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Lymphogranuloma venereum emerging in Europe

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EDITORIAL

EMERGENCE OF LGV IN WESTERN EUROPE: WHAT DO WE KNOW, WHAT CAN WE DO?

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Lymphogranuloma venereum (LGV), a systemic sexually transmitted disease (STD) caused by a variety of the bacterium *Chlamydia trachomatis*, rarely occurs in the Western world [1]. However, in January 2004, public health officials in the Netherlands noted an outbreak of LGV proctitis cases among men who have sex with men (MSM) [2]. Since then, cases have been reported from several European countries, the United States of America and Canada. In this issue three countries report on the current status of LGV [3-5].

Initial reports and current status

The first 13 cases among MSM were diagnosed between April and November 2003 and reported to the local health authorities in Rotterdam in December 2003 [2,6]. Most of the men were HIV positive, and the majority had reported unprotected anal intercourse in the past year. Only one patient, with onset of illness in April 2003, had symptoms usually associated with the classical picture of LGV (i.e., buboes and a painful genital ulcer). All other patients had gastrointestinal symptoms, (e.g., bloody proctitis with a purulent or mucous anal discharge and constipation) [6]. The majority of LGV patients had participated in casual sex gatherings during the 6–12 months period before onset of symptoms. LGV patients also reported having numerous sex contacts in cities in Europe and the United States. An alerting report was sent to the EWRS (Early Warning and Response System), the ESSTI (European Surveillance of Sexually Transmitted Infections) Network [7,8], and to the CDC [9]. Subsequently, case reports were received from Antwerp [10], Paris [11,12] Stockholm [13,14] Hamburg [15,16], Barcelona [17], the USA [9] and – later – Canada [18] suggesting that the LGV outbreak was not restricted to the Netherlands.

Active case-finding and contact tracing should be a priority in the control of LGV among this specific high-risk network of MSM in Europe before it becomes endemic

Since LGV is not a reportable disease in most European countries, it complicated the public health response. Enhanced surveillance was started in the Netherlands (January 2004), France (April 2004), Germany (May 2004), Sweden (June 2004) and the UK (October 2004) [19,14]. Except for Sweden [20], these surveillance systems yielded hundreds of cases: 244 rectal cases in France by December 2005 [4], 61 confirmed cases in Germany by November 2005 [3], 179 cases in the Netherlands by December 2005, and 344 cases in the United Kingdom by March 2006 [21]. In addition, several countries reported a few cases each. Considering no active case-finding was implemented in many countries, the actual number of cases may be higher. In Sweden, however, no additional cases were detected during the intensified epidemiological surveillance or in the course of the retrospective analysis [20]. Comparison between countries is hindered due to their different surveillance methods and lack of harmonisation concerning case definitions and questionnaires, e.g. in France only rectal cases were included. Nonetheless, common features in these reports were: MSM, Caucasian race / ethnicity, mean age above 35 years, predominantly (>70%) co-infected with HIV and a relatively large proportion of MSM with unknown HIV status, and frequent concurrent STIs and HCV [21,22]. Most of them presented with rectal symptoms and only a few with inguinal lesions. The majority reported large number of partners and unprotected anal intercourse. The practice of 'fisting' and use of sex toys were also reported. However, the precise identification of risk factors for LGV has not been assessed so far and further analytical studies are needed.

An unusual clinical picture for LGV?

The classical picture of LGV usually involves adenopathy and is characterized by buboes [23]. This current epidemic, however, is mainly characterized by cases presenting with severe proctitis. LGV proctitis in MSM is well recognised [24]. In the early 80's, serovar L2 was found to be associated with more severe forms of proctitis than non-LGV strains [24-27]. Serovar L1/L2 was also identified in 68 cases of LGV among 101 rectal samples of symptomatic men in San Francisco [28] and L1 in proctitis cases in Seattle [29]. An epidemic of LGV among heterosexuals, recently described by Bauwens et al, was linked to crack cocaine use and HIV infection, suggesting that LGV is not just a tropical disease but that it also has the potential to interact with HIV as was observed before with herpes [30]. Recognition of the current epidemic of proctitis LGV was hampered by poor clinical awareness, poor public health intervention and atypical clinical presentation [31]. Clinicians in industrialised countries would not be expected to consider LGV as a likely cause for gastrointestinal illness [32-34]. The clinical presentation of LGV was therefore easily missed as evidenced by the retrospective case reports from the Netherlands [5,35,36], France [4] , England [37], and Switzerland [38]. LGV proctitis may be far more common among MSM than previously thought. Before 2003, however, it was unusual to perform additional testing if chlamydial proctitis was diagnosed [39,40]. LGV proctitis causes more rectal symptoms (pain, tenesmus) and clinical manifestations (rectal discharge, bleeding) than rectal infections with serovars D-K [40]. The clinical presentation remains to be studied in more detail as asymptomatic and sub-clinical cases were also identified [35,36]. For instance, it is still unclear why inguinal cases were found less frequently in these LGV cases. Only one case of urethritis due to genovar L2b has been reported so far [41]. Studies including asymptomatic individuals are needed to unravel the epidemiology of these infections, as suggested by Schachter in June 2005 [31]. In a retrospective case-control study among MSM, a positive HIV status, proctitis findings and elevated white blood cell counts in anal smears were the only clinical features that revealed to be predictive for LGV [42].

Will LGV become endemic?

Finally, we have to address the question whether we are dealing with an epidemic of LGV in Europe that was overlooked previously? An unexpected or adverse event in STI is defined as a greater number of observed cases than expected over a defined time period or any event related to STIs that required a public health intervention (available at: www.essti.org). Unfortunately, no baseline data before the recent case reports were available as LGV is not a notifiable disease in most countries (and when it is, only the classic form is usually considered). However, the increasing number of cases, the number of linked cases - through international travel and import of infection as well [10,14,17] - and the geographical clustering strongly favour the hypothesis of an epidemic. But these findings could be biased by the enhanced surveillance systems and the availability of diagnostic capacity. However, there is increasing evidence for rising STIs among MSM and their association with HIV and high risk behaviours [43-50].

Moreover, there has been very little systematic testing in the past 20 years, despite the rise in anorectal infections causing cases to

remain unnoticed. Diagnostic support for disease confirmation was not widely available and hampered the development of guidelines for testing anorectal specimens. The development of a real-time PCR, both in the Netherlands and the US, allowing to distinguish LGV from non-LGV serovars can facilitate a more timely diagnosis of LGV on a wider scale in routine microbiological laboratory conditions [51]. In this outbreak, the new strain identified, L2b, was found in all genotyped cases in Amsterdam and France (mainly Paris) [4,35]. This strain is also highly prevalent in the UK and Germany, but not exclusively as demonstrated by Meyer [16]. More retrospective testing of stored specimens is needed to help unravel some of these issues. Investigation of anal swabs confirmed that the L2b strain was already circulating in San Francisco in the early 80's and could be traced back in Amsterdam as early as 2000 [35-36]. However, retrospective testing in Sweden yielded no additional cases [20].

Over the past two years, LGV has become an increasingly important public health issue. LGV may be contributing to the HIV epidemic - and the transmission of hepatitis C virus [22] - in facilitating transmission through prejudicing the integrity of the anal skin and mucous membrane. That is certainly plausible and has been observed in heterosexual transmission. It is striking that LGV seems to be limited to a high-risk network of MSM and involves many who are living with HIV. The extent of serosorting, the selection of partners and risk behaviours in these networks remain to be determined [50,52]. Even so, Marcus and colleagues hypothesize in this issue that increasing HIV incidence rates could be due to transmission during highly infective early HIV infection in similar networks, acquired mostly from casual partners [53].

In this epidemic, information on new cases and new findings traveled fast via international electronic STI and public health practitioners networks and via peer-reviewed literature. European-wide collaboration was initiated to discuss the state of the art, the surveillance and epidemiology of LGV, and to identify knowledge gaps in clinical studies [54]. However, prospective clinical studies, ongoing surveillance and epidemiological studies need further European partnerships. The lack of harmonisation would rather represent a missed opportunity to gather more information on this once rare STI.

The LGV epidemic seems to be evolving at a relatively slow pace with an undeterrmined dynamics so far. By now, it may have peaked in the Netherlands; the number of cases seems to have doubled quite rapidly in the UK, although LGV may not have been introduced at all in some other countries. However, LGV cases may still be missed easily if its diagnosis is not considered or if appropriate diagnostic tools are not available. Individual patients may remain undiagnosed and develop severe complications. Active case-finding and contact tracing ensuring effective treatment and prevention of further transmission of STIs and HIV should be a priority in the control of LGV among this specific high-risk network of MSM in Europe before it becomes endemic. In addition, primary prevention of STIs should be addressed more thoroughly within sexual health programmes for those living with HIV.

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EDITORIAL

IS THERE A NEED FOR A PUBLIC VACCINE PRODUCTION CAPACITY AT EUROPEAN LEVEL?

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In this issue of *Eurosurveillance*, Rouaud et al report a protracted outbreak of meningococcal B invasive diseases (BMD) in the northern French department of Seine-Maritime, linked to the local expansion of a clonal strain of B:14:P1.7,16 phenotype, belonging to the ST32/ET5 clonal complex.

This strain had already been responsible for an increased incidence in that department in 1997, and the incidence rose again in 2003, and has since remained high.

The paper summarises the main features of this outbreak. First restricted to the city of Dieppe and the surrounding area in 2003 and 2004, cases due to this specific strain were notified from other areas of the department in the first six months of 2005. The proportion of cases presenting with septicaemia was higher than usually observed for invasive meningococcal B diseases in France. However, the initially high case-fatality rate (25% in 2003) has decreased over time. This may in part reflect the impact of local efforts to raise awareness of both the general public and health professionals about the early signs of the disease, in order to optimise the management of cases, including systematic pre-admission parenteral injection of a third-generation cephalosporin for all cases where purpura fulminans is suspected.

Since the paper was first drafted, the situation has evolved, both as regards the epidemiological situation and the implementation of control measures. The hyper-endemicity situation is persisting. The incidence of BMD in the department as of early July for the last 12 months is 2.4 /100 000, compared with 0.7/100 000 for the rest of France. The strain has continued to spread and has been identified in several neighbouring departments, causing moderate increases in incidence.

The hyper-endemicity of meningococcal B invasive diseases in Northern France re-emphasises the need for generic vaccines against meningococcal diseases of serogroup B, and the limitations of the market forces that govern the private vaccine production when faced with such a situation

Mass chemoprophylaxis, which was considered in 2004, has been discarded, after taking into account the geographical spread of the cases due to this specific strain and its long-standing presence in the department. There is no generic serogroup B vaccine available. The only B vaccines to have been used are tailor-made outer membrane vesicle (OMV), protein-based vaccines developed against specific strains. Several of these vaccines have been used in the context of local outbreaks in Cuba, Chile, Brazil, Norway and currently in New Zealand, with efficacy estimates against homologous strains of at least 70% in children over five years [1-5]. Fortunately, the OMV vaccine developed in Norway in 1983 by the National institute of public health (Folkehelseinstituttets, FHI), MenBvac, was directed towards a B:15:P1.7,16 strain, which was responsible for most of the high excess incidence observed nationwide since 1974. As the

response induced by those vaccines is mainly directed towards the Por A protein, defining the sero-subtype, (here P1.7,16), it was anticipated that the Norwegian vaccine could be effective against the Seine-Maritime strain, which shares a common sero-subtype (PorA antigen) with the Norwegian strain. An experiment measuring the response in 19 Norwegian adolescents immunised with the MenBvac vaccine did indeed show a similar bactericidal activity against both the Norwegian and the Seine-Maritime strains. A total of 25 clinical trials have been performed with this MenBvac, including a phase III study carried out with 173 000 students. An immunogenicity study nested in this trial yielded an estimate of protection rate of 87% after 10 months [6]. The safety profile of the vaccine appears satisfactory. With this information on mind, the French Advisory Board on Immunisation, based on the advice of the Meningococcal Emergency Taskforce, which is made up of all the local and national stakeholders involved in the management of meningococcal outbreaks, in December 2005 recommended the vaccination of all children and teenagers under 20 years old living in the department, starting with the Dieppe area. In its statement, the Board urged the French Ministry of Health to take all necessary steps to make a sufficient amount of MenBvac vaccine available as soon as possible. Preliminary discussions held with the drug company that held the rights for MenBvac had been unsuccessful. In the specific context of the use of the vaccine in Seine-Maritime, a direct agreement with the FHI was reached. FHI sold us its available stock and increased its production in order to meet our needs of more than one million doses of the vaccine. The implementation of the vaccination campaign was phased to fit in with the anticipated release of new vaccine lots.

Vaccination started in early June 2006 with the 9000 available doses. It has been targeted at the group of children (considered to be most at risk), based on epidemiological data, that is, children aged between 1 to 5 years living in Dieppe and the surrounding area. Preliminary data suggest that coverage has been close to 80% for the first dose.

This outbreak re-emphasises the need for generic vaccines against meningococcal diseases of serogroup B, which represent 64% of invasive meningococcal diseases in Europe [7]. It shows us once again how little we can fight local outbreaks of BMD, because mass antibioprophylaxis is restricted to very limited situations where outbreaks are restricted in place and time. There was, understandably, considerable distress caused in the general population and among healthcare workers by three consecutive winters of BMD cases in the Seine-Maritime department. Cases were occurring at a rate of more than one per week at the peak of the epidemic, with a significant risk of permanent sequelae or death.

This experience also re-emphasises the importance of close cooperation between epidemiologists and biologists. The contribution of our national reference centre has been crucial in the vaccination decision process, through its ongoing phenotyping and genotyping of the strains and the exchange of the B:14:P1.7,16 strains with the institution involved in the development of OMP vaccines.

Thirdly, this experience has shown the limitations of the market forces that govern the private vaccine production when faced with such a situation. This raises the issue of maintaining a public vaccine production capacity, at European level if not at national level, to deal with public health emergencies. This capacity could be managed at the European level, as it might not be feasible or even necessary to have such a capacity at national level. However, the mechanisms to make such an enterprise work would have to be identified. The Institut de Veille Sanitaire, the French Ministry of Health and its agencies, the local authorities, the families and the health professionals of Seine-Maritime are all greatly indebted to the FHI for its active support in helping us to control this outbreak, but such international collaborations do need more formal mechanisms.

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A SLOW EPIDEMIC OF LGV IN THE NETHERLANDS IN 2004 AND 2005

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In 2004, an outbreak of LGV was detected in MSM in the Netherlands. By January 2006, 179 confirmed cases of LGV had been reported; 65 (retrospectively) in 2002/2003, 76 in 2004 and 38 in 2005. The evolution of the LGV outbreak appears to have slowed down and only a few cases were found in the first months of 2006.

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Key words: Lymphogranuloma venereum, outbreak, The Netherlands

Introduction

LGV was very rarely reported in Western Europe until January 2004, when a cluster of LGV cases in men who have sex with men (MSM) who were predominantly HIV positive was reported by the Health Service Rotterdam area [1]. Laboratory results confirmed infection with *Chlamydia trachomatis* serovar L2 [2]. The majority of the men reported unprotected sexual contact with numerous partners from several European countries. Immediate alerts with information about the clinical signs and symptoms of LGV were sent to STI and HIV clinics, gastroenterologists, public health services across the country and *Nederlands tijdschrift voor geneeskunde* (the Dutch Medical Journal). The gay community was informed via peer group oriented websites, periodicals for gay men and via the Schorer Foundation (a national foundation promoting sexual health of gay men and lesbians). International alerts were sent out through the European Surveillance of Sexually Transmitted Infections network (ESSTI), the European Early Warning and Response System (EWRS), and the United States Centers for Disease Control and Prevention's Epidemic Information Exchange (EPI-X) and Morbidity and Mortality Weekly Report (MMWR) [1,3]. A national investigation team was established in January 2004 to discuss the current outbreak and decide future actions.

Methods

Between 2003 and 2005, surveillance of sexually transmitted infections (STIs) in the Netherlands consisted of a sentinel surveillance network of five low threshold STI clinics that were free of charge, and nine STI services at Public Health Services throughout the country. A standardised questionnaire was used to collect anonymous demographic and epidemiological key parameters, including date of consultation, sex, year of birth, 4 digits of the postal code, sexual preference, previous HIV testing, previous STIs, injecting drug use, concurrent STIs and commercial sex work, for every new consultation. Laboratory tests for gonorrhoea, chlamydial infection, syphilis, hepatitis B, HIV and other infections were also registered together with the test results and site of infection (if applicable). Data were entered into a web based surveillance application called SOAP.

Enhanced surveillance of LGV was begun shortly after the first report, in January 2004. An additional questionnaire was developed which addressed clinical signs and symptoms, microbiology and diagnostics, sexual behaviour (meeting places, number of partners, the kind of sexual intercourse and condom use). The two questionnaires were matched using a unique number generated by SOAP. Data on LGV cases diagnosed at the STI clinic in Amsterdam were sent to RIVM in a Microsoft Excel worksheet that included date of consultation (or diagnosis), information on the site of infection (proctum, inguinal), sexual preference, HIV status, and current co-infections. No additional information was obtained on clinical aspects, microbiological tests or sexual behaviour.

Cases in this outbreak were managed as follows: Cases were further investigated if (a) a patient presented with clinical signs of inguinal syndrome, anorectal syndrome (proctitis), oropharyngeal syndrome or (b) a patient was known to be a sexual contact of a confirmed LGV case. Further classification followed the results of laboratory testing as detailed below. The case definition was deliberately broad, so as to include highly suspect clinical cases reported retrospectively by physicians shortly after the initial alert. A broad case definition enabled the investigating team to get a rapid idea of the size of the outbreak [TABLE].

The sentinel STI clinics were asked to report on suspected LGV cases voluntarily using both the routine STI and the enhanced LGV questionnaires. The alerts and the *Nederlands Tijdschrift voor Geneeskunde* [4] gave information on clinical signs and symptoms of LGV, e.g. for example this specific rectal syndrome, to increase awareness among medical professionals nationwide. They were invited to report any suspect case of LGV either to local MHS or to RIVM. If cases were reported directly to RIVM, additional information was requested using the questionnaires. RIVM notified the local MHS to contact the physician for contact tracing and interviewing.

Genotyping was performed in two microbiological laboratories, the Erasmus University Medical Centre in Rotterdam, and the Public Health Laboratory in Amsterdam.

Results

By January 2006, 179 confirmed cases had been reported with additional epidemiological information, although this is not yet complete. In 2004-2005, 114 cases were seen in patients and reported: 76 in 2004 and 38 in 2005. Of these, 78 (68%) were reported from the STI outpatient clinic in Amsterdam. Several cases were reported with dates of consultation in 2003 and 2004, but some could not be confirmed as L2 because specimens were not available. In 2002-2003, 65 confirmed cases were reported retrospectively. The epidemic curve

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Table

LGV outbreak in the Netherlands 2004-2006: LGV case definition

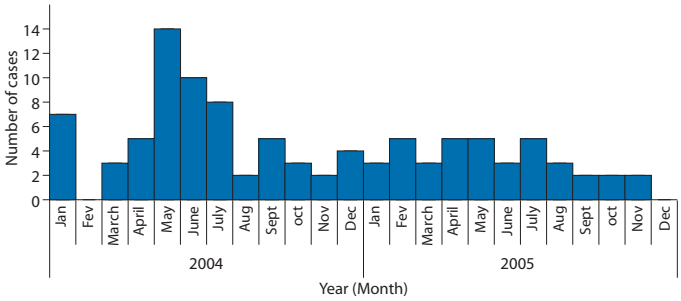
Case definition	Genotype	PCR urine or PCR rectum	*C. trachomatis* serology	Histology*
Confirmed	L1 or L2 or L3	Positive	High positive Unknown	-
Probable	Unknown	Positive	High positive	-
Possible	Unknown	Positive	Unknown	-
Possible	Unknown	Unknown or Negative	High positive	-
Possible	Unknown	Positive / Unknown	Unknown	Chronic inflammation
Rejected	Other genotype	Negative or Unknown	Low or negative or Unknown	Unknown or Other description

** Histology is mainly used for retrospective diagnosis of cases reported by gastroenterologists*

of cases, by date of consultation from January 2004, shows a slowly increasing outbreak with the highest number reported in May 2004 [FIGURE]. Genotyping demonstrated that all positive L2 samples in Amsterdam contained a new variant, L2b [5]. This genotype was identified in both symptomatic and asymptomatic patients in a study in Amsterdam that retrieved 87 cases retrospectively [5,12]. In the first few months of 2006 only a few cases were reported.

