Seen after travel	819 (99)	779 (97)	934 (99)	4,616 (93)	4,296 (94)	4,895 (95)
Seen during travel	12 (1)	21 (3)	8 (1)	375 (8)	259 (6)	249 (5)
Inpatient (%)	261 (31)	290 (36)	390 (41)	379 (8)	461 (10)	682 (13)
Pre-travel consultation (%)						
Yes	203 (24)	212 (27)	221 (24)	2,647 (53)	2,182 (48)	2,321 (45)
No	329 (40)	381 (48)	472 (50)	1,111 (22)	1,116 (25)	1,524 (30)
Do not know	299 (36)	207 (26)	249 (26)	1,233 (25)	1,257 (28)	1,299 (25)
Live in Europe (%)						
Yes	817 (98)	782 (98)	934 (99)	4,640 (93)	4,324 (95)	4,933 (96)
Born in Europe (%)						
Yes	260 (31)	239 (30)	264 (28)	4,570 (92)	4,214 (93)	4,757 (93)

AW: aid worker; M: missionary; R: researcher; V: volunteer; VFR: visiting friends and relatives.

[a] Risk travel: intended to identify travellers who will, by their behaviour, encounter a substantial number of the risks faced by the local population. This classification would generally include travelling without pre-booking accommodation for most or all nights, using accommodation specific to budget travellers and/or staying in local residents' homes.

Table 4

Number of cases and proportional morbidity for selected diagnoses with identified pathogens in people with long-term exposure seen at EuroTravNet sites, 2008–2010 (n=4,785)

Diagnosis Number (proportional morbidity)	Immigrants (n=2,416)					Expatriates (n=2,369)				
	2008 excluding new sites[a] n=656	2009 excluding new sites[a] n=489	2010 excluding new sites[a] n=632	2010 all sites n=639	P value	2008 excluding new sites[a] n=479	2009 excluding new sites[a] n=548	2010 excluding new sites[a] n=659	2010 all sites n=683	P value
Plasmodium falciparum malaria	13 (2)	6 (1)	20 (3)	21 (3)	0.080	12 (3)	10 (2)	11 (2)	14 (2)	0.581
P. vivax malaria	2 (0)	9 (2)	3 (1)	3 (1)	0.008	3 (1)	0 (0)	0 (0)	0 (0)	0.023
Severe malaria[b]	0 (0)	2 (<1)	2 (<1)	2 (<1)	0.294	3 (1)	1 (<1)	0 (0)	1 (<1)	0.095
Non-falciparum malaria (includes P. vivax)	3 (1)	10 (2)	6 (1)	6 (1)	0.033	6 (1)	3 (1)	3 (1)	3 (<1)	0.246
Dengue fever	0 (0)	0 (0)	2 (<1)	2 (<1)	0.163	7 (2)	6 (1)	10 (2)	10 (2)	0.801
Chikungunya	0 (0)	1 (<1)	0 (0)	0 (0)	0.268	2 (<1)	0 (0)	1 (<1)	1 (<1)	0.279
Giardia	6 (1)	5 (1)	4 (1)	4 (1)	0.755	8 (2)	7 (1)	9 (1)	10 (2)	0.858
Campylobacter	0 (0)	0 (0)	0 (0)	0 (0)	-	2 (<1)	1 (<1)	2 (<1)	3 (<1)	0.787
Salmonella[c]	1 (<1)	0 (0)	4 (1)	4 (1)	0.103	6 (1)	0 (0)	3 (<1)	3 (<1)	0.022
Active tuberculosis (all cases)	60 (9)	90 (18)	155 (25)	156 (24)	<0.001	2 (<1)	2 (<1)	0 (0)	0 (0)	0.272
Pulmonary tuberculosis	26 (4)	51 (10)	93 (15)	94 (15)	<0.001	0 (0)	0 (0)	0 (0)	0 (0)	-
Schistosomiasis	11 (2)	18 (4)	23 (4)	24 (4)	0.057	14 (3)	17 (3)	28 (4)	29 (4)	0.402
Chronic Chagas disease	93 (14)	30 (6)	58 (9)	58 (9)	<0.001	0 (0)	0 (0)	0 (0)	0 (0)	-
Cutaneous larva migrans	0 (0)	0 (0)	2 (<1)	2 (<1)	0.163	2 (<1)	1 (<1)	0 (0)	0 (0)	0.256

n: total number of ill patients (all diagnoses including those not due to an infectious cause)

[a] Cases reported by sites that joined EuroTravNet after mid-2008 were excluded to allow a reliable comparison by year.

[b] Severe malaria was defined according to World Health Organization criteria [7].

[c] Salmonella Typhi and other species and S. Paratyphi.

Table 5

Number of cases and proportional morbidity for selected diagnoses with identified pathogens in people with short-term exposure seen at EuroTravNet sites, 2008–2010 (n=22,703)

Diagnosis Number (proportional morbidity)	People visiting friends and relatives (n=3,419)					Other short-term travellers (n=19,284)				
	2008 Excluding new sites[a] n=831	2009 excluding new sites[a] n=800	2010 excluding new sites[a] n=846	2010 all sites n=942	P value	2008 Excluding new sites[a] n=4,991	2009 excluding new sites[a] n=4,555	2010 excluding new sites[a] n=4,594	2010 all sites n=5,144	P value
P. falciparum malaria	169 (20)	192 (24)	243 (29)	277 (29)	<0.001	73 (2)	88 (2)	119 (3)	136 (3)	<0.001
P. vivax malaria	9 (1)	3 (<1)	20 (2)	21 (2)	0.001	17 (<1)	27 (1)	30 (1)	55 (1)	0.078
Severe malaria[b]	1 (<1)	6 (1)	14 (2)	15 (2)	0.003	8 (<1)	4 (<1)	15 (<1)	17 (<1)	0.027
Non-falciparum malaria (includes P. vivax)	36 (4)	25 (3)	42 (5)	43 (5)	0.166	59 (1)	43 (1)	65 (1)	94 (2)	0.114
Dengue fever	16 (2)	22 (3)	25 (3)	27 (3)	0.368	108 (2)	144 (3)	290 (6)	319 (6)	<0.001
Chikungunya	2 (<1)	0 (0)	4 (1)	4 (<1)	0.149	8 (<1)	17 (<1)	23 (1)	25 (1)	0.015
Giardia	10 (1)	8 (1)	10 (1)	11 (1)	0.913	169 (3)	165 (4)	172 (4)	190 (4)	0.630
Campylobacter	3 (<1)	14 (2)	8 (1)	11 (1)	0.019	82 (2)	82 (2)	118 (3)	160 (3)	0.003
Salmonella[c]	13 (2)	17 (2)	24 (3)	27 (3)	0.202	59 (1)	55 (1)	72 (2)	93 (2)	0.189
Active tuberculosis (all cases)	28 (3)	39 (5)	24 (3)	26 (3)	0.076	12 (<1)	6 (<1)	15 (<1)	17 (<1)	0.154
Pulmonary tuberculosis	11 (1)	24 (3)	16 (2)	17 (2)	0.053	2 (<1)	3 (<1)	8 (<1)	10 (<1)	0.075
Schistosomiasis	18 (2)	23 (3)	23 (3)	24 (3)	0.635	85 (2)	76 (2)	70 (2)	75 (2)	0.767
Chronic Chagas disease	1 (<1)	0 (0)	2 (<1)	2 (<1)	0.387	0 (0)	0 (0)	0 (0)	0 (0)	-
Cutaneous larva migrans	2 (<1)	4 (1)	4 (1)	4 (<1)	0.659	93 (2)	103 (2)	96 (2)	106 (20)	0.390

n: total number of ill patients (all diagnoses including those not due to an infectious cause)

[a] Cases reported by sites that joined EuroTravNet after mid-2008 were excluded to allow a reliable comparison by year.

[b] Severe malaria was defined according to World Health Organization criteria [7].

[c] Salmonella Typhi and other species and S. Paratyphi.

hookworm-related cutaneous larva migrans (CLM), schistosomiasis and chronic Chagas disease.