Figure

Number of LGV cases by date of consultation, The Netherlands, January 2004 – December 2005



Source: RIVM – enhanced surveillance of LGV

Epidemiology

Routine STI surveillance data are available for 92% (104/114) of the confirmed LGV cases in 2004 and 2005. Additional data from the enhanced surveillance is available for 33% (34/104). Preliminary evaluation reveals the following characteristics: 101/104 (97%) were MSM (1 heterosexual, 2 missing), at least 70/104 (67%) were HIV positive (HIV status was unknown in 16 cases); 86% were of Dutch origin, and the mean age was 40 years (range 26-58). Concurrent STIs were frequently diagnosed: 24% (25/104) had gonorrhoea, 21% (16/104) had early syphilis, 10% (10/104) had hepatitis C, 6% (8/104) had genital chlamydial infection and 21% (16/104) were diagnosed with another STI (such as herpes or genital warts).

Clinical manifestation

The majority of the cases attended because of clinical signs, 82% (74/90; 14 cases missing). The majority (n = 95) were diagnosed with LGV proctitis and 6 with the inguinal syndrome. Most cases presented with proctitis symptoms: rectal discharge (85%; 29/34), rectal pain (74%; 25/34) and bloody rectal discharge (65%; 22/34). Genital symptoms were reported less frequently: swollen lymph nodes (24%; 8/34) or systemic symptoms, including general malaise (41%; 14/34). Most cases (91%; 23/26) were treated with a 21 day course of doxycycline.

Sexual behaviour

Detailed information on sexual behaviour was only obtained for 24 cases. The mean lifetime number of partners was 275 (range: 6-1000), the mean number of new partners in the last 12 months was 18 (range: 0-100), and the mean number of partners in the last 6 months was 11 (range: 0-50). Only one case reported always having used a condom with a steady partner, and five cases reported always having used a condom with a casual partner. Half (11/24) reported unprotected anal intercourse (both insertive and receptive), 18/24 reported oral sex without the use of a condom; 29% reported having shared sex toys without using protection or cleaning the toys while sharing. Another 55% (12/22) reported having taken part in group sex; most of them did not change condoms between partners. Of the 18 HIV infected MSM, 10 reported that they had never disclosed their HIV status before having sex.

Discussion

This LGV epidemic is occurring in a group of MSM in the Netherlands, a large proportion of whom were infected with HIV and other STIs.Erreur ! Signet non défini. We report what is undoubtedly a minimum estimate of disease occurrence: the majority of the cases in MSM presented with gastrointestinal problems such as bleeding and inflammation of the colon and rectum, which are not symptoms commonly associated with STIs. Clinicians in industrialised countries rarely make the diagnosis of LGV, and would not be expected to consider LGV as a likely cause of gastrointestinal illness [6-9]. The clinical presentation of LGV might therefore easily be missed, as evidenced by the large number of retrospective cases identified in Amsterdam [5,10]. Furthermore, before 2003 no additional testing was performed routinely when chlamydia proctitis was diagnosed based on positive anal swabs [11]. Further investigation of stored samples of MSM who attended the Amsterdam STI outpatient clinic demonstrated that LGV was circulating already in Amsterdam in 2000 [10]. Also, L2b was identified in patients who had no symptoms at all, suggesting that physical examination alone may not exclude LGV [5,12]. We believe that the actual number of cases is much higher than we have reported, due to underdiagnosis, lack of adequate diagnostics, misclassification and underreporting.

This current epidemic may reflect an increase in unsafe sexual behaviour, as has also been suggested by recent increases in several other STIs in MSM, such as syphilis, rectal gonorrhoea, and quinolone-resistant *N. gonorrhoeae*. [13-16]. It is important from a public health perspective because consequences for HIV transmission are as yet unclear. Behavioural data from the enhanced LGV surveillance is limited due to the small number, however preliminary results suggest that this group of MSM had multiple sex partners, practised 'rough' insertive techniques, and used condoms infrequently. This behaviour, together with their positive HIV status, can result in increased transmission of HIV. In a retrospective case-control study a positive HIV status was identified as the strongest risk factor for LGV [12]. If both partners are HIV positive, the risk of causing a new infection is reduced, but the effects of super-infection are yet unclear. In the here presented group, 10 HIV positive individuals reported that they never disclosed their HIV status to their sex partners.

The ulcerative character of LGV may facilitate transmission and acquisition of HIV, other STIs and bloodborne diseases, particularly in combination with specific sexual techniques that may lead to mucosal damage [6,7]. In Rotterdam, at least two cases with seroconversion for HIV were confirmed and five cases of recent hepatitis C virus (HCV) infection were found [17]. Hepatitis C is not normally considered as an STI, but ulcerative lesions in one of the partners together with high-risk behaviour

may enable the transmission of HCV during sex [7]. Furthermore, a rise was observed in the number of notified cases of HCV in 2004 in the Netherlands [18]. The increase coincided with the LGV outbreak in time and in most cases sexual contact between men was the most likely route of transmission reported for these new HCV infections [18].

The enhanced surveillance of LGV is currently being evaluated in the Netherlands. Our results so far suggest that non- response increases with the sensitivity of the topics. The response to the routinely collected attributes on STI surveillance was 92%. However, the basic dataset lacks the sensitivity to identify the risk factors for this outbreak in this specific group of MSM. In the enhanced surveillance questionnaire, specific questions were included, based upon the investigation of the first cluster of cases in Rotterdam, and yet, detailed information on sexual behaviour was available for only a few individuals. This may reflect not only the reluctance of the patients to disclose the information, but other reasons as well, such as low levels of staffing at MHS or clinic, no extra time available, patient could not be reached, etc. Obtaining reliable information on sexual behaviour requires professional and time-consuming interviewing. Furthermore, detailed information on the patients attending the Amsterdam STI outpatient clinic is not yet available. As 68% of the cases were diagnosed in this STI clinic, this affects our current insight into the epidemiological features.

The number of recently reported cases in the Netherlands is relatively low, suggesting that the epidemic may have already peaked. The rapid dissemination of information to healthcare providers may have facilitated the recognition of clinical signs. Also, adequate diagnostics (e.g. real time PCR) and treatment may have contributed to have prevented further spread of cases. However, LGV cases may still be missed if appropriate diagnostics are not available or if the diagnosis of LGV is not considered. LGV has occurred in a network of MSM in several different countries, and clinicians and health authorities in Europe and the US should remain alert to the occurrence of LGV and associated infections.

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ORIGINAL ARTICLES

Surveillance report

LYMPHOGRANULOMA VENEREUM EMERGING IN MEN WHO HAVE SEX WITH MEN IN GERMANY

V Bremer[1], T Meyer[2], U Marcus[1], O Hamouda[1]

A resurgence of lymphogranuloma venereum (LGV) has been observed in several European countries. LGV is not a mandatorily notifiable disease in Germany. Reports of LGV cases have actively been collected by the Robert Koch-Institut since 2004 to describe the outbreak and estimate the extent of the LGV problem in Germany. Updates on the LGV outbreak were published in the German national epidemiological bulletin. Physicians were asked to send

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2. Laboratory Prof. Arndt und Partner, Hamburg, Germany

their samples to a laboratory for genotyping. A possible case was defined as a person with symptoms of proctitis and/or inguinal lymph node swelling and a positive chlamydia serology. A probable case had in addition a positive chlamydia rectal or urinary PCR test. A case was confirmed if the genotype L1-L3 was identified based on sequence analysis of omp1 gene sequences.
Since 2003, LGV has been reported in 78 male patients in Germany. Of these, 61 patients were confirmed as genotype L2. Fifty eight out of 78 patients (74%) are known to be men who have sex with men (MSM). Fifty five patients (71%) had rectal symptoms and 49 (63%) knew they were HIV positive. Sixty two (79%) of the patients were residents of Berlin or Hamburg.
LGV has emerged in MSM in Germany at the same time as in other European countries. It is thought that LGV may become endemic in the MSM community in German metropolitan areas, because the number of reported patients with LGV continues to increase. The increase in the number of LGV cases and the high HIV prevalence in LGV patients are of great public health concern. Clinicians and MSM may not be sufficiently aware of the disease, and existing efforts to promote awareness and prevention of sexually transmitted infections and HIV need to be strengthened.

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Introduction

Lymphogranuloma venereum (LGV) was a notifiable disease under the old veneral disease legislation (Bundesseuchengesetz) in Germany, which was in use until the end of 2000. No case definition was used and the system provided only aggregated case numbers, without information on patients' risk factors [1]. The number of reported LGV infections declined from a median of 35 infections per year between 1990 and 1995) to seven infections per year between 1996 and 2000. Under the new Infektionsschutzgesetz (Protection Against Infection Act) introduced in 2001, the only sexually transmitted infections (STIs) to remain notifiable were HIV and syphilis. At the end of 2002, a nationwide sentinel surveillance system for STIs was introduced by the Robert Koch-Institut to collect information on HIV, chlamydia, gonorrhoea, trichomonas, anogenital warts and genital herpes. LGV was not included, because it was considered a rare tropical disease. After the first alert from the Netherlands in 2004 [2] and the report of the first LGV cases in Germany [3, 4], we asked sentinel and all other physicians and laboratories performing L1-L3 genotyping to voluntarily report LGV cases to the Robert Koch-Institut in order to describe the outbreak and estimate its magnitude.

Methods

The German sentinel surveillance system for STIs collects data from 60 local health offices, 13 hospital-based STI clinics and 159 private practitioners. Private practitioners such as specialists in dermatovenerology, gynaecology, urology and HIV have been chosen at randomin all federal states. Sentinel physicians are asked to report LGV cases to the Robert Koch-Institut using sentinel reporting forms.

Updates on LGV were published in the German national epidemiological bulletin [5, 6] which is read by local health authorities and private practitioners. All physicians were asked to send their samples to laboratories that perform chlamydia genotyping. Reports on cases were received from sentinel physicians, other physicians, hospitals and laboratories. We also provided information about LGV to magazines aimed at a gay readership.

A possible case was defined as a person with symptoms of proctitis and/or inguinal lymph node swelling and a positive chlamydia serology. A probable case also had a positive chlamydia rectal or urinary polymerase chain reaction (PCR) test. A case was confirmed if the genotype L1-L3 was identified, even if the patient's symptoms were unknown.

Chlamydia trachomatis infections sent to the Arndt and Partner diagnostic laboratory were diagnosed by DNA amplification of lesional swabs or lymph node aspirates using PCR (Cobas TaqMan CT, Roche, Mannheim) or strand displacement amplification (ProbeTec ET, Becton-Dickinson, MD). *C. trachomatis* genotypes were identified by sequence analysis of variable omp1 gene regions (VS1, VS2, and VS4), amplified by PCR using primer pairs MF21/MB22 and MF44/MB4 [6].

Additional patient information was obtained by asking physicians. We described confirmed, probable and possible LGV cases by demographic characteristics and symptoms.

Results

Between May 2004 and November 2005, 61 confirmed and 17 probable or possible cases were reported to the Robert Koch-Institut. All confirmed cases were genotype L2. Reports were received from two local health offices, seven hospital-based STI clinics and 17 private practitioners.

The epidemic curve is shown in figure 1. The median number of monthly reported cases has increased from two in 2004 to four in 2005. All cases were in men, and the mean age was 39 years. Main characteristics of LGV patients are shown in the table. All 58 patients from whom an information on sexual orientation was obtained were MSM. Twenty seven of all 78 cases (35%) had proctitis and 31 had unspecified rectal symptoms. Ten patients showed an inguinal lymph node swelling. Of those, one patient showed confluent lymph nodes with signs of extensive inflammation. Whether this patient was MSM is unknown.

Table

Demographic characteristics and clinical picture of possible, probable and laboratory confirmed cases of LGV in Germany, 2003-2005

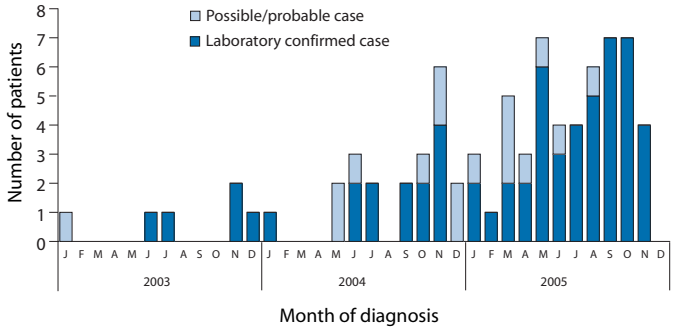
	Confirmed n=61	Probable n=10	Possible n=7
Sexual orientation			
Men who have sex with men	50	4	4
Unknown sexual orientation	11	6	3
Symptoms*			
Proctitis	14	8	5
Unspecified rectal symptoms	31		
Inguinal lymph node swelling	5	3	2
Unspecified genital symptoms	1		
Unknown symptoms	10		
HIV positive serostatus			
HIV positive	42	3	5
HIV negative	2	0	0
Unknown serostatus	17	7	2

Note: All cases were male
** One patient had rectal and genital symptoms*

Of the 52 patients with a known HIV status, 50 (96%) were known to be HIV-positive. Two patients were HIV-negative while the HIV status of 26 patients remains unknown. Patients originated from eight different federal states. Forty five patients (58%) were diagnosed in Hamburg, 17 (22%) in Berlin and 6 (8%) in Munich. The geographical distribution is shown in figure 2.

FIGURE 1

Number of possible, probable and laboratory confirmed cases of Lymphogranuloma venereum by month of diagnosis in Germany, January 2003 – November 2005, n=78



Of 24 patients for whom information on sexual contacts in other countries was available, three reported sexual contacts in the Netherlands and in Belgium. The other 21 patients did not report any contacts outside of Germany.

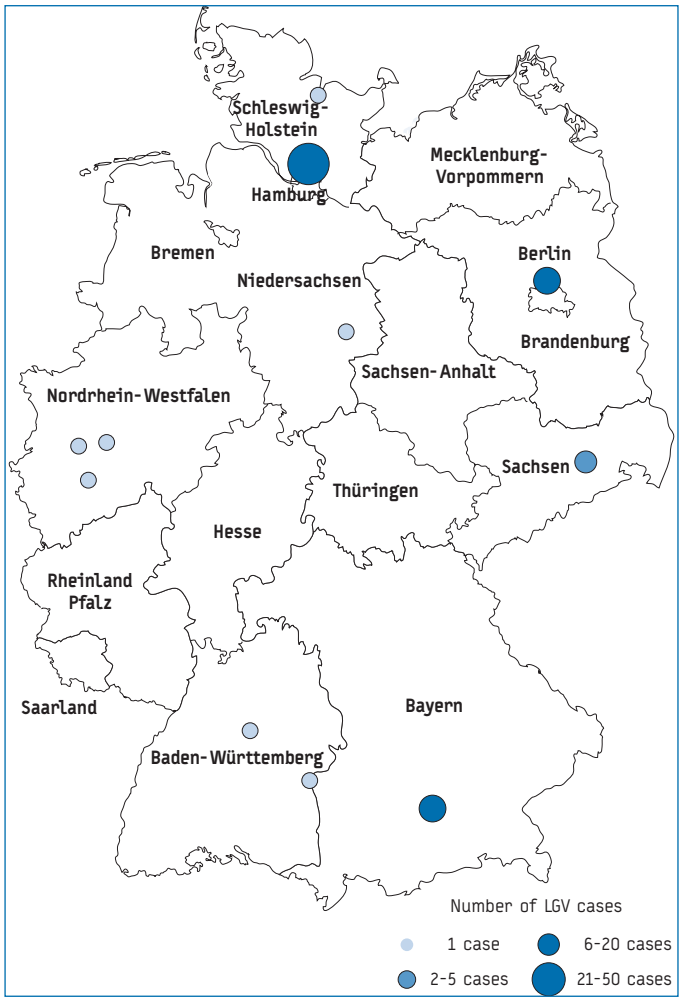
Discussion

In Germany, the first cases of LGV in MSM were observed at approximately the same time as the first cases in the Netherlands, France, Belgium and the United Kingdom [7-10]. It is possible that the outbreak began among MSM in the Netherlands and subsequently spread to Germany, but this remains unproven. Although information on sexual contacts in other countries was only available for a few German patients, the majority of these patients appear to have become infected in Germany. LGV may therefore have become endemic in the MSM community within two years of detection of the first cases in Germany. Furthermore, the number of reported patients with LGV has increased over the past few months and there are no signs that the epidemic is over. Over 80% of the reported cases have been diagnosed in large cities with a substantial MSM community such as Berlin, Hamburg and Munich. LGV may be more prevalent in these cities, but the difference could also reflect a diagnostic bias. Since the main diagnostic laboratory is situated in Hamburg, awareness among physicians may be higher in Hamburg than elsewhere.

About two thirds of LGV patients knew they were HIV positive at the time of their LGV diagnosis, a feature which has been observed in other countries as well [7, 9]. Reported cases of HIV and syphilis among MSM have also increased over the past three years in Germany [11, 12]. Since LGV facilitates HIV transmission, the emergence of LGV in the MSM community in the context of increasing numbers of newly acquired HIV infections should not be ignored. Clinicians and MSM may not be sufficiently aware of the disease, and existing efforts to promote awareness and prevention of sexually transmitted infections and HIV need to be strengthened.

FIGURE 2

Geographical distribution of LGV cases in Germany (n=78), January 2003 – November 2005



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Original Articles

Surveillance report

Rectal lymphogranuloma venereum surveillance in France 2004-2005

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Lymphogranuloma venereum (LGV) is a sexually transmitted infection (STI) caused by *Chlamydia trachomatis* strains belonging to the L1, L2 or L3 genotype.

An alert about an outbreak of LGV among MSM in the Netherlands was published in January 2004. The first cases of rectal LGV in France were retrospectively diagnosed in March 2004 and sentinel surveillance for LGV was implemented in April 2004.

Most of the participating centres were located in the cities of Paris and Bordeaux. Only confirmed rectal LGV cases were included in the surveillance. Rectal specimens from men that were found to be positive for *C. trachomatis* by PCR were sent to the National Reference Centre for Chlamydia infection for genotyping. Simple epidemiological data provided by clinicians and genotyping results were sent to the Institut de Veille Sanitaire (InVS) where data were anonymously recorded.

A total of 328 *C. trachomatis* rectal strains isolated in men were genotyped by the end of December 2005. Of these, 244 (74%) were LGV strains belonging to the L2 genotype. No L1 or L3 *C. trachomatis* genotype was found.

Diagnosis was made retrospectively for 46 cases. The median age of patients with LGV was 39 years. HIV status was known for 96 patients: 82/96 (85%) were HIV-infected. Most LGV cases were diagnosed in the Paris area (92%). Among the remaining 26% C. trachomatis strains, genotypes Da and G were the most frequent.

As with syphilis in recent years, the emergence of LGV in Europe is mainly affecting HIV-infected MSM. The screening and treatment of STIs should be included in the clinical follow-up of all HIV-infected MSM.

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Key words: Lymphogranuloma venereum, MSM, France

Introduction

An outbreak of rectal lymphogranuloma venereum (LGV) was detected among men who have sex with men (MSM) in Rotterdam during the summer of 2003 [1]. LGV, a sexually transmitted infection (STI) caused by *Chlamydia trachomatis* genotype L1, L2 or L3 is endemic in tropical countries but remains rare in industrialized countries. The classical clinical presentation of the infection is a genital ulcer with buboes. Rectal presentations have also been described, especially in MSM [2].

After the Dutch alert, a retrospective investigation was conducted in France which identified 21 cases of rectal LGV. Epidemiological information obtained for 14 of these 21 cases showed that all the patients were MSM, 8 were infected with HIV and 9 had also another sexually transmitted infection (STI). The mean duration of symptoms before diagnosis was lengthy (50 days), suggesting that clinicians were not aware of this STI [3].

In April 2004, as a public health response to these findings, a large-scale information campaign aimed at microbiologists, clinicians and groups focusing on MSM was begun, and a voluntary-based sentinel LGV surveillance system was launched in France. The results of this surveillance are presented in this paper.

Methods

Sentinel Surveillance design

In April 2004, six centres were recruited on a volunteer basis. They included two STI clinics, a laboratory, an outpatient proctology clinic and two microbiology laboratories, and all were located in Paris. The national reference centre, which is located in Bordeaux, also participated. In 2005, six additional laboratories located in other large cities were recruited

All rectal swabs positive for *C. trachomatis* by PCR were sent to the national reference centre, where genotyping was performed. Participating clinicians and microbiologists were also asked to provide basic epidemiological data such as age, HIV status, date of symptom onset, and date of sampling. Anonymised microbiological and clinical data were sent to InVS for analysis.

Case definition

Only confirmed rectal cases were included in the LGV surveillance. A confirmed rectal case was defined as a male patient with symptomatic proctitis due to *C. trachomatis* diagnosed using polymerase chain reaction (PCR) [Cobas Amplicor Roche Diagnostic System, Meylan, France] with the *C. trachomatis* strain belonging to L1, L2 or L3 genotype.

C. trachomatis strain genotyping was performed at the national reference centre for *Chlamydia* infection using a nested *omp1* PCR-restriction fragment length polymorphism assay [4].

Since a new LGV *C. trachomatis* variant characterised by a single mutation in the *omp1* gene of the major outer membrane protein (MOMP) and named L2b had recently been identified [5], the *omp1* gene of a random sample of L2 strains isolated in France during 2004-2005 was sequenced.

Results

From March 2004 to December 2005, 328 rectal *C. trachomatis* strains were genotpyed.

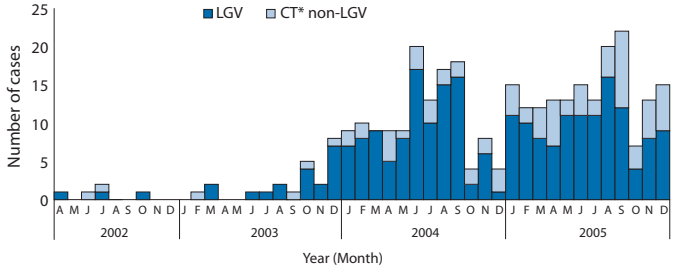
1. Institut de veille sanitaire, Saint-Maurice, France
2. National Reference Centre for Chlamydia infection. Université Bordeaux 2, Bordeaux, France
3. Institut Alfred Fournier, Paris, France
4. Bacteriology Laboratory. Hôpital Saint-Louis, Paris, France
5. Hôpital Léopold Bellan, Paris, France
6. Bacteriology Laboratory Chemin Vert, Paris, France
7. Hôpital Saint-Louis, Paris, France

Of these, 244 (74%) belonged to the L2 genotype, which confirmed the diagnosis of rectal LGV. No *C. trachomatis* strain belonging to the L1 or L3 genotype was found.

For 22 rectal LGV cases which occurred between April 2002 and December 2003, the diagnosis was made retrospectively in March 2004. For 2004, 104 rectal LGV cases (24 cases retrospectively from January to March and 80 prospectively from April onwards) were reported to the LGV surveillance system. For 2005, 118 rectal cases were recorded [FIGURE].

FIGURE

Monthly rectal LGV and rectal CT non-LGV cases, France 2002-2005



* *Chlamydia trachomatis*

Of the 244 identified rectal LGV, 174 (72%) were sequenced, and all these exhibited the *omp1* gene mutation of the MOMP that characterises the newly described L2b variant. The median age of patients with a rectal LGV infection was 39 years (range: 34-44). HIV status was available for 96 patients, and 82 (85%) were known to be infected with HIV. Most of the patients with rectal LGV lived in the Paris area (92%). Of the remaining patients, 5% lived in Bordeaux and 3% were diagnosed in other cities, includingTourcoing, Lille and Marseille.

Eighty five of the genotyped *C. trachomatis* rectal strains (26%) did not belong to the LGV genotypes. For these 85 strains, the genotypes were found to be mainly Da (10%) and G (9%). In 2004, the proportion of non-LGV genotypes was 20%, in 2005 this proportion increased significantly from 20% to 30% (c2= 4.4, P=0.03). Patients with *C. trachomatis* proctitis were younger than patients with LGV proctitis, with a median age of 34 years (range: 21-58), and were less likely to have an HIV infection (60%) (c2=8.1, P=0.004) than those with LGV proctitis.

Discussion

Since the French surveillance system includes only confirmed cases which require strain genotyping, and there are only a small number of participating centres, mainly located in Paris, the number of reported rectal LGV cases is certainly underestimated for France. However, the number of reported rectal LGV cases in 2004-2005 higher than in previous years. A study in the late 1980s at a STI clinic in Paris found two rectal forms diagnosed in MSM among a total of 27 LGV cases [6], and no further cases were reported in France until the current epidemic.

The genotyping of *C. trachomatis* strains appears to be necessary to confirm the diagnosis of LGV, because a quarter of *C. trachomatis* strains isolated in men were not LGV strains.

The number of LGV cases in 2004 and 2005 are similar, but reports of non-LGV *C. trachomatis* proctitis increased during this period, almost certainly due to a surveillance bias (more participating centres).

LGV cases have been diagnosed in several Europeans countries [7] and in some cities in the United States [8]. In all these countries, LGV proctitis has only been seen in MSM, most of whom were HIV-infected. A recent case-control study (LGV proctitis versus non-LGV *C. trachomatis* proctitis) showed that HIV infection was strongly associated with LGV [9]. This result is consistent with the French data in which patients with LGV are more frequently HIV-infected than those with a non-LGV proctitis (82% versus 60%). The new variant L2b recently described in the Netherlands was found in all the sequenced L2 *C. trachomatis* stains in France suggesting that this specific LGV strain has spread in the two countries.

The LGV emergence is a serious concern for gay men and in Europe. LGV diagnosis should be prompt and appropriated treatment administered to avoid serious sequels as rectal stricture (2) and to interrupt transmission. Furthermore, rectal LGV characterised by deep mucosal lesions could facilitate HIV transmission. Patients with rectal LGV are often infected with several others pathogens such as herpes simplex virus or human papillomavirus. Screening and treating STIs should be included in the clinical follow–up of all HIV-infected MSM.

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Original Articles

Surveillance report

HIV incidence increasing in MSM in Germany: factors influencing infection dynamics

U Marcus, L Voss, C Kollan, O Hamouda

After an initial peak in the mid-1980s, HIV incidence in men who have sex with men (MSM) declined in most western industrialised countries and then levelled off during the 1990s. Since the late 1990s, increasing numbers of newly diagnosed HIV infections in MSM have been observed in the majority of countries with large and visible MSM communities.

Based on a review of national and international behavioural surveillance studies of MSM and national HIV surveillance data, we propose a model for the HIV epidemic in MSM in Germany.

The model includes aspects such as individuals' increasing numbers of sexual partners and increasing frequency of unprotected anal intercourse, conditional condom use based on real or perceived HIV status of sexual partners (HIV 'serosorting') and sexual role assignments (insertive versus receptive based on HIV status (HIV 'seropositioning'), selection of partners and formation of sexual networks through seeking sexual partners on the internet, the introduction of HAART and changing HAART treatment strategies. All these aspects have been shown or are suspected to increase or decrease HIV transmission risk in MSM.

We conclude that increasing HIV incidence in MSM in recent years has been fuelled by a spread of HIV in high-risk sexual networks with an increasing proportion of infections transmitted during highly infective early HIV infection, acquired mostly from casual sexual partners.

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Key words: MSM, HIV incidence, sexual risk behaviour, sexual networks

Background

By the end of 2005, the number of people living with HIV (PLWHIV) in Germany was estimated at about 49 000, among a total population of 82.5 Mio. Around two thirds of all PLWHIV in Germany are estimated to be men who have sex with men (MSM) [1]. Since 2001, there has been a continuous increase in the number of newly diagnosed HIV infections in MSM. Over the same time period, similar increases of HIV diagnoses in MSM have been reported from the majority of western European countries in which HIV surveillance systems are established. These simultaneous increases of newly diagnosed HIV infections were preceded, accompanied or followed by increasing incidences of other sexually transmitted diseases in MSM, such as syphilis, gonorrhea and lymphogranuloma venereum [2,3].

Introduction

Among the first consequences of the growing awareness of the HIV epidemic in gay communities in the early to mid-1980s was a dramatic reduction of partner numbers, followed in the late 1980s and early 1990s by the increasing use of condoms within the context of casual sexual encounters. This decrease in sexual risk-taking resulted in reductions of transmission events and a shift of HIV transmission in MSM from casual sexual encounters towards more long-term partnerships, because internal relationship dynamics within such partnerships favour unsafe sexual behaviour [FIGURE 1].

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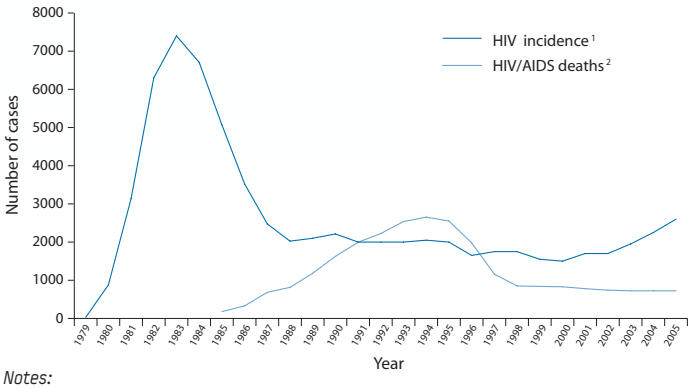
Figure 1

Model of incident HIV infections and incident HIV/AIDS-related deaths in Germany, 1979-2005



Notes:
Estimates for HIV incidence from 1979 to 1991 based on AIDS back-calculation model (AIDS cases diagnosed up to 1995), from 1991 onwards based on numbers of newly diagnosed HIV infections
1. HIV incidence = estimated number of incident cases of HIV infection in Germany resp. in persons residing in Germany at the time of HIV infection (i.e. migrants from high prevalence areas excluded)
2. HIV/AIDS deaths = estimated number of deaths among people infected with HIV independent of the actual cause of death (estimates based on cause-of-death statistics, corrected for non-AIDS-related deaths based on the proportion of such deaths in selected regions, where HIV clinics match their patient data with vital statistics)

It is clear that something changed in the second half of the 1990s, because the incidence of sexually transmitted infections in MSM began to increase again, not just in selected countries or regions, but in all countries of the developed and developing world (such as Thailand and Brazil) that had large, organised and visible MSM communities.

Based on the findings of national and international behavioural surveillance data in MSM from recent years, and on the HIV surveillance data from Germany, we propose a model for the HIV epidemic in MSM in Germany that could explain the trends observed and identify relevant areas for future epidemiological and behavioural research.

Methods

The construction of a model for the MSM HIV epidemic in Germany is based on a review of national and international behavioural surveillance studies of MSM and HIV surveillance data.

The German HIV surveillance system has been described in

detail elsewhere [4]; briefly, newly diagnosed HIV infections must be reported by laboratories with complementing patient history and clinical data provided by the primary care physician on a duplicate of the laboratory reporting form.

For Germany, the main data source for sexual behaviour changes in MSM are the national surveillance studies that have been performed every 2-3 years since 1987 [5].

Behavioural surveillance studies of MSM in western developed countries were identified by a Medline search using the search criteria 'MSM' and 'sexual risk behaviour', including studies published since 1998 from western Europe, Australia and North America.

Results

Behaviour changes in MSM

Recent studies on sexual risk behaviour of MSM have described a range of changes in sexual risk-taking behaviours in MSM in recent years. Many MSM report increased numbers of partners, there has been an apparent revival of anogenital practices and an increase in the proportion of unprotected episodes of anogenital intercourse. Other behavioural features are frequent HIV testing (in a recent internet-based survey in which over 45 000 MSM from Germany participated, 70% reported that they had been tested for HIV at least once, and 53% reported having had between two and five tests [6]), HIV 'sero-sorting', and HIV 'sero-positioning' , and the growing importance of the internet for seeking and selecting sexual partners [3,5-12].

Number of sexual partners

German behavioural surveillance of MSM has found that MSM have been having increasing numbers of sexual partners since the early 1990s, after a short period during which MSM had decreasing numbers of partners, from approximately 1984 until 1989 [4].

While there was no clear evidence from the HIV surveillance system that increasing numbers of partners in MSM resulted in accelerated HIV transmission in subsequent years, the incidence of some sexually transmitted infections, which are more easily transmissible than HIV, may already have increased during this period, despite widespread condom use, because of transmission through sexual practices, which were usually performed without protection (e.g. genital-oral sex: no data available for Germany, but see [13]).

Increase of unsafe sex

Sexual behaviour surveys in MSM in Germany [5] have repeatedly found evidence of increasing unsafe sexual contact in MSM since 1996, after a decade of continuously declining occurrence of unsafe sexual behaviour. The proportion of men reporting unsafe anal intercourse with partners of unknown HIV status, and the reported number of partners with whom unsafe sex is practised, have been increasing since 1996 [FIGURE 2].

Urban-rural differences, the internet, and the formation of high risk networks

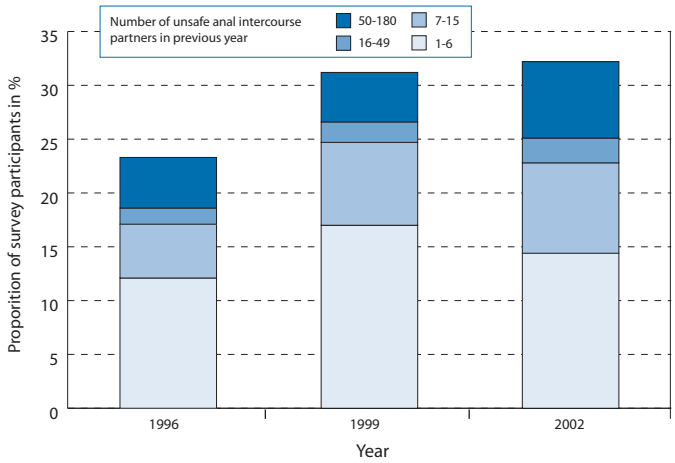
The wish to fulfil sexual desires, unconstrained by social and family supervision, results in a concentration of MSM in large cities, where gay bars, discotheques, bath houses, and a wide range of gay community organisations make it easier for MSM to seek and find sexual partners. Therefore, MSM living in metropolitan areas usually report higher numbers of sexual partners and higher incidences of sexually transmitted infections than MSM living in rural areas. Since the late 1990s, the increasing availability of the internet has led to more opportunities to seek and meet new sexual partners. The decreasing gap between MSM residing in metropolitan and rural areas in terms of partner numbers and (self-reported) STI incidences observed in the German behavioural surveys (data not shown) probably reflects the increased use and availability of the internet. However, the internet not only makes the search for new partners easier, it also allows for a more effective selection of partners, based on sexual preferences, HIV status, and also on the willingness to practise unsafe sex. This results in the formation of sexual networks suitable for fast and efficient spread of STIs [DIAGRAM] [14-16].

Improvement of antiretroviral therapy and changing treatment strategies

Since the availability of highly active antiretroviral therapies (HAART) from 1996, the number of people being treated with HAART (calculated based on antiretroviral drug sales) increased rapidly until 1998, and then levelled off, when problems associated

FIGURE 2

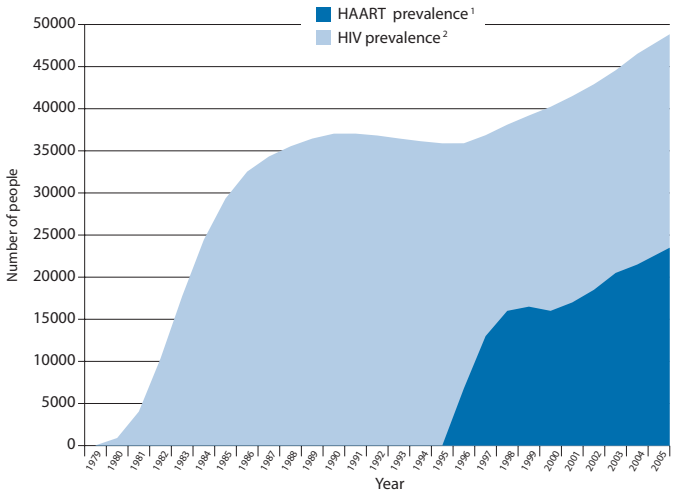
Proportion of MSM from metropolitan areas (Berlin, Hamburg, Munich, Frankfurt, Cologne) participating in behavioural surveys (N=1906), who reported unsafe sexual encounters (unprotected anal intercourse) during the year before the survey and the number of partners with whom unsafe sex was practised



Source: Repeated behavioural surveys among German MSM by Bochow/ Wright [4]

FIGURE 3

HIV prevalence model for Germany, 1979-2005



Notes:
1. HAART prevalence = total number of people infected with HIV and treated with highly active antiretroviral combination therapy (usually three or more antiretroviral agents in combination). The numbers are estimated based on monthly drug doses sold by pharmacies in Germany
2. HIV prevalence = total number of people living with HIV in Germany at the respective time point, calculated by subtracting the cumulative number of deaths among people with HIV from the cumulative number of people infected with HIV

with long term toxicities of HAART began to emerge in 1999/2000. HAART is nowadays initiated later in the course of HIV infection. The numbers of people living with HIV, but being not treated with HAART, decreased sharply from 1996 to 1999, but has since begun to increase slowly [FIGURE 3].

After 1996, HIV transmission risks were reduced within stable partnerships between serodiscordant partners (where one partner is infected with HIV, and the other partner is not infected) by widespread use of highly active antiretroviral therapies (HAART), because of the reduced infectivity of those being treated. However, prolonged survival and improved quality of life for HIV-infected people resulted in a growing number of people living with HIV, and an increase in their sexual activity. Since the late 1990s, the change of HIV treatment strategies has led to treatment interruptions and delayed initiation of antiretroviral treatment in people newly diagnosed with HIV [DIAGRAM].