Febrile systemic illnesses

Malaria

There was an increase in malaria cases reported from 2008 to 2010 at the EuroTravNet sites, even after the exclusion of sites that joined EuroTravNet after mid-2008 (Figure 1). The proportionate morbidity from malaria was dramatically higher in VFRs than in other groups. A significant increase over time in numbers and proportionate morbidity was observed in both the group of VFRs and other traveller groups (Figure 2). The increase was observed in patients returning from all main countries of exposure for malaria with the exception of Burkina Faso where no variation was seen over-time (Figure 1). There was a significant increase in the proportion of patients with malaria seen at the sites in Paris (France) and Brescia (Italy), which together contributed more than half of the cases (57% in 2010), as well as in those seen in Munich and Hamburg (Germany) and Madrid (Spain) (Figure 2).

***Plasmodium falciparum* malaria** was the most commonly reported species with 426 cases in 2010. *P. falciparum* malaria proportionate morbidity (number of *P. falciparum* malaria cases per 100 ill travellers) increased from 4% in 2008 to 6% in 2010 (p<0.001), primarily in patients returning from sub-Saharan Africa. Most cases were in VFRs and other short-term travellers. There were 31 patients with severe *P. falciparum* malaria (one death) in 2010 compared with 13 in 2009 (no deaths) and 12 in 2008 (one death) (p=0.002). In 2010, the mean age of patients with severe malaria was 39.6 years (range 3–73 years), four patients were children. Eight of those patients were tourists, seven were business travellers, volunteers, research or aid workers, while the remaining 16 were immigrants or VFRs (54%).*

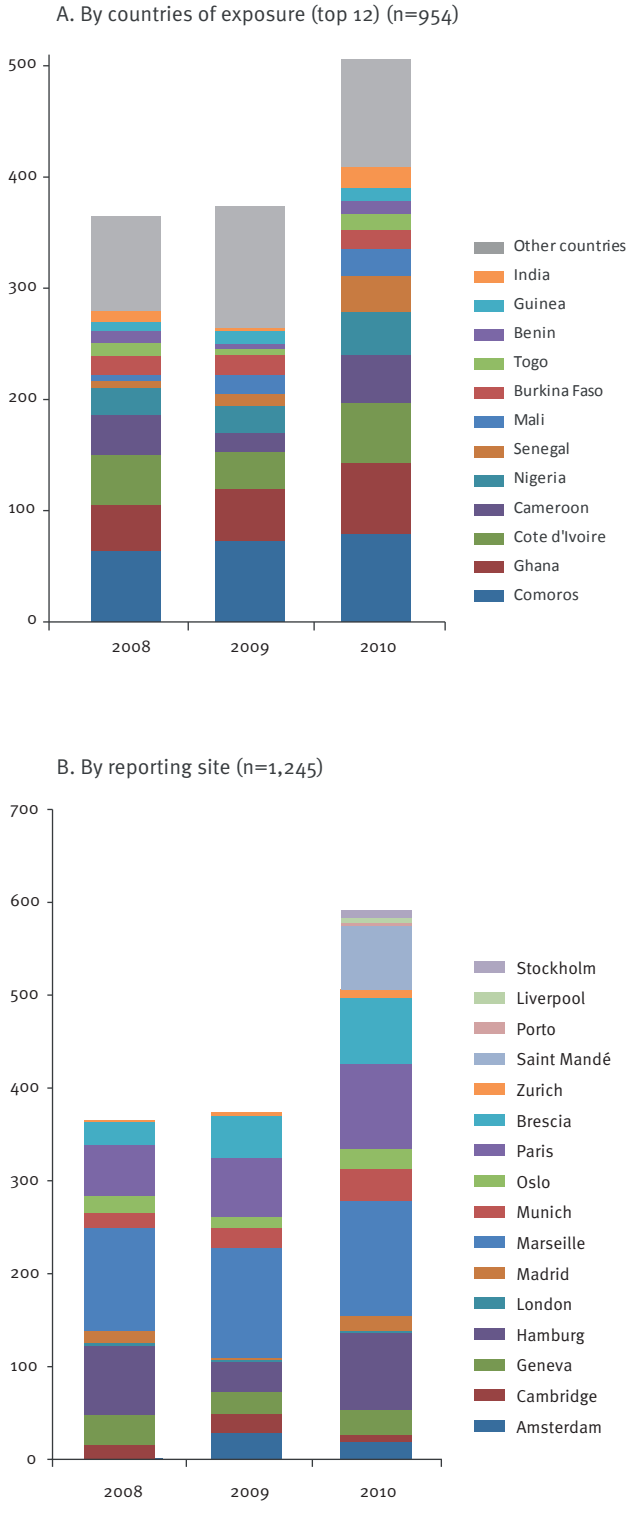
***Plasmodium vivax* malaria** proportionate morbidity (number of *P. vivax* malaria cases per 100 ill travellers) increased from 0.5% in 2008 to 1% in 2010 (p=0.038). Most cases were VFRs and other short-term travellers returning from India.*