Therefore, by the early 2000s, increasing risk behaviour and increased transmission risk were no longer being compensated for by the effects of antiretroviral therapy. New infections with HIV increased in frequency in the partners of chronically HIV-infected people, and mostly in the age group in which most sexually active HIV-infected men are found (35-40 years). However, an increase in risk-taking behaviour by uninfected MSM and the formation of subpopulations of MSM with high partner numbers and a high prevalence of unsafe sexual behaviour introduced new opportunities for HIV to spread quickly and efficiently within high risk sexual networks, where high incidences of other STIs further enhanced the spread [17] [DIAGRAM]. These high risk networks are found within and across all age groups of MSM between the ages of 25 and 45-50. The diffusion of HIV from the core age group of 35-40 into the neighbouring age groups via sexual networks occurs with some smaller time delays, which are reflected in the successive increase of HIV diagnoses incidence in different age groups [FIGURE 4].

Conclusions

The increase in number of partners in the early 1990s probably had few consequences for HIV incidence, because during that time period, an overwhelming proportion of penetrative sexual contacts within the context of casual sex were protected by condom use. A few exceptions may have permitted isolated infection clusters, but these did not spread extensively, because of widespread condom use. During this period, a comparatively high proportion of HIV transmission in MSM occurred within committed, short or long-term partnerships, and therefore increased emphasis on HIV testing was a highly appropriate part of prevention strategies.

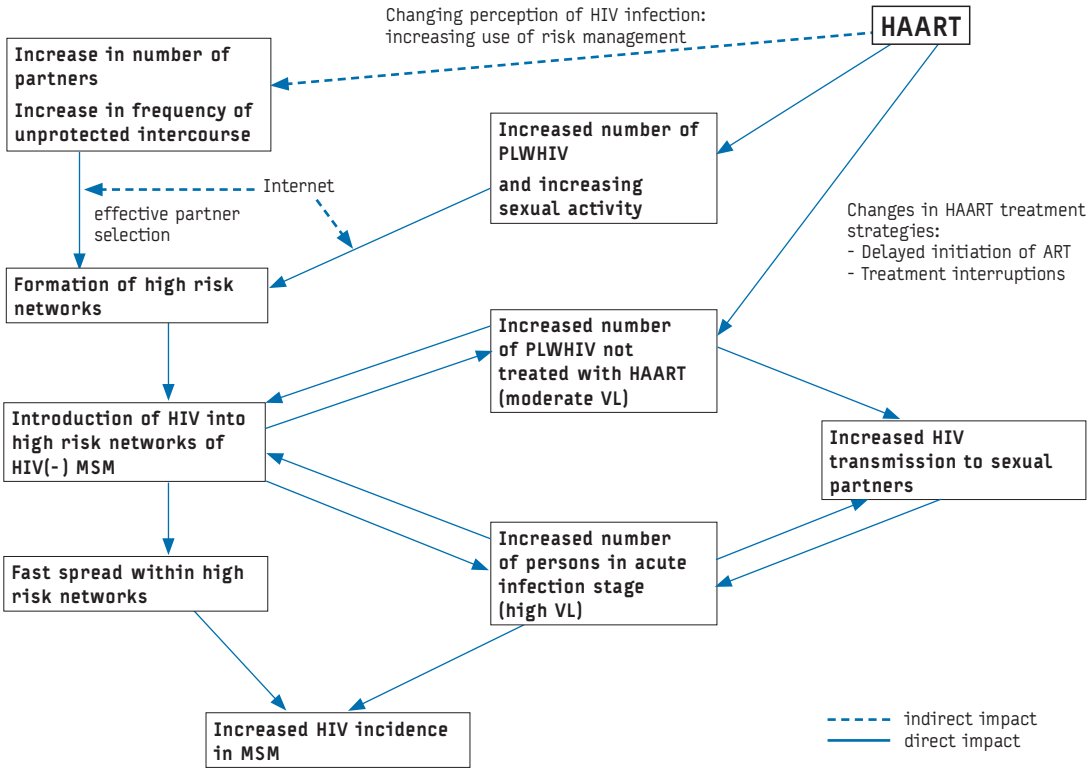
Risk minimisation strategies based on better knowledge or assumptions on HIV status developed during the 1990s and were appropriate for the above described epidemiological situation, but they tended to fail in the situation that developed after 1996, in which an increasing proportion of new infections are transmitted during acute HIV infection, and outside of stable partnerships. Emphasising HIV testing as a cornerstone of HIV prevention in the current situation in the mentioned high risk subgroups of MSM may even be counterproductive if it encourages men with a high number of partners and frequent practice of unsafe sex to be overly confident of a negative HIV status and to abandon condom use [17].

Outlook

While surveillance of newly diagnosed HIV infections allows for a more up to date monitoring of the HIV epidemic than AIDS case surveillance, it cannot provide accurate information on HIV incidence. The challenges are to apply methods to determine HIV incidence and

DIAGRAM

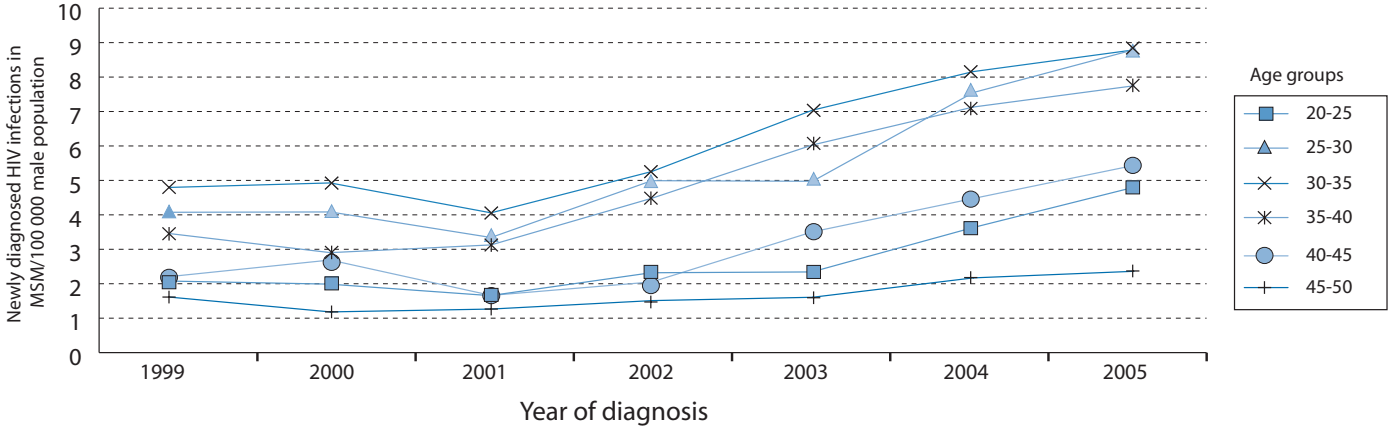
Behaviour and context factors leading to increased HIV incidence among MSM



PLWHIV = people living with HIV; VL = viral load; (HA)ART = (highly active) antiretroviral therapy

FIGURE 4

Newly diagnosed HIV infections in MSM per 100 000 population in the respective male age groups in Germany, 1999-2005



to monitor risk behaviour to detect changes in risk behaviours early enough to modify prevention messages and prevention strategies before these changes have a large impact on HIV incidence.

Our goal therefore is to build a system of second generation surveillance in Germany. Currently, the following elements of such a system are being implemented or planned:

1) A pilot study to establish a surveillance system and laboratory assays to define the proportion of recent infections among newly diagnosed HIV infections (ongoing).
2) Extension of behavioural surveillance of MSM. In addition to the repeated behavioural surveillance studies that have been conducted in the past and that focused on HIV-related risks, a new survey on MSM's knowledge, attitudes and behaviours regarding STIs has been executed in 2006. In a pilot sub-study within this survey we tested the feasibility of self-collected blood filter samples, with the aim of connecting behavioural and serological data (results are currently analyzed).
3) Qualitative research on risk factors of incident HIV infections and motives for unsafe sex in newly diagnosed HIV-infected MSM (ongoing).
4) A study on partner-seeking and risk communication by internet users (results are currently analyzed).

While we are aware that not all aspects of our proposed model are strongly corroborated by epidemiological and behavioural data, we think the model represents a reasonable interpretation of epidemiological trends based on available data, and as such, may be helpful for generating research questions for further studies.

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DIAGNOSIS OF NON-VIRAL SEXUALLY TRANSMITTED INFECTIONS IN LITHUANIA AND INTERNATIONAL RECOMMENDATIONS

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To evaluate the range, quality and availability of diagnostic services for non-viral sexually transmitted infections (STIs), i.e. *C. trachomatis, N. gonorrhoeae, T. vaginalis* and *T. pallidum*, in Lithuania from September 2002 to December 2003.

Surveillance data describing the organisation and performance characteristics of non-viral STI diagnostic services in Lithuania were collected using a questionnaire and subsequent site-visits. International evidence-based recommendations for non-viral STI diagnosis were used to evaluate the quality of the STI diagnostics.

There were 171 facilities providing non-viral STI diagnostic services for the 3.5 million inhabitants of Lithuania. However, only 6% (n=9) of the respondents (n=153) could provide a confirmatory diagnosis, in accordance with international recommendations, for the full minimum range of relevant non-viral STIs in Lithuania, i.e. *C. trachomatis, N. gonorrhoeae, T. pallidum,* and *T. vaginalis*. In addition, accessibility to STI diagnostic services differed significantly among the different counties in Lithuania. Several of the respondents analysed low numbers of samples each year, and overall the sampling size was extremely low, especially for *C. trachomatis* diagnostics.

In Lithuania, optimisation of non-viral STI diagnostics as well as of epidemiological surveillance and management of STIs is crucial. It may be worth considering a decrease in the number of laboratories, with those remaining having the possibility of performing STI diagnostic services that are optimised, in concordance with international recommendations, standardised, and quality assured using systematic internal and external quality controls and systems. In addition, establishment of national inter-laboratory networks and reference centres for non-viral STIs is recommended.

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Key words: non-viral STIs, laboratory diagnosis, Lithuania, diagnostic quality

Introduction

Sexually transmitted infections (STIs) are recognised as major public health threats worldwide. However, in most of the countries of the former Soviet Union, including Lithuania, STIs and reproductive health have received insufficient attention, contributing to a decrease in the birth rate and an increase in the rate of medical abortions [1]. Lithuania has a population of 3.5 million inhabitants and comprises 10 different counties. In 2002, the population of the counties ranged from 133 000 to 848 000 (in the country which includes the capital city, Vilnius). The estimated incidences of non-viral STIs in Lithuania, especially genital chlamydial infection and gonorrhoea, are comparatively low at present, and have tended to decline during the past decade [2, 3]. However, reliable figures for the incidences of non-viral STIs are lacking, primarily due to suboptimal diagnostics, incomplete epidemiological surveillance, and self treatment.

Since the re-independence of Lithuania in 1991, the national healthcare system has undergone several major changes. For example, state-controlled mandatory hospitalisation has been replaced by a more decentralised system based on an outpatient primary care approach, and there are many new private STI outpatient clinics and laboratories with an anonymous care and treatment approach. Previously, it was mandatory for local dermatovenereological diagnostic facilities to report all diagnosed STI cases to the central dispensary (dermatovenereological out-patient clinic). Cases must now be reported to newly established regional public health centres, which then report to the National Centre for Prevention and Control of Communicable Diseases [4]. Many of these changes have contributed to distortion of the epidemiological data.

International evidence-based recommendations regarding diagnostics [5-7] are still mainly unknown in non-viral STI diagnostic services in Lithuania. In many cases, the choice of diagnostic strategies and assays is consequently based on empirical knowledge or even on the economic status of the particular facility, which significantly affects the quality of the diagnostics. Unfortunately, highly sensitive and specific laboratory-based diagnoses of several non-viral STIs are quite expensive. Issues regarding laboratory quality control have recently emerged in Lithuania but these have not yet attracted sufficient attention on the part of healthcare administrators. Thus, there are still no accredited clinical microbiological laboratories in Lithuania [8].

In the absence of effective vaccines, the mainstay in the prevention of non-viral STIs is based on the availability of adequate healthcare, effective diagnostics and treatment, and epidemiological surveillance. Consequently, the number of physicians specialising in STIs and in counselling afflicted patients, and the number and geographical location of adequate healthcare institutions and laboratory facilities that can provide sensitive and specific STI diagnostics are highly important.

The aim of the present study was to evaluate the range, quality and availability of diagnostic services for non-viral STIs (*Chlamydia trachomatis, Neisseria gonorrhoeae, Treponema pallidum* and *Trichomonas vaginalis*) in Lithuania from September 2002 to December 2003.

Material and methods

Surveyed Lithuanian laboratories and demographic data

All Lithuanian laboratories and other facilities that performed diagnostic tests for *C. trachomatis*, *N. gonorrhoeae*, *T. pallidum*, and *T. vaginalis* from September 2002 to December 2003 were included in the present study. Laboratories were identified from information obtained from the Lithuanian Department of Accreditation (LDA; in Lithuanian, the Lietuvos akreditacijos tarnyba), which is responsible for the certification of facilities performing laboratory diagnostics. In addition, the county-level STI management groups in all 10 Lithuanian counties [9] updated the information received from LDA. The study questionnaire was sent to all laboratories that had confirmed they performed non-viral STI diagnostics. Demographic

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data on each of the counties in Lithuania (n=10) were obtained from the Lithuanian Statistical Department (in Lithuanian, the Lietuvos statistikos departamentas) [10].

Survey questionnaire and data collection procedure

The utilised questionnaire consisted of 150 questions focussing on (a) organisation of the STI diagnostic service (type of laboratory, number of personnel, professional qualifications of the personnel, existence of a laboratory quality assurance system, etc.), and (b) performance characteristics (STI agents diagnosed, number of tests performed per month, diagnostic methods employed for the different STIs, etc.). The laboratories provided surveillance data by email, fax, or telephone interviews. In addition, follow up visits for validation of these data were performed at many of the laboratories.

In the final data analysis, the laboratory diagnostics for the full minimum range of relevant non-viral STI agents in Lithuania underwent more comprehensive evaluation.

Adherence of Lithuanian STI diagnostics to international evidence-based recommendations

For evaluation of the quality of the non-viral STI laboratory diagnostic strategies and assays used at the Lithuanian laboratories, international evidence-based recommendations for non-viral STI diagnostics and definitions of STI surveillance cases [5-7] were used.

Results

STI diagnostic laboratories in Lithuania and response rates

In total, 171 laboratories in Lithuania, of which 28 (16%) were private, were LDA certified for STI diagnostics and currently performed non-viral STI diagnostics. Consequently, the median number of inhabitants served by one STI diagnostic laboratory in Lithuania was 20 470 (range: 10 400-30 600) in the different counties. Of the 171 laboratories identified, 153 (89%) agreed to participate in the assessment study and provided all the surveillance data that were requested. The remaining 18 laboratories gave various reasons for declining to participate, for example only performing STI diagnostics occasionally, testing very few samples or not wishing to be involved in the present study. Minor discrepancies were identified between the data provided in the questionnaires and observations at the site visits; however, these were associated only with incomplete filling in of the questionnaire or occasional misunderstanding of a question.

Laboratory diagnostics for non-viral STIs in the responding Lithuanian laboratories

Microscopy of genital samples

In all, 150/153 (98%) respondents used microscopy of genital samples for non-viral STI diagnostics. Of note 34/153 (22%) respondents reported microscopy of genital samples as the only method used for STI diagnostics. In 49/153 (32%) responding laboratories, only specialists with a master's degree in medicine or biology, and who also specialised in laboratory medicine, were responsible for evaluation of the genital samples. Six respondents (6/153, 4%) reported that practicing, non-specialist physicians performed the microscopy in their laboratories. In 31/153 (20%) of the responding laboratories, laboratory technicians were solely responsible for evaluating the genital samples, and in 67/153 (44%), technicians and/or laboratory physicians performed the microscopy.

Laboratory diagnostics for the main non-viral STIs in Lithuania

No accredited clinical microbiological laboratories exist in Lithuania and all respondents also lacked a complete and thoroughly implemented laboratory quality assurance system; that is, one which included internal and external quality controls, written guidelines describing the entire procedure for processing of samples, interpretation of results, equipment control measures, etc. Only 10% of respondents could provide diagnostics for the full minimum range of relevant non-viral STIs in Lithuania. The main characteristics of the diagnostics for these pathogens are summarised in the table.

Laboratory diagnostics for *C. trachomatis* was available in only six of the 10 counties in Lithuania and, in total, only in 16 (10%) of the responding laboratories [TABLE]. Consequently, the number of samples was much lower than for the other main non-viral STI pathogens [TABLE]. Two thirds of the analyses were performed in the largest county. Most respondents used an enzyme immunoassay (EIA) or a direct immunofluorescence (DIF) assay [TABLE].

For diagnosis of *N. gonorrhoeae*, the number of samples each month varied dramatically among the different counties in Lithuania and ranged from 22 to 1629 for men and from 270 to 8888 for women. Almost 75 per cent of all samples from men were tested in the two largest counties of Lithuania. Most respondents diagnosed *N. gonorrhoeae* exclusively by microscopy of stained (methylene blue or Gram stained) genital samples [TABLE]. In seven of the 10 Lithuanian counties at least one respondent was able to perform culture of *N. gonorrhoeae*, but the number of samples was low.

Regarding the diagnostics of *T. pallidum*, respondents in the larger Lithuanian counties analysed almost equal numbers of samples from men and women, while respondents in most of the smaller counties tested more samples collected from women. For screening purposes, the majority (60%) of respondents performed rapid plasma reagin (RPR) tests of STI samples, units of donated blood and plasma, pregnant women, etc. For RPR positive samples, mainly *T. pallidum* haemagglutination (TPHA) was used for subsequent specific confirmation [TABLE].

For diagnosis of *T. vaginalis*, the number of samples analysed and the women/men ratio of samples tested were very similar to that of *N. gonorrhoeae* [TABLE]. Almost 75% of the men tested were tested in the

Table

Diagnosis of non-viral sexually transmitted infections, monthly average, Lithuania, 2002-2003

	C. trachomatis (n=16)[a]	*N. gonorrhoeae* (n=152)[a]	*T. pallidum* (n=92)[a]	*T. vaginalis* (n=114)[a]
Total number of samples (range)[b]	1 551 (11-1253)	27 247 (465-10 517)	24 829 (405-10 749)	25 704 (405-9735)
Female/male ratio (range)[b]	1.3 (1.2-6.7)	6.8 (1.4-36)	1.5 (0.5-59)	6.1 (1.6-57)
Number of samples per 100 000 inhabitants (range)[b]	44 (5.8-148)	784 (307-1334)	709 (205-1267)	734 (217-1165)
Diagnostic methods[c] (%)[d]	EIA (5.9) DIF (5.2) REIA (3.3) NAATs (2.0) Serology (1.3) Cell culture (0.7)	Microscopy of genital smears (94) Culture (5.0) DIF (0.7) NAATs (0.7)	RPR (60) TPHA (53) DFM (6.0) Serology for newborns (6.5) VDRL (2.6) REIA (2.0) FTA (1.3)	Microscopy of genital smears (75; i.e. 75% used methylene blue, 42% Gram, 14% Giemsa and 23% wet smear) Culture (0.7)

a. Number of respondents that diagnosed the pathogen

b. Range of numbers of samples or of the female/male ratio of samples in different counties in Lithuania

c. EIA, enzyme immuno assay; DIF, direct immunofluorescence; REIA, rapid enzyme immuno assay; NAATs, nucleic acid amplification tests; RPR, rapid plasma reagin; TPHA, *T. pallidum* hemagglutination; DFM, dark field microscopy; VDRL, Venereal Disease Research Laboratory assay; FTA, fluorescent treponemal antibodies

d. Percentage of responding STI diagnostic laboratories in Lithuania (n=153) that perform the method

two largest counties. The vast majority of the respondents diagnosed *T. vaginalis* using microscopy of genital samples [TABLE].

Discussion

The present study highlights several shortcomings in the diagnostics and management of non-viral STIs in Lithuania. A similar situation has previously been described in one of the neighbouring Baltic countries, Estonia [11]. In Lithuania, there is mandatory reporting of syphilis, gonorrhoea and genital chlamydial infections [4]. Before the re-independence of Lithuania in 1991, patients with non-viral STIs were managed exclusively by specialists in dermatovenereology, mainly at dermatovenereological (DV) dispensaries. Each case of syphilis and gonorrhoea was reported by the local DV dispensary to a central dispensary. The chief dermatovenereologist at the central DV dispensary would then be kept up to date with the progress of each case, including partner tracing. Each primary healthcare facility had its own dermatovenereologist who managed all the non-viral STI patients. There were no private practices or laboratories. Following the re-independence of Lithuania, there was no ready concept within healthcare reform for the diagnostics and management of non-viral STIs. Many private clinics and laboratories arose, which introduced and usually used the cheapest available methods for STI diagnostics. There was a lack of expertise and financial resources for controlling the STI diagnostic strategies and the quality of the diagnostic methods used in these laboratory services. As revealed in the present study, the 3.5 million inhabitants in Lithuania during 2002-2003 had 171 facilities providing non-viral STI diagnostic services, but the availability of STI diagnostic services for each inhabitant and the number of inhabitants served by each laboratory varied significantly between counties. Several of the responding laboratories were small and received low number of samples for STI diagnostics. This may not be cost-effective, there may be insufficient experience, inadequate use or even lack of standardised controls, and it may be more difficult to implement systematic internal and external quality assurance controls and systems.

Only 10% of the respondents that diagnosed any STI in Lithuania were able to provide *C. trachomatis* diagnostics and there were only 532 samples per 100 000 inhabitants per year. In contrast, 4726 samples per 100 000 inhabitants are tested each year in Estonia [11]. The low sampling size in Lithuania may partially explain why the estimated incidence of *C. trachomatis* infection in Lithuania (11.08 per 100 000 inhabitants in 2004) is significantly lower than in the neighbouring countries of Estonia [11], Belarus, Poland, Sweden, and Denmark [2]. Although Latvia has also reported a low incidence of *C. trachomatis* infection [2], more information about the reliability of these figures is needed. In Lithuania, older diagnostic assays such as EIA or DIF were most often used, which may not give optimal sensitivity and specificity. However, with the exception of two respondents who used serology only, the diagnostics used by the laboratories that diagnosed *C. trachomatis* corresponded well with international recommendations [5, 7], using at least one antigen detection assay (DIF or EIA), nucleic acid detection method, or culture.

It is alarming that for *N. gonorrhoeae*, most respondents reported using microscopy of stained genital samples as their sole method, because it is cheaper to use, and only 5% of the respondents were able to culture the bacteria. Consequently, most respondents were only able to provide definitive diagnosis of male symptomatic gonococcal urethritis [6, 7, 12]. According to international recommendations, to provide a definitive diagnosis, the following kinds of samples should be cultured: urethral and cervical samples from women, samples from asymptomatic patients of both sexes, and tests of cure, as well as all extra-genital samples [5, 6, 12]. Failing this, antigen or nucleic acid of the bacteria should be identified [5, 7]. Culture allows subsequent identification of antimicrobial resistance in *N. gonorrhoeae* and there is a complete lack of in depth knowledge about the level of antimicrobial resistance in Lithuania.

Concerning diagnosis of syphilis in Lithuania, all respondents that performed syphilis diagnostics could identify probable cases of primary and secondary syphilis according to international guidelines [5, 7]. However, only 6% of the respondents reported using IgM or DFM (or another direct detection method such as PCR) and therefore being able to provide a confirmatory diagnosis of early primary or secondary syphilis [5, 7]. These data are mainly in agreement with the results of our previous study in the neighbouring country of Estonia [11].

As for *N. gonorrhoeae*, the sample size for *T. vaginalis* diagnostics reflected the number of genital samples for microscopy from STI patients and from women attending gynaecology clinics, which is mirrored in the female/male sample ratio. Only 23% of the respondents used wet smear microscopy, which is considered to be the most sensitive method for microscopic diagnosis of the agent [13].

As mentioned previously, only 10% (n=16) of the respondents could provide diagnostics for the full minimum range of relevant non-viral STIs in Lithuania, and only 6% (n=9) of the respondents were able to provide confirmatory diagnoses in accordance with international recommendations for diagnostics [5, 7] for all the non-viral reportable STIs in Lithuania (*C. trachomatis* infection, gonorrhoea, and syphilis).

The comparatively low and declining estimated incidences of non-viral STIs in Lithuania may, in part, reflect incomplete case reporting and epidemiological surveillance, the low number of samples for some of the STIs, the availability of STI diagnostic services, and, in many cases, the suboptimal diagnostics [present study, 14]. The main reason for this situation is the low level of funding in the healthcare budget for each non-viral STI patient, which should cover the cost of clinical investigation and all laboratory analyses. For more thorough and complete laboratory diagnostics the patient may have to pay for each additional assay himself/herself [15].

In conclusion, for optimisation of non-viral STI diagnostics, epidemiological surveillance and management of non-viral STIs in Lithuania, improved adherence to international recommendations for diagnostics, increased accessibility of diagnostic services, and overall improvements of reproductive healthcare are crucial. To achieve this, we propose that: (i) national inter-laboratory networks be established; (ii) the number of STI diagnostic laboratories be decreased; (iii) the diagnostics of some STIs be centralised to larger laboratories in order to ensure diagnostics in accordance with international recommendations and quality assurance; (iv) internal and external quality control (EQC) systems be introduced; (v) reference centres for STIs other than HIV be established, which will be responsible for recommendations of adequate diagnostic methodologies, coordination of EQC systems, performance of confirmative diagnostics for smaller laboratories, as well as guidance and education regarding STI diagnostics and quality assurance issues; and (vi) patient insurance be introduced, to cover expenses for thorough laboratory-based diagnostics for each STI patient.

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ORIGINAL ARTICLES

Surveillance report

ANTIBIOTIC RESISTANCE IN THE SOUTHEASTERN MEDITERRANEAN – PRELIMINARY RESULTS FROM THE ARMED PROJECT

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Sporadic reports from centres in the south and east of the Mediterranean have suggested that the prevalence of antibiotic resistance in this region appears to be considerable, yet pan-regional studies using comparable methodology have been lacking in the past.

Susceptibility test results from invasive isolates of *Staphylococcus aureus, Streptococcus pneumoniae, Escherichia coli, Enterococcus faecium* and *faecalis* routinely recovered from clinical samples of blood and cerebrospinal fluid within participating laboratories situated in Algeria, Cyprus, Egypt, Jordan, Lebanon, Malta, Morocco, Tunisia and Turkey were collected as part of the ARMed project.

Preliminary data from the first two years of the project showed the prevalence of penicillin non-susceptibility in *S. pneumoniae* to range from 0% (Malta) to 36% (Algeria) [median: 29%] whilst methicillin resistance in *Staphylococcus aureus* varied from 10% in Lebanon to 65% in Jordan [median: 43%]. Significant country specific resistance in *E. coli* was also seen, with 72% of isolates from Egyptian hospitals reported to be resistant to third generation cephalosporins and 40% non-susceptible to fluoroquinolones in Turkey. Vancomycin non-susceptibility was only reported in 0.9% of *E. faecalis* isolates from Turkey and in 3.8% of *E. faecium* isolates from Cyprus.

The preliminary results from the ARMed project appear to support previous sporadic reports suggesting high antibiotic resistance in the Mediterranean region. They suggest that this is particularly the case in the eastern Mediterranean region where resistance in *S. aureus* and *E. coli* seems to be higher than that reported in the other countries of the Mediterranean.

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Key words: antibiotic, resistance, Mediterranean, ARMed, EARSS, MRSA

Introduction

Data from the European Antimicrobial Resistance Surveillance System (EARSS) [www.earss.rivm] indicate that the highest levels of antibiotic resistance have been found within the Mediterranean countries participating in the system. On the other hand, information about the prevalence of antimicrobial resistance in the non-European countries of the southern and eastern Mediterranean has, in the past, been sparse. Nevertheless, high levels of resistance have been reported in *Streptococcus pneumoniae* [1,2], *Staphylococcus aureus* [3] as well as within species of the Enterobacteriacae [4,5]. Unfortunately, besides being few in number, these studies have been totally unrelated, using different methodologies and, as a result, are difficult to compare [6].

This deficiency has been addressed by the Antibiotic Resistance Surveillance & Control in the Mediterranean Region (ARMed) project [www.slh.gov.mt/armed] which began in January 2003,7 and is funded by the European Commission under the INCOMED programme of the DG Research Fifth Framework Protocol (ICA3-CT-2002-10015). Over its four year funding period, this study is documenting the prevalence of antibiotic resistance in southern and eastern Mediterranean countries, as well as attempting to investigate potential factors such as antibiotic consumption and infection control. We report on the midway findings of ARMed-EARSS, the resistance epidemiology subcomponent of the project.

Methodology

ARMed-EARSS collects susceptibility test results from invasive isolates of *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Escherichia coli*, *Enterococcus faecium* and *faecalis* routinely isolated from clinical samples of blood and cerebrospinal fluid in the participating laboratories situated in Algeria, Cyprus, Egypt, Jordan, Lebanon, Malta, Morocco, Tunisia and Turkey. These laboratories are asked to send information only about the first isolate of each organism from each patient. ARMed-EARSS uses almost identical protocols to those adopted and validated by the EARSS project, enabling comparison between data from the two projects. The laboratories follow their routine procedures and breakpoints, which in 86.8% of the participants were based on CLSI (formerly NCCLS) guidelines.

S. aureus testing determines oxacillin susceptibility by an oxacillin screen plate (6 mg/l) or alternatively, by an oxacillin disk test (1 µg or 5 µg) and a cefoxitin disk. ARMed laboratories screen invasive S. pneumoniae isolates for oxacillin resistance which, when found to be non-susceptible, is confirmed and determined to intermediate or high-level resistance to penicillin by determination of minimum inhibitory concentration (MIC) using E-test (AB Biodisk, Solna, Sweden). The protocol for *E. coli* susceptibility testing requires disc diffusion testing, amongst others, of a fluoroquinolone (ciprofloxacin and/or ofloxacin) and a third-generation cephalosporin (cefotaxime or ceftriaxone and/or ceftazidime). E-test confirmation is requested in cases of resistance to third generation cephalosporins in *E. coli* and vancomycin in enterococci. ARMed-EARSS protocols are accessible at the ARMed website (http://www.slh.gov.mt/armed/earss.asp). The website also includes an interactive function where maps for specific drug-bug combinations for any of the participating countries can be generated, as specified by the user.

To assess the reliability and comparability of susceptibility test results, two external quality assurance (EQA) exercises were performed in September 2003 and 2004 by all ARMed participating laboratories. These exercises were performed in collaboration with UK NEQAS (United Kingdom National External Quality Assessment Service) and undertaken concurrently with those run by EARSS for their laboratories.

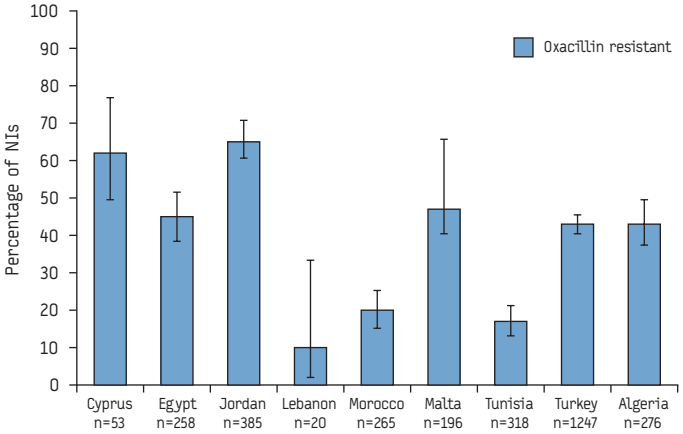
Results

A total of 5883 isolates were investigated, as reported in the first 21 months of the project by the 53 participating ARMed laboratories, which in turn serve 60 hospitals. Of these, 3017 (51.3%) were *S. aureus*, 1567 (26.6%) were *E. coli*, 745 (12.7%) were *S. pneumoniae*, 390 (6.6%) were *E. faecalis*, and 164 (2.8%) were *E. faecium*. Resistance to penicillin in isolates of *S. pneumoniae* was reported from all the collaborating countries except for Malta and Cyprus [FIGURE 1]. When only data from countries reporting at least 10 isolates during the study period were evaluated, the prevalence of penicillin non-susceptibility *S. pneumoniae* ranged from 0% (Malta) to 36% (Algeria) (median: 29% [interquartile range 18% – 33%]). Except for Tunisia, macrolide non-susceptibility in *S. pneumoniae* was generally lower than penicillin non-susceptibility for each country, particularly in Turkey, where the difference was statistically significant (P=0.001).

There was considerably greater variability for resistance within *S. aureus* isolates [FIGURE 2]. Percentages of oxacillin resistance - used as a marker for methicillin resistant *Staphylococcus aureus* (MRSA) - varied from 10% in Lebanon to 65% in Jordan (median: 43% [IQR: 20 – 47%]). The most common resistance pattern showed co-resistance to methicillin, erythromycin and gentamicin. These isolates were particularly evident in Turkey where they accounted for more than a third of all *S. aureus* isolates.

FIGURE 2

Percentage of non-susceptiblity to oxacillin (methicillin) in *Staphylococcus aureus* isolates reported by participating ARMed centres



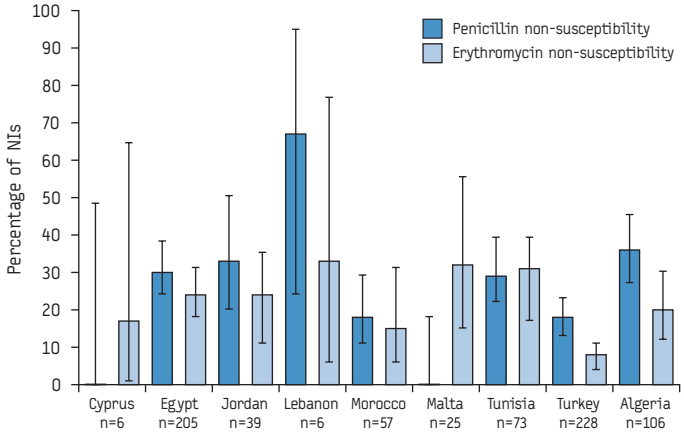
I: 95% confidence interval

Note: ARMed centres are grouped by country and reported number of isolates

Even greater disparity was seen in the resistance patterns for *E. coli*, mainly for fluoroquinolones and third generation cephalosporins [FIGURE 3]. Resistance to third generation cephalosporins varied from 3% in Malta to 72% in Egypt (median 18% [16 – 26%]) and in the fluoroquinolones ranged from 5% in Algeria to 40% in Turkey (median 27% [18 – 33%]). Multiresistant isolates were also particularly evident. In fact, simultaneous resistance to four major antimicrobial classes (aminoglycosides, third generation cephalosporins, aminopenicillins, fluoroquinolones) was the second most common resistance pattern seen and accounted for 13.7% of all isolates reported. Multiresistant *E. coli* isolates were most commonly found in Egypt, comprising more

FIGURE 1

Percentage of non-susceptibility to penicillin and erythromycin in *Streptococcus pneumoniae* isolates reported by participating ARMed centres

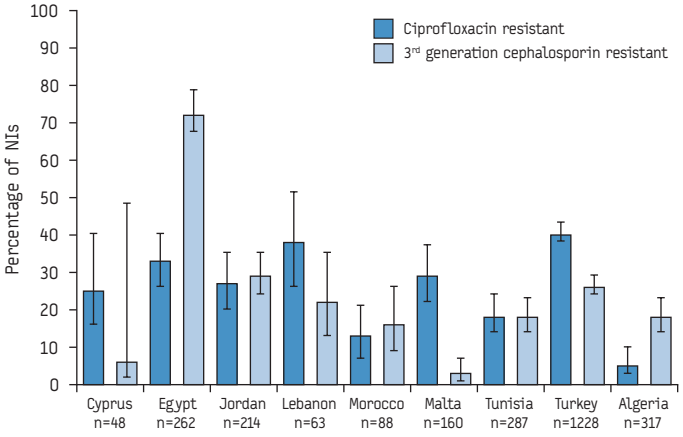


I: 95% confidence interval

Note: ARMed centres are grouped by country and reported number of isolates

FIGURE 3

Percentage of non-susceptibility to fluoroquinolones and third generation cephalosporins in *Escherichia coli* isolates reported by participating ARMed centres



I: 95% confidence interval

Note: ARMed centres are grouped by country and reported number of isolates

than half of all resistant isolates from that country, followed by Turkey and Lebanon where around 30% were similarly multiply resistant to three or more antibiotic groups.

Out of the five countries (Cyprus, Malta, Morocco, Tunisia and Turkey) that provided data on more than 10 isolates of each of the enterococcal species under investigation, only two reported vancomycin non-susceptibility (intermediate or resistant): Turkey, with 0.9% (95% CI 0%–2%) *E. faecalis* and 3.8% (2 – 7 %) *E. faecium*; and Cyprus, with 2% (0%–14%) *E. faecalis*.

Discussion

ARMed results have provided, for the first time, a standardised, comparable snapshot on the prevalence of resistance in important clinically relevant pathogens within hospitals in the southeastern Mediterranean. A median of 43% for methicillin resistance within isolates of *S. aureus* confirms that the Mediterranean region indeed constitutes a high prevalence region for MRSA. It also correlates well with previous sporadic reports from individual countries within the region [8-10]. It appears that MRSA seems to be more widespread in the eastern Mediterranean than in the south. Overall data from the hospitals in Cyprus, Egypt, Jordan and Turkey all showed MRSA proportions in excess of 40%. Results from the EARSS network, using the same methodology, have reported MRSA proportions in excess of 30% from Croatia, France, Greece, Israel and Portugal [11,12]. This would therefore indicate that the whole of the Mediterranean region is a high prevalence region for MRSA.

On the other hand, resistance within *E. coli* to third generation cephalosporins, and by association possibly extended-spectrum beta-lactamase (ESBL) and/or Amp-C enzyme production, appears to be more significant to those previously reported in the region. This seems especially the case in the eastern Mediterranean where the centres in Turkey, Lebanon, Jordan and Egypt reported average proportions in excess of 20%. The figure of 72% resistance to third generation cephalosporins reported from Egypt is one of the highest figures recorded for this resistance trait. Nevertheless indications of high level resistance within Gram negative pathogens in this region are not new. Bouchillon and colleagues, studying isolates from 38 centres in 17 countries, reported the incidence of ESBL production in Enterobacteriacae to be at its highest in their Egyptian centres at 38.5% [13]. El Kholy et al noted that 62% of *E. coli* isolated from blood cultures in three Cairo hospitals were non-susceptible to ceftazidime [14]. The ARMed results seem to confirm these previous reports and indicate that the situation may be even more acute and widespread throughout the Mediterranean region than previously indicated. In addition the presence of co-resistance to other antibiotic groups further compounds the challenge posed by such pathogens.