Dengue virus infection

Dengue virus was the second most frequent cause of fever among ill returning travellers, with 357 patients in 2010. There was a statistically significant increase in proportional morbidity, from 2% in 2008 to 5% in 2010 (p<0.001). Most cases were in non-VFR short-term travellers. The 2009–10 increase was primarily due to a peak of cases between May and October 2010 (Figure 3). In 2010, patients returning from south-east Asia accounted for 40% of dengue patients, those from the Caribbean for 24% and those from South America for 12%. The seasonal pattern could be partly explained by preferential destinations of different traveller

Figure 1

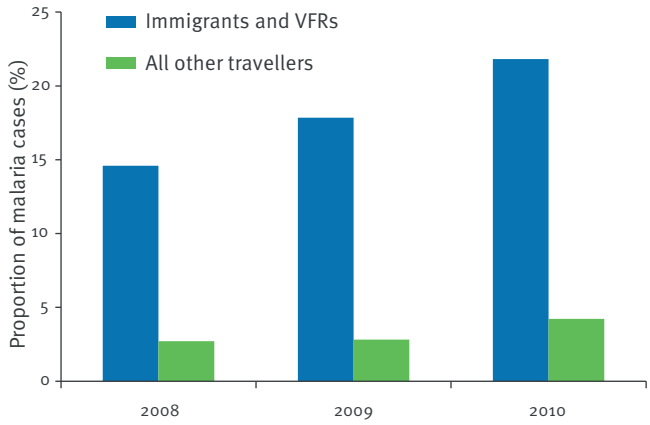
Number of all malaria cases per year reported by EuroTravNet sites, 2008-2010 (n=1,245)



Cases reported by sites that joined EuroTravNet after mid-2008 were excluded to allow a reliable comparison by year.

Figure 2

Proportion of malaria cases among all ill immigrants, people visiting friends and relatives, and other travellers returning to EuroTravNet sites, 2008–2010 (n=1,245 malaria cases)



VFR: visiting friends and relatives.

groups. Consequently, in September 2010, there were more patients, predominantly Germans, with exposure in south-east Asia, mainly Thailand. From June to September 2010, there were more French patients with exposure in Guadeloupe and Martinique. The increase in October 2010 was spread over different EuroTravNet sites and exposure countries, but German patients returning from Indonesia were overrepresented. Cases were also seen in 2010 in travellers returning from Brazil, Surinam and India. Unexpected places of exposure, such as the Comoros Islands, Zanzibar and Benin were also recorded. There was one case of haemorrhagic dengue fever in a 53 year-old French male VFR from Martinique.