In contrast, the proportions of penicillin non-susceptibility in *Streptococcus pneumoniae* (PNSP) isolates from the ARMed laboratories are broadly in line with those already reported in centres within other Mediterranean and Middle Eastern countries [15,16]. PNSP levels seem to be uniform throughout the region and the apparent differences seen between eastern and southern Mediterranean centres in *S. aureus* and *E. coli* were not found in pneumococci. It is also interesting to note that, contrary to reports from the European countries of the region where macrolide resistance in pneumococci often exceeds that of penicillin [15, 16], erythromycin non-susceptibility appears to be less prevalent in the southeastern Mediterranean countries. Finally, the presence of vancomycin resistance in enterococci from ARMed laboratories in Turkey supports previous reports from this country [17].

The use of routinely collected clinical laboratory data provides the advantage that epidemiological conclusions mirror the day-to-day situation in the participating institutions. Furthermore, the choice of blood culture isolates minimises sample bias and reflects the clinical situation in the more severe infections. Unlike patients with less critical infections, such as those of the respiratory and urinary tract, most patients with signs of sepsis or meningitis will probably have a microbiological sample taken. In addition, the major strength of the ARMed study resides in the common methodology used throughout the different centres in the nine participating countries. Any such study has the limitation of depending on the accuracy and validity of the individual participating laboratories, which can vary, especially in limited resource countries. It is also hampered by the inability to perform third party reference laboratory verification and do more detailed investigation in results of particular significance. Nevertheless, the concurrent satisfactory quality assurance results would suggest that this potential limitation did not prejudice the conclusions reached from the preliminary data collected by ARMed-EARSS to any significant degree [18].

In addition to the direct repercussions for the countries of the Mediterranean region [19], the epidemiology of resistance in the southern and eastern Mediterranean also has European implications. Human mobility in this region is highly significant, in terms of both recognised travel (particularly tourism) and the results of migration. The importation of multiresistant organisms to European hospitals via patients arriving from countries within the Mediterranean region is well documented [20,21]. Such an occurrence may result in the possibility of subsequent intra-institutional spread with the potential for an outbreak [22,23]. Prior knowledge of the epidemiology of resistance in the Mediterranean region will therefore facilitate the introduction of effective interventions on initial contact with patients originating from this region and who may be potentially colonised or infected with multiresistant organisms. It should also prove beneficial for stakeholders in the countries involved to plan and implement correct antibiotic stewardship programmes to attempt control and possibly reduction of the incidence of antimicrobial resistance in pathogens of critical importance [24].

Conclusion

The preliminary results from the ARMed project have started to shed new light on the incidence of antimicrobial resistance in the south and east of the Mediterranean. They appear to support and accentuate previous sporadic reports suggesting a high prevalence in this region and indicate that this is particularly the case in the eastern region where multiresistance in *S. aureus* and *E. coli* seem to be especially high, and higher than that reported in the other countries of the Mediterranean. This picture will become clearer once the full duration of the study is completed and a more comprehensive isolate database is established.

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ORIGINAL ARTICLES

Surveillance report

HEALTHCARE ASSOCIATED INFECTIONS IN UNIVERSITY HOSPITALS IN LATVIA, LITHUANIA AND SWEDEN: A SIMPLE PROTOCOL FOR QUALITY ASSESSMENT

J Struwe[1,2], U Dumpis[3], J Gulbinovic[4], Å Lagergren[1,2], U Bergman[5]

Surveillance of healthcare associated infections is an overlooked parameter of good clinical practice in most healthcare institutions, due to the workload demanded in the absence of adequate IT-systems. The aim of the present study was to investigate whether a simple protocol could be used to estimate the burden of healthcare associated infections in three university hospitals in Huddinge in Sweden, Riga in Latvia and Vilnius in Lithuania and form the basis for initiating a long term follow up system.

The medical records of all patients receiving antibiotics were reviewed according to a standardised protocol, focusing on the indications for the drugs and on the frequency of hospital acquired infection (HAI) in a point-prevalence survey. Only comparable specialities were included.

The proportion of patients treated with antibiotics (prophylaxis not included) were 63/280 (22%) in Huddinge, 73/649 (11%) in Riga and 99/682 (15%) in Vilnius. The proportion of admitted patients treated for a HAI were 15%, 3% and 4%, respectively, (both comparisons Huddinge versus other centres P<0.001). Surgical site infections were most common, followed by infections with an onset more than 2 days after admission without any of the other registered risk factors present. Our inexpensive and simple method showed that healthcare associated infections were a significant problem among patients admitted to Huddinge. The figures obtained can be used for further discussion and form a baseline for follow up at the local level. The comparison of figures between centres was far less relevant than the process the study created.

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Key words: Healthcare associated infection, hospital acquired infection, antibiotics, quality assessment

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Introduction

Despite its relevance, the surveillance of healthcare associated infections is overlooked as a parameter of good clinical practice in most healthcare institutions. Apart from purely scientific projects, most of which have time limits, most registration initiatives are hampered by the workload for data collection, administration, feedback and long term sustainability. When long term registration is started, it often relies on a few devoted enthusiasts, rather than a broad acceptance among clinicians. Some of the major obstacles are that the purpose and ambition is ill-defined, protocols and criteria are too extensive and, when computer-based medical records exist, integration with microbiological results is poor.

In order to estimate the burden of healthcare associated infections in Karolinska University Hospital, Huddinge, Sweden (Huddinge), and to initiate a system for follow up over the years, we recently made a survey using a rather simple protocol based on patients receiving antibiotic treatment [1]. The specific aims of the present study were to see whether our protocol was useful for the assessment of the

prevalence of antibiotic use and healthcare associated infections in university hospitals in adjacent countries, i.e. Stradins University Hospital in Riga, Latvia (Riga) , and Vilnius University Hospital in Lithuania (Vilnius). Furthermore we wanted to address some of the questions that had arisen from a previous study in Huddinge and Vilnius where we made the somewhat surprising finding that antibiotic resistance was higher in Vilnius despite higher antibiotic pressure in Huddinge [2]. That study raised the question that perhaps differences in duration of hospital stay, healthcare associated infection rates and infection control practices (in particular access to alcohol-based hand-disinfectants) and use of antibiotics outside the hospital could explain this unexpected finding.

Material

Huddinge, Riga and Vilnius all are tertiary care university hospitals with about 1000 beds each.

The infection control team in Huddinge consisted of one doctor specialising in clinical bacteriology, two infection control nurses and a hospital epidemiology team of one doctor (infectious disease specialist) one nurse and one molecular epidemiologist. There was an infection control committee, led by the chief medical officer, with about 15 representatives from major clinics, operation theatres, sterilisation unit and building and construction that meets twice yearly. The infection control team in Riga consists of one infectious disease consultant, one half time hospital epidemiologist and one nurse assistant. Clinical microbiology is not recognised as a speciality in Latvia and its responsibilities are divided between the microbiologists and the infectious disease consultant. Vilnius university hospital has an infection control department divided between the sections for disinfection, sterilisation and epidemiology. The epidemiology section is responsible for infection control, and has three epidemiologists and three nurses.

While therapeutic antibiotics can be given on clinical grounds by any doctor in all three hospitals, some substances are restricted to specialist use in Riga and Vilnius. Consultants in infectious disease are available in Huddinge and Riga. Huddinge has had a dedicated infection control programme since the year 2000 (including rational use of antibiotics), guidelines for rational antibiotic use were recently distributed in Vilnius, while no specific activities, other than occasional lectures, existed in Riga at the time of this survey.

Methods

A point-prevalence study was carried out so that every ward was visited once during May 2002. In order to avoid interference from public holidays, data were collected on Tuesdays, Wednesdays and Thursdays. All patients receiving antibiotics were identified. The authors reviewed the medical records according to the same protocol. If a patient was surveyed twice due to transfer between clinics (which was rare), only the first treatment episode was registered. Only infections treated with antibiotics were counted. The accuracy of the diagnosis made by the treating physician was not evaluated.

Based on the definition used by the Swedish National Board of Health and Welfare that a healthcare associated infection is 'any infection resulting from any treatment or investigation associated with health care, regardless of whether the causing agent originates from the patient or the hospital environment' [3], the following definitions for healthcare associated infections were used in this study:

- Surgical site infections (SSI): Infection in a surgical site within 30 days of surgery (within one year after implant surgery).
- device-related infections: infections associated with intravascular or urinary catheters or any other foreign material
- antibiotic associated diarrhoea (AAD): diarrhoea starting after admission, and after beginning treatment with antibiotics, with or without a positive test for *Clostridium difficile*
- neutropenic fever/ septicaemia associated with immune suppressive therapy in a patient with a neutrophil granulocyte count of less than 0.5 x 109/l.
- infections with onset more than 2 days after admission due to a non-infectious cause.

Access to hand disinfectants was calculated as the number of dispensers in patient rooms (or by the entrance of the room) divided by the number of patient beds.

Since no patient identification was collected and the surveillance was part of the quality assurance, approval of ethics committees was not considered necessary.

Results

During the year of the study (January-December 2002), the total number of admitted patients and bed-days were 46 063 and 220 453 in Huddinge, 35 421 and 293 375 in Riga, and 28 737 and 295 990 in Vilnius, respectively. This corresponds to an average hospital stay of 4.8, 8.3 and 10.3 days per patient, respectively

Table 1 show the number and proportions of patients treated with antibiotics for community acquired (CI) and healthcare associated infections (nosocomial infections, NI) in the hospitals. The comparable clinics accounted for 280/679 (41%) of all patients admitted at the time for the survey at Huddinge, 649/938 (69%) in Riga and 682/850 (80%) in Vilnius. The mean age of patients treated with antibiotics in the comparable departments was 61 years (range 0-82) in Huddinge, 56 years (range 0-99) in Riga and 53 years (range 0-88) in Vilnius. The mean duration of stay in the hospital before survey was 10 days (range 1-57) in Huddinge, 9 days (range 1 - 76) in Riga and 13 days (range 1-86) in Vilnius.

The proportion of patients treated with antibiotics in comparable departments was significantly higher in Huddinge, 63/280 (22%), compared to 73/649 (11%) in Riga and 99/682 (15%) in Vilnius, $P<0.001$, respectively. The rate of NIs was also significantly higher in the departments investigated at Huddinge (42/280, 15%) than in Riga (22/649, 3%) and in Vilnius (27/682, 4%), $P<0.001$, respectively. There was no significant difference between Riga and Vilnius with regard to proportions of treated patients and patients with NIs. Intensive care units and transplantation clinics had the highest rates of NIs in all hospitals. In Huddinge and Riga, nephrology also had comparatively high rates (40% and 24% respectively), whereas thoracic surgery had the highest rate in Vilnius (10%).

Surgical site infections were the quantitatively most important NI in all hospitals, and in Vilnius accounted for over 70% of all NIs [FIGURE]. New symptoms of infection appearing more than two days after admission without any other obvious reason was another common type of NI at Huddinge and Riga.

The prevalence of dispensers for alcohol-based hand disinfection in comparable departments was highest in Huddinge, 263/325 beds (81%) compared to 27/769 (4%) in Riga and 161/754 (21%) in Vilnius [TABLE 2].

Discussion

One of our aims in this first international survey of healthcare associated infections in Latvia, Lithuania and Sweden was to test a simple tool for quality assessment, which does not request major human and financial resources. All participants agreed that the protocol was useful even if the obtained figures should be interpreted carefully. In a comparative study between the Netherlands and Belgium, one of the major conclusions was that even though comparison of crude infection rates did not seem meaningful due to differences in the case mix, patient turnover and post-discharge surveillance, international comparisons yield 'interesting insights regarding quality of care' [4]. We agree with this and think that although it was useful to compare experiences during the process, and valuable discussions were held while interpreting the results, the figures we obtained are mainly useful for comparison and analysis at the local level.

Our present finding of prevalence's of healthcare associated infections of 15% among the included clinics in Huddinge, 3% in Riga and 4% in Vilnius, shows that antibiotic treatment of healthcare associated complications was a significant problem, at least in Huddinge. The figures from this study confirm the magnitude of the problem from previous surveys when the same protocol was used in Huddinge one year earlier. At that time 11% of the inpatients were

Table 1

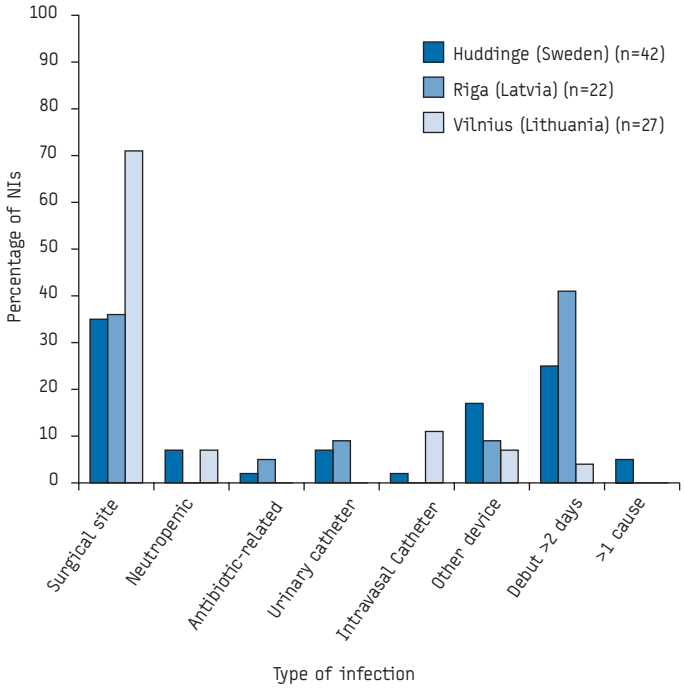
Proportion of patients treated with antibiotics for a nosocomial infection (NI) in three university hospitals in Sweden, Latvia, and Lithuania

	Huddinge (Sweden)				Riga (Latvia)				Vilnius (Lithuania)			
Comparable departments	NI	(%)	treated/ admitted	(%)	NI	(%)	treated/ admitted	(%)	NI	(%)	treated/ admitted	(%)
Abdominal surgery	1	(3)	5/40	(13)	3	(4)	7/72	(10)	3	(4)	9/75	(12)
Cardiology	2	(6)	3/36	(8)	1	(1)	7/166	(4)	0	(0)	2/120	(2)
Gastroenterology	5	(33)	6/15	(40)	0	(0)	3/48	(6)	0	(0)	3/45	(7)
Gynaecology	1	(13)	1/8	(13)	1	(3)	2/29	(7)	0	(0)	0/17	(0)
Intensive care unit												
-General	4	(50)	6/8	(75)	3	(38)	4/8	(50)	3	(33)	6/9	(67)
-Thoracic	2	(50)	2/4	(50)	0	(0)	0/6	(0)	2	(10)	2/20	(10)
Nephrology	8	(40)	10/20	(50)	5	(24)	5/21	(24)	0	(0)	3/37	(8)
Neurology	2	(4)	5/45	(11)	0	(0)	0/41	(0)	0	(0)	3/51	(6)
Otolaryngology	1	(7)	3/14	(21)	0	(0)	5/24	(21)	1	(2)	14/49	(29)
Pulmonology	2	(18)	4/11	(36)	1	(2)	17/57	(30)	0	(0)	22/48	(46)
Rehabilitation	0	(0)	0/15	(0)	0	(0)	1/46	(2)	1	(7)	2/15	(13)
Thoracic/cardiac surgery	2	(14)	2/14	(14)	5	(6)	8/87	(9)	12	(10)	18/126	(14)
Transplantation	10	(32)	10/31	(32)	3	(18)	3/17	(18)	3	(20)	3/15	(20)
Urology	2	(11)	5/19	(26)	0	(0)	11/27	(41)	2	(4)	12/55	(22)
Subtotal comparable departments	42	(15)	63/280	(22)	22	(3)	73/649	(11)	27	(4)	99/682	(15)
Subtotal of all other departments	49	(12)	122/399	(30)	14	(5)	31/289	(11)	3	(2)	6/168	(4)
Total entire hospitals	**91**	**(13)**	**185/679**	**(27)**	**36**	**(4)**	**104/938**	**(11)**	**30**	**(4)**	**105/850**	**(12)**

being treated with antibiotics for a healthcare associated infection [1]. In 2001, using British National Prevalence Survey definitions, 4.1% of inpatients in Riga were found to have a healthcare associated infection [5,6]. The rate of healthcare associated infections, which we found in Lithuania, was lower than the 9.2% previously reported from other Lithuanian university hospitals using the above mentioned British criteria [5,7]. In studies from the other Nordic countries, a nationwide Norwegian survey in mixed types of hospitals showed a prevalence of 6.1% [8]. In iterated surveys of Norwegian university hospitals the rate has been 6-9.1% [9,10] while prevalence's of 10.4 % and 12.1% were found in Danish surveys of a mix of hospitals and clinics [11]. In surveys of university hospitals in other European countries, where somewhat different criteria and methods have been used, prevalence rates ranging from 4.3% to 13.5 % have been reported [12-16]. Though these figures cannot be adequately compared due to variation in criteria and case mix between the studies, they still illustrate that the numbers obtained with our protocol seemed to be in a reasonable order of magnitude. We, like others [17], do not think that extension of a survey beyond one day significantly affected our data quality.

Figure

Relative occurence of different nosocomial infections (NIs) in comparable departments in three university hospitals in Sweden, Latvia, and Lithuania



Contrary to expectations, we found that the prevalence of healthcare associated infections was higher in Huddinge than in Riga and Vilnius, despite Huddinge's better facilities and infection control resources. The climate in all three countries is quite similar. There were no registered epidemics at the time of the survey. There was no major difference in demographic characteristics of patients. All three hospitals are referral centres for complicated cases. Furthermore, the survey was performed by a small number of experienced investigators at the same time of the year (May). Thus, we do not believe that any of these factors were related to the differences. Although our attempt to record risk factors as indicators of the severity of the patients' illnesses failed, our impression was that the shorter mean admission time at Huddinge meant that the patients were more severely ill when discharged, while comparatively healthier patients were admitted to hospital more easily in Riga and in Vilnius. Furthermore, while high levels of C-reactive protein (CRP) per se, without focal symptoms or clinical findings, was probably too frequent an indication for treatment with antibiotics in Huddinge, the limited use of CRP in Riga and Vilnius might, rightly or wrongly, spare some patients from antibiotic treatment. Testing a scoring system for rational antibiotic prescribing might be a useful quality indicator for future studies [16]. Absence of restrictions may further have contributed to a more liberal use of antibiotics at Huddinge.

Based on our previous finding that antibiotic resistance was higher in Vilnius despite lower antibiotic pressure [2], we thought that inferior hygienic routines and lower compliance for hand disinfection might be an explanation. In this study, however, the rate of healthcare associated infections was higher in Huddinge despite easier access to hand disinfectants, a factor that has been proven to reduce the rate of NIs [18]. However, due to the lack of hand washing basins, staff in Riga and Vilnius is instead encouraged to use pocket containers of alcohol containing solutions. As such containers were not registered in the survey, the difference in availability may actually not be as big as it seems. One way to assess the relative importance of insufficient hygiene practices would be to detect clonal spread by epidemiological typing of prospectively collected bacterial isolates.