Chikungunya virus infections

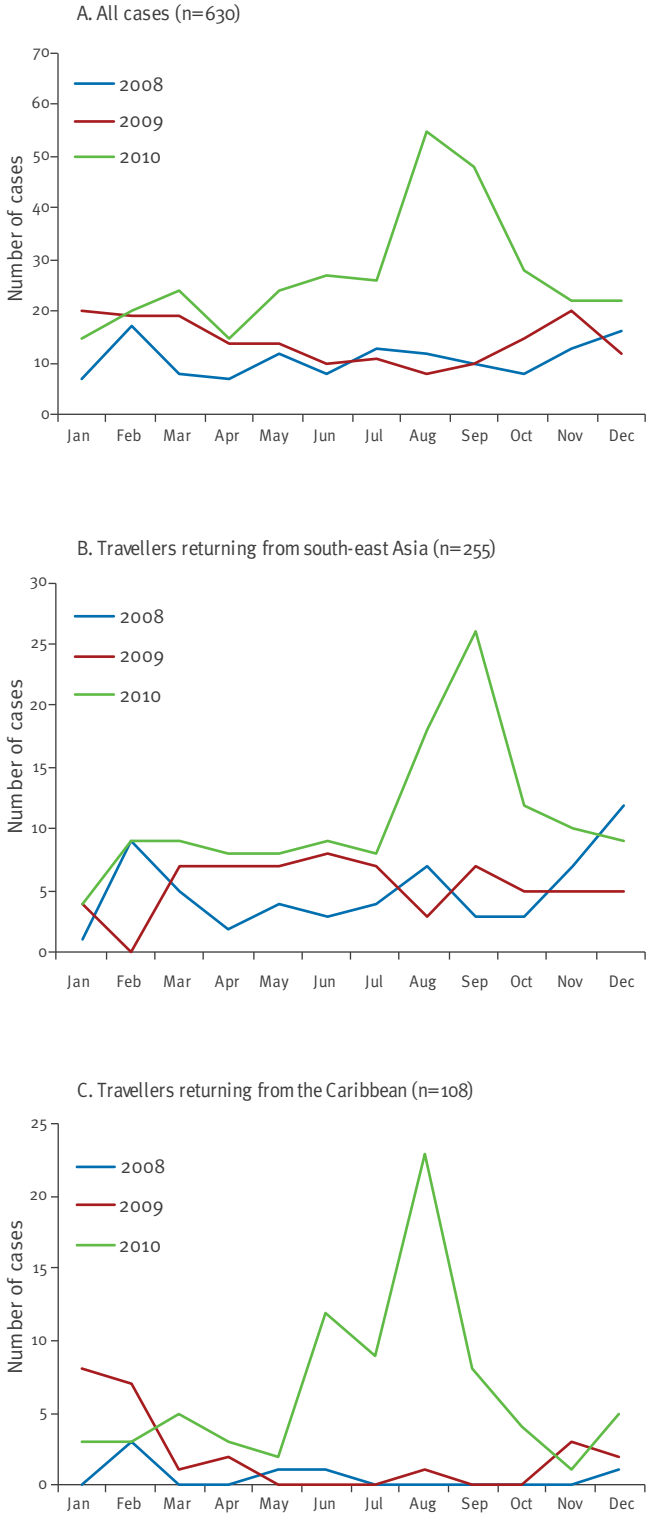
The proportionate morbidity for diagnosed chikungunya virus infections was 0.2% in 2008 and 0.4% on 2010. Most patients had exposure in India and Indonesia and occurred in early 2010.

Gastro-intestinal diseases

A total of 215 G. lamblia infections were recorded in 2010. While *G. lamblia* and *Salmonella* spp. proportionate morbidity remained constant over time, the proportionate morbidity of *Campylobacter* spp. infections increased from 1.3% in 2008 to 1.9% in 2010 (p=0.008), mainly in patients returning from India, Thailand and Pakistan. *G. lamblia* was identified in 16% of patients with acute diarrhoea. The proportion of patients with acute diarrhoea due to *Campylobacter* increased from 7% in 2008 to 12 % in 2010 (p=0.002).*

Figure 3

Number of dengue fever cases seen at EuroTravNet sites, per month, 2008–2010 (n=630)



Cases reported by sites that joined EuroTravNet after mid-2008 were excluded to allow a reliable comparison by year.