Table 2

Number of available beds in comparable and non-comparable clinics, and percentage of beds with dispenser for alcohol based hand disinfectants in university hospitals in Sweden, Latvia, and Lithuania

	Huddinge (Sweden)		Riga (Latvia)		Vilnius (Lithuania)	
	Hand disinfection/ available beds	(%)	Hand disinfection/ available beds	(%)	Hand disinfection/ available beds	(%)
Comparable departments						
Abdominal surgery	38/38	(100)	0/101	(0)	26/90	(29)
Cardiology	39/47	(83)	13/195	(7)	8/117	(7)
Gastroenterology	9/47	(50)	0/50	(0)	4/50	(8)
Gynaecology	15/15	(100)	0/39	(0)	1/28	(4)
Intensive care unit						
-General	8/8	(100)	4/10	(40)	5/12	(42)
-Thoracic	4/4	(100)	3/9	(33)	15/20	(75)
Nephrology	20/20	(100)	1/26	(4)	1/40	(3)
Neurology	35/54	(65)	0/48	(0)	2/64	(3)
Otolaryngology	10/26	(38)	0/35	(0)	9/45	(20)
Pulmonology	12/14	(86)	0/65	(0)	4/55	(7)
Rehabilitation	8/16	(50)	0/45	(0)	2/18	(11)
Thoracic/cardiac surgery	17/17	(100)	1/96	(1)	62/143	(43)
Transplantation	26/26	(100)	5/20	(25)	12/22	(55)
Urology	22/22	(100)	0/30	(0)	10/50	(20)
Subtotal comparable departments	263/325	(81)	27/769	(4)	161/754	(21)
Subtotal of all other departments	326/441	(74)	11/301	(4)	18/172	(10)
Total entire hospitals	**589/766**	**(77)**	**38/1070**	**(4)**	**179/926**	**(19)**

We believe that restricting surveillance to patients receiving antibiotic treatment is justified if one is satisfied with detecting the most significant bacterial infections, rather than aiming to pinpoint the true prevalence of all healthcare associated infections. Although others have pointed out that as many as 6% of infections are missed [19], we believe that the advantages out rule the disadvantages when resources are limited. The patients are easy to identify (even if there are a few cases with poor documentation, leading to difficulties in distinguishing treatment from prolonged prophylaxis), the workload is smaller, since, in our experience, only 10%-40% of all admitted patients need to be surveyed. Furthermore, the need for training of those who register is less extensive. Our model, in which representatives from the infection control team and consultants in infectious disease performed the survey, created an additional opportunity to pick up questions related to antibiotic treatment or infection control when making rounds of the wards, a measure which has been proven to contribute to lower infection rates [20]. Important limitations were that neither untreated infections nor healthcare associated infections treated with antiviral or antifungal therapy were included. This risk for underestimating the true prevalence might be overestimated by the fact that we did not evaluate the accuracy of the indications for antibiotic treatment, which were probably too broad. Finally, our inclusion of all neutropenic fevers regardless of duration of hospital stay, culture findings and port of entry, led to a higher number of healthcare associated cases than would have been included by criteria used in other studies.

We conclude that our methodology with a simple protocol for point-prevalence surveys of antibiotic treatment and healthcare associated infections was applicable in three countries with differing economic circumstances. We think that direct comparisons of infection rates between countries should be interpreted with caution, because of the different organisation of hospital healthcare systems, but that such comparisons can nevertheless give rise to valuable discussions and contribute to identifying problematic areas in different countries. Our simple approach makes repeated studies easy to perform with limited economic and human resources. Such repeated procedures could be used for internal quality assurance in the long term.

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A copy of the protocol can be obtained from the authors on request.

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ORIGINAL ARTICLES

Euroroundup

PNEUMOCOCCAL DISEASE SURVEILLANCE IN EUROPE

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Pneumococcal disease (Pnc) is responsible for invasive pneumococcal disease (IPD) – mainly meningitis and septicaemia - and is an infection of public health importance in Europe. Following the licensure of an effective conjugate vaccine (PCV) in Europe, several European countries, including France, Germany, the Netherlands, Norway, Spain and the United Kingdom, are introducing universal Pnc childhood immunisation programmes. As part of a European Union (EU) funded project on pneumococcal disease (Pnc-EURO), a questionnaire was distributed in late 2003 to each of the current 25 European Union member states as well as Norway and Switzerland to get a clearer picture of national surveillance for invasive pneumococcal disease (IPD) in Europe. All respondents were contacted in 2006 and asked to provide an update to the questionnaire.

Twenty two of the 27 countries targeted completed and returned the questionnaire. Four of the 22 responding countries have no reporting requirement for IPD. Eighteen countries reported a total of 27 national surveillance systems. Case definitions employed in these systems differed. Fourteen of the 18 countries reported collection of IPD strains to a single reference lab for serotyping and in 12 countries to a single laboratory for susceptibility testing. Thirteen countries undertook laboratory quality assurance. Information on age and sex were widely collected, but only 11/27 systems collected information on pneumococcal polysaccharide vaccine status, while 5/27 systems collected information on pneumococcal conjugate vaccine status. The incidence of IPD reported in each of the 18 countries ranged from 0.4 to 20/100 000 in the general population, with a total of 23 470 IPD cases reported over a 12 month period. Surveillance for IPD in Europe is very heterogeneous. Several countries lack surveillance systems. Large differences in reported disease incidence may reflect both true differences, and also variations in patient and healthcare factors, including surveillance. If IPD surveillance in Europe can be strengthened, countries will be able to make informed decisions regarding the introduction of new pneumococcal vaccines and also to monitor and compare the impact and effectiveness of new programmes.

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Introduction

Pneumococcal disease (Pnc) has been highlighted as an infection of public health importance in Europe [1]. It has a wide range of clinical manifestations, particularly in young children and older persons. These range from less frequent invasive disease (IPD), presenting mainly as meningitis and septicaemia, to more common but generally non-invasive conditions such as pneumonia, sinusitis and otitis media. Increasing antimicrobial resistance, particularly to penicillin and erythromycin, has occurred in certain parts of Europe [2]. However, the true burden due to pneumococcal disease in Europe is uncertain. Differences in the incidence of IPD have been well-documented, and explained (at least partly) by patient and healthcare factors such as blood culture practice and pre-admission antibiotic administration [3].

A 23-valent Pnc polysaccharide vaccine (PPV) was licensed in Europe during the 1980s and targeted at groups at higher risk of invasive pneumococcal disease. In recent years, many European countries have introduced PPV into national immunisation schedules for all elderly people [4]. A new 7-valent Pnc conjugate vaccine (PCV) has been recommended in the United States national immunisation programme for all children since 2000, where reductions in IPD due to vaccine serotypes in both vaccinated and - indicative of a herd immunity effect - in older, unvaccinated cohorts have been observed [5,6]. In the US, there is now increasing evidence of the emergence of non-vaccine serotypes ('serotype replacement') for both invasive and non-invasive disease [6,7,8]. In 2001, PCV was licensed in Europe [9]. At first, a number of European countries introduced PCV for children at higher risk of Pnc disease [4]. More recently, several countries in Europe, including Norway [10], France [11], Germany [12], the Netherlands [13], Spain and the UK [14], have introduced or are planning to introduce PCV into their routine childhood immunisation programmes. Programmes vary both in the number of doses recommended in the primary course (two doses in UK and Norway versus three in France, Germany and the Netherlands), the age of administration (3 and 5 months in Norway and 2, 3 and 4 months in France, Germany and the Netherlands), the use of a catch up campaign (e.g. UK) and co-administration with other vaccines.

One of the main objectives of the EU funded project, Pneumococcal Disease in Europe (Pnc-Euro) was to establish the epidemiology of *Streptococcus pneumoniae* in a variety of European countries prior to

the large-scale introduction of new pneumococcal conjugate vaccines, and to implement an inventory of existing pneumococcal surveillance programmes. This paper summarises the findings of a questionnaire survey of Pnc surveillance practice in the EU.

Methods

A standardised questionnaire was designed and sent in late 2003 to the national public health institutes of each of the current 25 European Union member states, and to Norway and Switzerland. Ten of the EU countries were in the accession phase at this time. The countries included in the survey (including initial non-responders) were approached again early in 2006, with a request for an update on any changes in pneumococcal surveillance since the original questionnaire. Data from the returned questionnaires were entered into a database using EpiData software and analysed using Epi Info 6.

Results

Twenty two of the 27 countries included in the survey completed and returned the questionnaire (response rate 81%). The non-responders were Austria, Greece, Hungary, Portugal and Spain.

Four (Cyprus, Estonia, Latvia and Luxembourg) of the 22 responding countries stated there was no specific reporting requirement for pneumococcal disease within their national communicable disease surveillance system. The remaining 17 countries reported 26 routine Pnc surveillance systems, and Germany reported a system initially established as a research programme [TABLE 1]. Four of these 18 countries (Czech Republic, Denmark, Ireland and Poland) reported two surveillance systems for pneumococcal disease and two countries (France and Belgium) reported three. The earliest of these systems were established in the 1930s, although the majority began during the 1990s. One of the Belgian surveillance systems (Pedisurv) was only established in 2005.

System objectives

Only one the 27 reported Pnc surveillance systems had no specific objective [TABLE 1]. The main system objectives mentioned were to monitor IPD incidence/trends (n=20), to monitor antimicrobial susceptibility (AMR, n=15), to monitor the impact of interventions (n=15), to monitor circulating serotypes (n=12), to detect outbreaks/clusters (n=4), to monitor Pnc meningitis incidence (n=2) and to identify risk factors (n=1).

TABLE 1

Pneumococcal disease surveillance systems in the European Union and the stated system objectives (23 countries), 2006[1]

Country	Surveillance system	Name of Pnc surveillance system	Year started	Monitor incidence	Monitor AMR	Monitor impact	Monitor serotypes	Detect outbreaks
Belgium	Yes	ID sentinel laboratory system	1986	Y		Y		Y
		Pedisurv	2005	Y		Y	Y	
		National Pnc reference laboratory	1980	Y	Y	Y	Y	
Cyprus	No	-	-	-	-	-	-	-
Czech Republic	Yes	EPIDAT	1994	Y				
		National Streptococci Reference Lab	1997		Y		Y	
Denmark	Yes	National notification system	1980	Y		Y		Y
		National laboratory surveillance	1938	Y	Y	Y	Y	
England & Wales	Yes	National enhanced surveillance	1996	Y	Y	Y	Y	
Estonia	No	-	-	-	-	-	-	-
Finland	Yes	National ID register	1995	Y	Y		Y	
France	Yes	EPIBAC	1995	Y		Y		
		CNRP-ORP	2001		Y	Y	Y	
		GPIP-ACTIV (meningitis)	2001		Y	Y		
Germany	Yes	ESPED	1997	Y	Y		Y	
Ireland	Yes	EARSS-Ireland	1999		Y			
		Pnc meningitis system	1999	Y		Y		Y
Italy	Yes	Bacterial meningitis surveillance	1994	Y				
Latvia	No	-	-	-	-	-	-	-
Lithuania	Yes	Pnc meningitis surveillance						
Luxembourg	No	-	-	-	-	-	-	-
Malta	Yes	EARSS-Malta	2000		Y			
Netherlands	Yes	NRBM	1975	Y	Y	N#	N#	
Norway	Yes	MSIS	1977	Y	Y	Y	Y	Y
Poland	Yes	National ID surveillance	1970	Y				
		NRCBM	1997	Y	Y	Y	Y	
Scotland	Yes	SPIDER	1999	Y	Y	Y	Y	
Slovak Republic	Yes	EPIS	1960	Y		Y		
Slovenia	Yes	Epidemiology invasive disease	1993			Y		
Sweden	Yes	Laboratory reporting system	1990	Y				
Switzerland	Yes	National surveillance of IPD	1999	Y	Y		Y	

Y: Yes N: No

From 2006, will include these objectives when Pnc conjugate vaccine (PCV) is introduced

1. In the table, Scotland and England and Wales were counted separatly. In the text, both countries are grouped under UK

Table 2

Pneumococcal disease surveillance systems in the European Union and case definitions used (19 countries), 2006[1]

Country / Name of surveillance system	Surveillance of *S. pneumoniae*	Statutory system	Clinical syndrome surveillance	Clinical surveillance		Case definition	Case definition			
				Meningitis	Sepsis		Isolation from CSF	Isolation from blood	Non-culture methods	Time interval between cases
Belgium										
ID sentinel laboratory system	Y	N	N	N	N	Y	Y	Y	Y	10 weeks
Pedisurv	Y	N	N	N	N	Y	Y	Y	Y	
National Pnc reference laboratory	Y	N	N	N	N	Y	Y	Y		
Czech Republic										
EPIDAT	Y	Y	Y	Y	N	Y	Y	Y	Y	
National Streptococci Reference Lab	Y	N	Y	Y	Y	Y	Y	Y	Y	
Denmark										
National notification system	N	Y	Y	Y	N	Y	Y	N		
National laboratory surveillance	Y	N	N	N	N	Y	Y	Y		30 days
England & Wales	Y	N	Y	Y	Y	Y	Y	Y		
Finland	Y	Y	N	N	N	Y	Y	Y		3 months
France										
EPIBAC	Y	N	N	N	N	Y	Y	Y		
CNRP-ORP	Y	N	N	N	N	Y	Y	Y	N	
GPIP-ACTIV (meningitis)	N	N	Y	Y	N	Y	Y	Y	Y	
Germany	Y	N	N	N	N	Y	Y	Y	N	1 week
Ireland										
EARSS-Ireland	Y	N	N	N	N	Y	Y	Y		
Pnc meningitis system	N	N#	Y	Y	N	N##	N##	N##		
Italy	Y	N	Y	Y	N	Y	Y	N	Y	
Lithuania	N#	N#	Y	Y	N	Y	Y	Y		
Malta	Y	N	N	N	N	Y	Y	Y		3 months
Netherlands	Y	N	N	N	N	Y	Y	Y		
Norway	Y	Y	N	N	N	Y	Y	Y	Y	
Poland										
National ID surveillance	N	Y	Y	Y	Y	Y	Y	Y		
NRCBM	Y	Y	Y	Y	Y	Y	Y	Y	Y	
Scotland	Y	N	N	N	N	Y	Y	Y		2 weeks
Slovak Republic	N	Y	Y	Y	Y	Y	Y	Y		
Slovenia	Y	Y	Y	Y	Y	Y	Y	Y		
Sweden	Y	N#	N	N	N	Y	Y	Y		
Switzerland	Y	Y	N	N	N	Y	Y	Y	Y	

Y: Yes N: No

Since 2004, invasive pneumococcal disease (IPD) became mandatory notifiable ## Case definition implemented in 2004

1. In the table, Scotland and England and Wales were counted separatly. In the text, both countries are grouped under UK

Reporting systems

In 2003, nine of the 27 Pnc surveillance systems were statutory and 18 were non-statutory [TABLE 2]. By 2006, IPD notification had become mandatory in Ireland, Lithuania and Sweden.

In 21 of the 27 systems, surveillance was specifically for the pathogen *S. pneumoniae*. In 12 systems, surveillance for a clinical syndrome was undertaken. For these 12 systems, the clinical syndromes under surveillance were meningitis (n=12), sepsis (n=6) and other (n=1).

Case definitions

Twenty six of the 27 systems had reporting case definitions in 2003 [TABLE 2]. Ireland introduced a case definition in 2004. In general, the case definition included isolation of Pnc from CSF (n=26) and blood (n=24). Besides bacterial culture, at least nine countries included PCR as a method of laboratory confirmation in the case definition.

In those systems specifying a time interval between illness episodes to define a new case in the same individual, duration ranged from seven days to three months.

Target population

The target population under surveillance was all age groups for 24 of the 27 surveillance systems. The German ESPED, Belgium Pedisurv and French GPIP-ACTIV systems focused on children under 16, 15 and 18 years of age respectively. No country reported a specific Pnc surveillance system focused on a certain risk group (e.g. the military).

Twenty three of the Pnc surveillance systems were reported to be national, population based reporting systems and four were sentinel (three in France and one in Belgium). The latter were reported to have coverage of 73% for EPIBAC in France, 63% for CNRP-ORP in France, 70% for GPIP-ACTIV in France and 79% in Belgium for ID sentinel laboratory system.

Twenty of the Pnc surveillance systems were based on laboratory notifications and twelve on clinician notifications [TABLE 3]. Five countries (Belgium, Germany, Norway, Poland (NRCBM) and Switzerland) used both reporting sources, and in other countries, physicians were responsible for reporting laboratory confirmed cases to the national surveillance system.

Laboratory surveillance

Pnc findings reported by the laboratory were from CSF (n=21), blood (n=20) and other sites (n=16) [TABLE 3]. Other sites included any other normally sterile site (n=10 countries., Other sites specifically mentioned included (with some countries mentioning more than one

TABLE 3

Pneumococcal disease surveillance in the European Union and laboratory surveillance (27 surveillance systems), 2006

Country / Name of surveillance system	Notification by clinicians	Notification by laboratory	Laboratory notifications			Central reference laboratory	% samples serotyped	Collect information on AMR	% samples with susceptibility
			CSF	Blood	Other sites				
Belgium									
ID sentinel laboratory system	N	Y	Y	Y	Y	Y	NA	Y	99
Pedisurv	Y	Y	Y	Y	Y	Y	72	Y	72
National Pnc reference laboratory	N	Y	Y	Y	Y	Y	100	Y	100
Czech Republic									
EPIDAT	N	Y	Y	N	N	Y			
National Streptococci Reference Lab	N	Y	Y	Y	Y	Y	100	Y	100
Denmark									
National notification system	Y	N				Y	100	N	
National laboratory surveillance	N	Y	Y	Y	Y	Y	100	Y	100
England & Wales	N	Y	Y	Y	Y	Y	66	Y	70
Finland	N	Y	Y	Y	N	Y	90	Y	90
France									
EPIBAC	N	Y	Y	Y	N	Y	NA	N	
CNRP-ORP	N	Y	Y	Y	Y	Y	100 (≤15) 20 (>15)	Y	100
GPIP-ACTIV (meningitis)	Y	N	N	N	N	Y	68	Y	89
Germany	Y	Y	Y	Y	Y	Y	51	Y	48
Ireland									
EARSS-Ireland	N	Y	Y	Y	N	N		Y	100
Pnc meningitis system	Y	N				N		N	
Italy	Y	N				Y	NA	N	
Lithuania	Y	N	Y	Y	Y	N	3	Y	100
Malta	N	Y	Y	Y	N	N		Y	100
Netherlands	N	Y	Y	Y	Y	Y	100	Y	100
Norway	Y	Y	Y	Y	Y	Y	80	Y	0
Poland									
National ID surveillance	Y	N	N	N	N	N		N	
NRCBM	Y	Y	Y	Y	Y	Y	100	Y	100
Scotland	N	Y	Y	Y	Y	Y	85	Y	85
Slovak Republic	Y	N				N	5	Y	60
Slovenia	N	Y	Y	Y	Y	Y	100	Y	100
Sweden	N	Y	Y	Y	Y	N	25	N	
Switzerland	Y	Y	Y	Y	Y	Y	70	Y	70

Y: Yes N: No

site): joint (n=3), pleural effusion (n=3), peritoneum (n=2), middle ear (n=1) and sputum (n=2).

Fourteen of 18 countries reported that Pnc strains were collected to a single central reference level within the surveillance system for serotyping [TABLE 3]. In at least one country (Italy), the information was not integrated into the Pnc surveillance system. The proportion of Pnc isolates serotyped on average ranged between countries from 3% to 100%.