Respiratory and other diseases

Tuberculosis

The proportionate morbidity of active tuberculosis increased from 1.5% in 2008 to 2.9% in 2010 ($p<0.001$). A total of 121 patients with pulmonary tuberculosis were recorded in 2010, a threefold increase in the proportionate morbidity of pulmonary tuberculosis from 2008 to 2010 ($p<0.001$). Most cases were reported in immigrants and VFRs, originating mainly from India, Pakistan and Romania. *

Other parasitic infections

In 2010, 152 *Schistosoma* infections were recorded and most cases were diagnosed in patients returning from Africa. Egypt, Ghana, Malawi, Mali and Uganda accounted for 41% of infections. Six patients may have acquired schistosomiasis in south-east Asia and two in Brazil. Most *Schistosoma* infections (40%) occurred in missionaries, volunteers and aid workers, followed by tourists (19%), VFRs (16%) and immigrants (13%). In 2010, 112 CLM infections were recorded and most cases were acquired in Thailand, Brazil and Malaysia (46%) and mostly reported from tourists (80%) followed by business travellers (6%). In 2010, 60 cases of Chagas disease were recorded. All but two patients diagnosed with Chagas disease were immigrants from Bolivia; the other two were from Paraguay and Ecuador. Two thirds of the patients (67%) had symptoms that could be attributed to Chagas disease, and 21% of those had confirmed visceral involvement and 79% were in the indeterminate phase. The proportionate morbidities of schistosomiasis, CLM and Chagas disease did not increase significantly from 2008 to 2010.

Discussion

Between 2008 and 2010, 10 deaths were reported among travellers seen within our network. This may significantly underestimate the travel-related mortality in Europe, as it does not include patients who died overseas or patients not seen in our centres. In other series published in the last decade on patients with imported infections presenting with fever, malaria was found to be the most important cause of travel-related mortality [8]. Case fatality rates of imported malaria do not fluctuate much and have been about 0.5 to 1% of reported cases in the past 20 years [9,10] compared with less than 0.4% in our experience.

We observed distinct patterns of morbidity related to the duration of stay in tropical areas. Malaria, dengue and chikungunya virus infections, diarrhoea and CLM were mostly seen in short-term travellers, while tuberculosis, Chagas disease and *Schistosoma* infections were mostly seen in long-term travellers. Reason for travel was also associated with some infections, including malaria in VFRs, CLM in tourists, or tuberculosis and Chagas disease in immigrants.

Malaria remains the most common cause of fever among travellers to tropical countries receiving a diagnosis in the EuroTravNet/Geosentinel database. The significant increase in malaria cases reported to EuroTravNet in 2010 confirms the trend already observed in 2009 [3] and was not biased by the addition of new sites to the network in 2010 nor by an overall increase of patients seen at each EuroTravNet clinic. It may reflect a changing trend in imported malaria in Europe, possibly due to changes in destinations. However, the increase was statistically significant in only five EuroTravNet sites. Despite a global trend in declining malaria case numbers in endemic areas over the past decade, World Health Organization (WHO) statistics on imported malaria cases in Europe show a contradictory trend with increased case numbers in the past two years [11] which calls for intensified EuroTravNet surveillance of malaria in travellers and migrants. According to data from the WHO, the overall incidence of imported malaria in the European Union had decreased gradually from 2.9 cases per 100,000 population in 2000 to 1.64 per 100,000 in 2008, but there was a slight increase to 1.67 per 100,000 in 2009 [11,12]. This correlates with our own results, with national malaria surveillance data in France that estimated 3,990 imported cases in 2009 and 4,600 in 2010 [13], and also with data from the United Kingdom, where 1,370 imported cases were recorded in 2008, 1,495 in 2009 and 1,761 in 2010 [14]. Odolini et al, [3] emphasised the public health consequences of increasing importation of *P. vivax* malaria to Mediterranean Europe that could lead to the reappearance of autochthonous malaria. Sporadic cases of autochthonous *P. vivax* malaria have already been observed in southern France [15] and Spain [16] and more recently in Greece [17,18]. Given the high proportion of immigrants and VFRs among malaria patients, specific health education programmes should be launched in these populations who are known to seek pre-travel advice less frequently compared with other travellers [17], which is confirmed in our survey (see Tables 2 and 3). This is important because patients with *P.vivax* malaria could act as reservoirs for autochthonous transmission in Europe.

We highlight that dengue virus is an increasingly frequent cause of fever in travellers returning from the tropics, which corroborates results from single-centre surveys recently conducted in Germany, Denmark and the Netherlands [18-22]. The increased incidence of dengue fever in travellers returning from south-east Asia and from the Caribbean may be the consequence of outbreaks that occurred in these areas in 2010 [24,24]. Surveillance of sentinel travellers allows us to identify dengue virus circulation in areas where it was unknown or rarely described, notably in Benin and the Comoros Islands [25,26]. Whether this reflects extremely rare transmission from sylvatic animals to humans or transmission between humans, is not clear. A number of patients with dengue and chikungunya virus infections in our survey were recorded in southern France and Italy where autochthonous transmission has recently been observed [27-29]. Overall, 16% of patients with chikungunya fever were seen

in Marseille, where *Aedes albopictus* has recently been detected [30]. This emphasises the need for increased attention to surveillance of dengue and chikungunya fever in travellers returning to areas where *A. albopictus* is present.

The high proportion of G. lamblia infections among European travellers suffering from diarrhoea is noteworthy. Travellers should receive stool examinations especially in the context of chronic gastrointestinal complaints accompanied by intermittent diarrhoea. Data on imported resistant bacteria are not systematically reported to the EuroTravNet database. However, most cases of diarrhoea due to *Campylobacter* and *Salmonella* spp. followed exposure in Asian countries where fluoroquinolone resistance is common [31,32]. This suggests that fluoroquinolones should no longer be prescribed as first-line empiric treatment for travellers' diarrhoea. A macrolide such as azithromycin may be a better choice [31].

Our survey confirms that tuberculosis is an issue in immigrants coming to Europe from high-incidence countries. In the author's view, health systems should facilitate early access and treatment of patients with tuberculosis (regardless of their legal status) to prevent further spread of the disease. In addition, substantial numbers of chronic Chagas disease were reported to EuroTravNet in 2010, mainly at the site in Madrid among immigrants from Bolivia. This is comparable to the data from 2008–09 [33].

Schistosomiasis and CLM continue to cause a significant proportion of imported parasitic diseases in European travellers. Schistosomiasis is easily prevented by avoiding swimming in open water, and this recommendation should be re-enforced when giving pre-travel advice. CLM is more difficult to prevent because most tourist travellers acquire this disease during typical holiday leisure activities on the beaches and prevention is mainly by public health measures that keep dogs and cats off the beach.

The major strength of our analysis is the multi-centre nature of EuroTravNet, which provided a large number of patients from many countries and captured many types of travellers, and its focus on proportionate morbidity. The limitations of this method of analysis have been discussed [1,5]. In particular, because the denominator data (number of travellers) cannot be ascertained, it is not possible to calculate incidence rates or absolute risk. Also, the data may not be representative of the overall population of travellers, and do not include the broad spectrum of illnesses typically seen at non-specialised primary care practices where people with mild or self-limited conditions present with higher frequency. Due to the nature of GeoSentinel/EuroTravNet clinics, illnesses acquired after travel to non-tropical destinations or non-infectious travel-related illnesses may be under-represented. However, the GeoSentinel database has been identified as a valuable source of data on the epidemiology of travel-related illnesses [34]. Surveillance over this three-year period also identified an increase in imported vector-borne diseases at European sentinel sites with significantly raised numbers of malaria and dengue fever. This has important public health implications and warrants close surveillance in view of the presence in Europe of *Anopheles* (competent for *P. vivax* transmission) and *Aedes* vectors (competent for dengue and chikungunya virus transmission), allowing real-time intervention to prevent subsequent autochthonous transmission.

Finally, it is of concern that there were more hospitalised patients and fewer patients who were known to have had a pre-travel consultation, compared with 2008–09. This should alert public health authorities to the need to reinforce preventive activities among international travellers.

In summary, we have investigated travel-associated morbidity in European travellers in 2010 and showed that illness patterns in sentinel travellers, captured through the activities of the EuroTravnet/Geosentinel Network, continue to highlight the potential role of travellers in the emergence of infectious diseases of public health concern in Europe.

* Authors' correction:

The sentences "All ill patients presenting to EuroTravNet sites are systematically and prospectively included in the GeoSentinel database provided the diagnosis is clinically or laboratory-confirmed and that the causality of travel is confirmed. All patients included in the study were symptomatic, including those with parasitic infections such as malaria and schistosomiasis. Patients with proven chronic Chagas infection, however, were included whether or not they were symptomatic, owing to the potential life-threatening course of the disease." were corrected to read: "All returned travellers presenting to EuroTravNet sites are systematically and prospectively included in the GeoSentinel database provided the diagnosis is clinically or laboratory-confirmed and that the causality of travel is confirmed. Travellers undergoing screening for asymptomatic infections or clinically cured travellers looking for a confirmation of the diagnosis established elsewhere are however also included in the database, with "healthy" as a diagnosis when the screening remains negative. Patients included in the study may be symptomatic or not. For example, patients with chronic infection such as Chagas disease, schistosomiasis, tuberculosis, hepatitis B, were included whether or not they had clinical symptoms at the time they presented." . This correction was made on 12 November 2012 at the request of the authors.

In addition, on 19 November 2012, some numbers were corrected at the request of the authors in the abstract and in the main text (making no interpretation difference).

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United States Centers for Disease Control and Prevention issue updated guidance for tackling carbapenem-resistant enterobacteriaceae

A Kallen (AKallen@cdc.gov)[1], A Guh[1]
1. Centers for Disease Control and Prevention, Atlanta, Georgia, United States

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On 21 June, the United States (US) Centers for Disease Prevention and Control (CDC) released a report [1] and updated recommendations [2] that detail how states and healthcare facilities should deal with carbapenem-resistant *Enterobacteriaceae* (CRE), deadly germs that cause healthcare-associated infections. The report documents the first case of person-to-person transmission in the US of CRE with New Delhi metallo-beta-lactamase (NDM), first reported in 2007. CRE with NDM are of particular concern because these enzymes allow drug resistance to be transferred easily from one bacterium to another.

CRE are resistant to almost all drugs and can contribute to death in 40% of patients who become infected [3]. In response to this emerging threat, the CDC have urged healthcare facilities and US state health departments to take action and follow several key steps to protect patients.

Healthcare providers should:

- place patients currently or previously colonised or infected with CRE on contact precautions;
- wear a gown and gloves when caring for patients with CRE;
- perform hand hygiene - use alcohol-based hand rub or wash hands with soap and water before and after contact with patients or their environment;
- prescribe and use antibiotics wisely; and
- discontinue devices like urinary catheters as soon as no longer necessary.

Klebsiella pneumoniae carbapenemase (KPC) is the most common carbapenemase in the US and has spread throughout many regions [4]. Although the prevalence of CRE likely varies from region to region, a review of data from CDC's National Healthcare Safety Network found that in 2009-2010 in the USt, about 13% of *Klebsiella* species reported from central line-associated bloodstream infections (CLABSIs) and catheter-associated urinary tract infections (CAUTIs) were carbapenem-nonsusceptible. About 2% of *Escherichia coli* reported from CLABSIs and CAUTIs were carbapenem-nonsusceptible.

Genes coding for KPC can be transmitted between bacteria via mobile genetic elements, potentially facilitating transmission of these organisms. Organisms producing metallo-beta-lactamase (NDM, VIM, and IMP) have also been identified in the US but appear to be less common than KPC-producing organisms.

In healthcare settings, CRE are usually transmitted from person to person, often via the hands of healthcare personnel or via contaminated medical equipment. To control CRE, healthcare providers should ensure the use of appropriate infection control procedures, including personal protective equipment during and good hand hygiene following exposure to the patient's immediate environment, especially when draining urine from a catheter bag or changing wound dressings.

The CDC CRE website [5] at has information and resources for US patients, clinicians, healthcare facilities, and state health departments.

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