Twelve countries reported that a single reference laboratory undertook susceptibility testing. In two countries, this was undertaken by more than one laboratory [TABLE 3]. In France and Slovenia, there were 22 and 10 laboratories respectively undertaking Pnc antimicrobial susceptibility testing as a reference function. Of the 27 Pnc surveillance systems, 20 collected information on Pnc antimicrobial susceptibility. At least one country (Italy) reported that the information was not integrated into the surveillance system. The proportion of Pnc isolates tested for antimicrobial susceptibility ranged from 0 to 100%.

Laboratory quality assurance

Ten of the 18 countries reported that national protocols/guidelines were in place for microbiology laboratories to guide sampling, transportation and identification of Pnc. In thirteen countries, clinical microbiology laboratories undertook national quality assurance for Pnc either regularly or occasionally. In twelve countries, laboratories took part in international quality assurance.

Data collected

Data collected on each case in the 27 Pnc surveillance systems in 2003 included age (n=26), sex (n=24), unique ID (n=17), clinical presentation (n=20), outcome (n=17), PPV vaccination status (n=11), PCV vaccination status (n=5) and risk factors (n=8). Several countries plan to collect information in the future on PCV vaccination status with the introduction of universal infant immunisation programmes. The proportion missing for each variable by system is summarised in table 4.

Using the available ID, all 13 countries that used unique ID, and plus Germany and Belgium (Pedisurv) which both use an algorithm comparing identifiers common to both systems, linked multiple laboratory notifications recorded within the timespan specified in the case definition into a single case.

Data dissemination

Data collected by the 27 surveillance systems was disseminated through a publicly available website for 17 systems and through a national epidemiological bulletin for 16 systems [TABLE 5]. Twelve

systems have published surveillance findings in biomedical journals. Three countries have original data publicly accessible outside the surveillance network.

Available data

Recent surveillance data for IPD and Pnc meningitis is summarised in table 6. The number of IPD cases reported in one year was 23 470 cases from 18 countries, with the incidence of IPD ranging from 0.4 (Lithuania and Italy) to 20/100 000 general population (Denmark and Norway).

Of all these IPD cases, the total number of Pnc meningitis cases was 2193 from ten countries. The reported incidence of Pnc meningitis ranged from 0.3 (Poland and Slovak Republic) to 1.8/100 000 (Denmark). The proportion of isolates non-susceptible to penicillin in all age-groups ranged from 0 (Malta) to 43% (France).

Key reported limitations

Respondents identified a number of limitations to the surveillance systems. This included the infection not being notifiable (Estonia) or not being statutorily notifiable (Ireland, Scotland, Sweden, Denmark, Germany). Case reporting was identified as being incomplete by several countries (including Lithuania, Ireland, Germany), compounded by factors such as low blood sampling rates (Germany and Poland) and the presence of a limited number of laboratories (Italy). Other reported limitations included lack of data on Pnc pneumonia and sepsis (Czech republic), lack of reliable data on Pnc septicaemia (Netherlands, Denmark); a lack of clinical data (Ireland, Slovenia, Norway, Denmark and Belgium); lack of outcome data (the Netherlands); lack of data on vaccination status (Belgium); lack of information on serotypes (Belgium, Norway, Sweden); only aggregate data available at national level (Lithuania and Poland); lack of data on vaccine coverage to interpret epidemiological changes (Belgium) and only limited personal identifiers available thus limiting the ability to link databases and to de-duplicate (Switzerland and Sweden).

Conclusions

This paper is the first to provide an overview of the structure and outputs of national surveillance systems for invasive *S. pneumoniae* infection in Europe. There are weaknesses to the study, including of the level of non-responders. However, a number of key points can be learnt:

- Surveillance systems for invasive pneumococcal disease in Europe are very heterogeneous;
- Although several countries have strengthened their surveillance since the original survey, a number of countries still had no IPD surveillance in place in 2006, and a number of others only had surveillance for Pnc meningitis;
- Although the European Union has established a standard case definition (2002/253/EC), at least for international reporting, case definitions (CD) for invasive pneumococcal disease are not standardised across Europe especially with regard to use of non-culture methods and of time interval between cases;

Table 4

Pneumococcal disease surveillance in the European Union and data collected (27 surveillance systems), 2006

Country / Name of surveillance system	Age	% age missing	Sex	% sex missing	Unique ID	Clinical present	% clinical missing	Outcome	% outcome missing	PPV status	PCV status	Risk factors
Belgium												
ID sentinel laboratory system	Y	1	Y	1	Y	N		N		N	N	N
Pedisurv	Y	0	Y	0	Y	Y	44	Y	NA	Y	Y	Y
National Pnc reference laboratory	Y	0	Y	1	Y	Y	46	Y	31	Y	N	N
Czech Republic												
EPIDAT	Y	0	Y	0	Y	Y	0	Y	0	N	N	N
National Streptococci Reference Lab	Y	NA	Y	NA	Y	Y	NA	Y	NA			
Denmark												
National notification system	Y	0	N		Y	Y	0	Y	5	Y	N	Y
National laboratory surveillance	Y	0	Y	0	Y	N		N		N	N	N
England & Wales	Y	NA	Y	NA	Y	Y	80	Y	80	Y	N#	Y
Finland	Y	0	Y	0	Y	N		N		N	N	N
France												
EPIBAC	Y	0	Y	1	N	N		N		N	N	N
CNRP-ORP	Y	NA	Y		N	Y	NA	N		N	N	N
GPIP-ACTIV (meningitis)	Y	0	Y	1	N	Y	0	Y	1	Y	Y	Y
Germany	Y	0	Y	1	N	Y	0	Y	41	Y	Y	Y
Ireland												
EARSS-Ireland	Y	1	Y	1	Y	N		N		N	N	N
Pnc meningitis system	Y	0	Y	0	Y	Y	0	Y	0	N	N	N
Italy	Y	2	Y	0	Y	Y	0	Y	15	N	N	N
Lithuania	N		N		N	Y	0	N		N	N	N
Malta	Y	0	Y	0	Y	N		Y	0	N	N	N
Netherlands	Y	1	Y	1	N	Y	50	N		N	N#	N
Norway	Y	0	Y	0	Y	Y	13	Y	25	Y	N	N
Poland												
National ID surveillance	Y	0	N		N	Y	0	N		N	N	N
NRCBM	Y	5	Y	5	Y	Y	5	Y	70	Y	N	Y
Scotland	Y	0	Y	0	N	Y	19	Y	8	Y	N#	Y
Slovak Republic	Y	1	Y	1	N	Y	10	Y	0	Y	Y	N
Slovenia	Y	1	Y	5	Y	Y	35	Y	100	N	N	N
Sweden	Y	5	Y	5	N	N		N		N	N	N
Switzerland	Y	0	Y	0	Y	Y	17	Y	35	Y	Y	Y

Y: Yes N: No

 # Vaccination status of cases is collected since 2006

Table 5

Pneumococcal disease surveillance in the European Union and data dissemination (27 surveillance systems), 2006

Country / Name of surveillance system	Web	URL	Bulletin	Bulletin name	URL
Belgium					
ID sentinel laboratory system	Y	www.iph.fgov.be/epidemio/labo	Y	Rapports mensuels sur la surveillance des maladies	
Pedisurv	Y	www.iph.fgov.be/epidemio/epien/index32	N		
National Pnc reference laboratory	Y	www.iph.fgov.be/epidemio/epien	N		
Czech Republic					
EPIDAT	N		N		
National Streptococci Reference Lab	N		N		
Denmark					
National notification system	Y	www.ssi.dk	Y	EPI-NYT/EPI-NEWS	www.ssi.dk (epi-data)
National laboratory surveillance	N		Y	Epi-Nyt/Epi News	
England & Wales	Y	www.hpa.org.uk/infections/topics_az/pneumococcal/data.htm	Y	CDR weekly	www.hpa.org.uk/cdr
Finland	Y	www.ktl.fi/ttr	Y	Kansanterveyslehti	www.ktl.fi/portal/suomi/julkaisut/kansanterveyslehti
France					
EPIBAC	Y	http://www.invs.sante.fr/surveillance/epibac/default.htm	N		
CNRP-ORP	N		Y	Bulletin Epidemiologique Hebdomadaire	
GPIP-ACTIV (meningitis)	Y	http://193.251.4.4:9000/index.html	N		
Germany	Y	www.esped.uni-duesseldorf.de/	N		
Ireland					
EARSS-Ireland	Y	www.ndsc.ie	Y	EARSS newsletter	
Pnc meningitis system	Y	www.ndsc.ie	N		
Italy	Y	www.simi.iss.it/meningite-batterica.htm	N		Same
Lithuania	N		N		
Malta	Y	www.slh.gov.mt/icunit/icuearee.asp	Y	Infection Control Newsletter	
Netherlands	N		Y	Annual reports	
Norway	Y	www.fhi.no/tema/smittvern/haandbok/pneumokokkinfeksjon.html	Y	MSIS - report	
Poland					
National ID surveillance	Y	www.pzh.gov.pl/epimed	Y	Kronika Epidemiologicza	
NRCBM	N		N		
Scotland	Y	www.show.scot.nhs.uk/scieh/	Y	HPS weekly report	www.ewr.hps.scot.nhs.uk/
Slovak Republic	N		Y	Bulletin of chief hygienist - annual report	
Slovenia	N		Y	Health Statistical Year Book	
Sweden	N	www.smittskyddsinstitutaet.se	Y	Communicable diseases in Sweden, annual report	Available on request
Switzerland	Y	www.bag.admin.ch/infreporting/mv/d/index	Y	BAG Bulletin (german) or Bulletin OFSP	www.bag.admin.ch/infreporting/bulletin/d/index.htm

Y: Yes N: No

- Laboratory surveillance practice, a vital component of IPD surveillance, also varied, particularly regarding provision of access to a central reference laboratory and to quality assurance. In a number of countries serotype information was missing, which is critical to ascertain coverage of the 7-valent conjugate vaccine in relation to the actual distribution of serotypes in the country. It is also required to monitor for serotype replacement post-PCV introduction. Several countries undertook surveillance for Pnc AMR, which is a potential emerging public health problem;
- In several instances, parallel surveillance systems for Pnc were operating in a single country, and the surveillance findings were apparently not integrated. This was raised by one country in relation to the surveillance of pneumococcal antimicrobial resistance, within the European Antimicrobial Resistance Surveillance System (EARSS) [15].
- Case-based data were available in almost all surveillance systems, with information usually collected on age, sex and clinical presentation. However, only a few countries routinely collected information on the vaccination status of cases. This is essential (together with population coverage) to estimate vaccine effectiveness (using the classical screening method);
- Most systems disseminated regular reports and aggregate data through websites and national epidemiological bulletins. However, in a small number of cases pneumococcal surveillance data was not disseminated.
- A large number of IPD cases were detected through these routine surveillance systems. However, as has been previously documented, there are large inter-country variations in reported IPD rates [3,16]. These large differences reflect a combination of true epidemiological differences and various patient and healthcare factors. The latter include antibiotic prescribing, blood culture practice, reporting practices and structural differences in surveillance system. Each of these components varies from country to country.

Recommendations

Pneumococcal surveillance is critical if countries are to be able to ascertain the pre-vaccination epidemiology and disease burden of Pnc and therefore make an informed decision on whether and how to introduce PCV. Pnc surveillance will also be important for monitoring and comparing the impact and effectiveness of the vaccine (including serotype replacement) after its introduction. This will be particularly important because countries will introduce a variety of schedules into their childhood immunisation programmes. Based on the results of this survey, a number of general recommendations can be made:

- The epidemiology of invasive pneumococcal disease remains poorly described in a number of European countries. In the present era of licensed conjugate and polysaccharide pneumococcal vaccines, there is a clear need for countries to improve national surveillance of IPD, including identification of serotype, in order both to ascertain local disease burden, and to monitor and compare the impact and effectiveness of various, new vaccination programmes as they are introduced;
- Standard case definitions for IPD and collection of minimum case data need to be established to ensure that any data collected is comparable across Europe. This should include standard clinical presentations (meningitis, septicaemia, pneumonia, etc.). The European Centre for Disease Prevention and Control (ECDC) is currently reviewing the case definitions in use across Europe with the aim of producing standard recommendations for use in Europe.
- Parallel surveillance systems for IPD, in particular Pnc antimicrobial susceptibility and serotype surveillance, need to be more integrated;
- All countries should have access to an identified central reference laboratory able to undertaken Pnc isolation and serotyping. Countries need to establish national surveillance systems based on these laboratory reports. The reference laboratory should undertake regular quality assurance and have access to external quality control.

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TABLE 6

Pneumococcal disease surveillance in the European Union and available data (27 surveillance systems), 2006

Country / Name of surveillance system	Year of report	Total IPD cases	IPD incidence/ 100 000	Total Pnc meningitis cases	Pnc meningitis incidence/ 100 000	IPD case fatality ratio	Pnc meningitis case fatality ratio	% Pnc isolates pen non-susceptible
Belgium								
ID sentinel laboratory system	2002	1072	13.0	48	0.6			15
Pedisurv	###							
National Pnc reference laboratory	2003	1674	16.1	91	0.9			13
Czech Republic								
EPIDAT	2003			61	0.6		18.0	
National Streptococci Reference Lab	2003	270	2.7	75	0.7			2.0
Denmark								
National notification system				95	1.8	20		3
National laboratory surveillance	2002	1089	20.3					3
England & Wales	2004	6171	11.6	276	0.5			7
Finland	2002	612	11.8					0.9
France								
EPIBAC	2003	6324	10.6	589	1.0			
CNRP-ORP	2003				0.95			43
GPIP-ACTIV (meningitis)	2004			120 (<18 y)	1.4 (<18 y)		10.4 (<18 y)	50.4 (<18 y)
Germany	2002	465 (# 560)	3.5 (#CRA 4)	166 (CRA: 177)	1.2 (CRA: 1.3)	17	11	0.9
Ireland								
EARSS-Ireland	2002	278	7.1					11.5
Pnc meningitis system	2002			15	0.4		6.7	
Italy		235##	0.4	235	0.4		12.5	12.2
Lithuania		15	0.4					
Malta		12	3.4			8.3		0
Netherlands	2005	1296	7.9	246	1.5			0.9
Norway	2002	918	20.2			7.4		
Poland								
National ID surveillance	2005	175	0.46	110	0.29			
NRCBM	2004			49	0.13			18.2
Scotland	2005	719	14.2					0.6
Slovak Republic		17##	0.3	17	0.3	0	5.9	40
Slovenia		92	4.6			6.5		24.2
Sweden	2003	1152	12.9					
Switzerland		884	12.3			13		13
TOTAL		**23 470**		**2 193**				

 # CRA = capture-recapture estimate
Meningitis cases only
Data only available from 2006

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ORIGINAL ARTICLES

Outbreak report

PROLONGED OUTBREAK OF B MENINGOCOCCAL DISEASE IN THE SEINE-MARITIME DEPARTMENT, FRANCE, JANUARY 2003 TO JUNE 2005

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Between January 2003 and June 2005, an outbreak of meningococcal disease occured in the department of Seine-Maritime in northern France. Eighty six cases were notified, giving an average annual incidence of 2.7 cases per 100 000 inhabitants, compared with 1.6 in France. An especially affected area was defined as the city of Dieppe and its surrounding area (26 cases, giving an annual incidence of 12 cases per 100 000). This outbreak was due to *N. meningitidis* phenotype B:14:P1.7,16 belonging to the clonal complex ST-32/ET-5. Over the 31 B14:P1.7,16 cases confirmed by phenotyping methods at the national reference centre for meningococci (CNR, Centre National de Référence des méningocoques) the case-fatality rate (19%) and the proportion of purpura fulminans (42%) were especially high. Teenagers aged between 15 and 19 years and children aged 1 to 9 years were the most affected. In 2003, health authorities put in place enhanced epidemiological surveillance and informed practitioners and population about the disease. In 2004, the national vaccination advisory board studied the opportunity of using a non licensed outer membrane vesicle vaccine developed in Norway which may be effective against the B14:P1.7,16 strain. The Ministry of health decided in 2006 to offer vaccination with this vaccine to people aged 1 to 19 years in Seine- Maritime.

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Introduction

In France, invasive meningococcal disease (IMD) is a mandatory notifiable disease [1] and strains isolated from patients are sent to the national reference centre for meningococci (CNR, Centre National de Référence des méningocoques). The last evaluation of IMD surveillance estimated the exhaustivity of mandatory reporting at 80% [2,3]. The goal of the surveillance is rapid detection of clusters or abnormal situations

for prompt response and monitoring of national trends. The IMD incidence rate has been below 2 cases per 100 000 inhabitants for the past 10 years. Ninety seven percent of IMD cases are sporadic and IMD is associated with serogroup B in 59% of cases. Close contacts of IMD cases are offered chemoprophylaxis, and if appropriate, vaccination, as documented in the national guidance [4].

At the beginning of 2003 the national institute for public health surveillance (InVS, Institut de Veille Sanitaire) was alerted by the high incidence of serogroup B IMD cases in the north of the department of Seine-Maritime, Haute Normandy region, population 1 237 263. A similar increase had been observed in the same department in 1997, associated with high incidence of the B serogroup serotype 14 and serosubtype P1.7,16 belonging to the electrophoretic type 5 [5].

From 2003, health authorities set up an enhanced surveillance, collecting data on demographic, clinical, epidemiological and biological characteristics of each new cases and raised awareness of the disease among health practitioners aware and the general public.

This report describes the outbreak in Seine-Maritime, between 1 January 2003 and 30 June 2005.

Methods

Since 2002 the case definition of IMD has been a patient with Gram negative cocci in direct examination of cerebrospinal fluid (CSF) or *N. meningitidis* isolated from a sterile site; a patient with purulent CSF with presence of meningococcal antigens or positive polymerase chain reaction (PCR); or a patient with purpura fulminans or purulent CSF and purpuric spots.

For this outbreak, B:14:P1.7,16 cases were identified by culture or PCR from a sterile site. IMD cases included in the analysis were patients living, studying or working in Seine-Maritime and with dates of hospital admission between 1 January 2003 and 30 June 2005.

In the Seine-Maritime department we assumed that all cases were reported because of the enhanced surveillance and the high medical awareness during the outbreak. Specific care was taken to send samples to the CNR quickly.

To calculate incidence, each case was assigned to the department where the patient was normally resident. An especially affected area was defined by tracing a circle around the city of Dieppe including the homes of all the cases, and a total of 84 500 inhabitants. The P values for comparisons were estimated using the Fisher exact test or the chi-square test. Population estimates in 2003 were issued from the national office for demographic studies (INSEE) and from the 1999 census data for Dieppe area.

Results

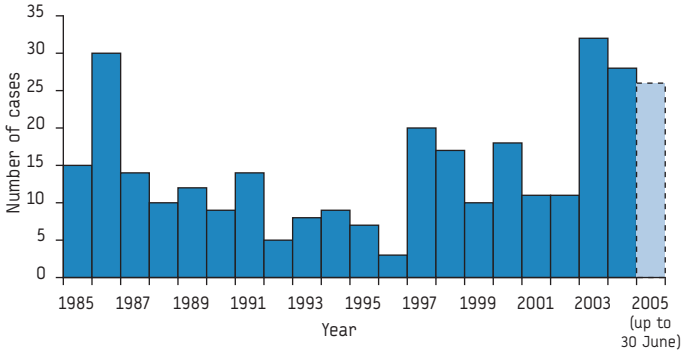
The outbreak in Seine-Maritime

From 1 January 2003 to 30 June 2005, 31 of the 86 IMD cases notified in the Seine-Maritime department were B:14:P1.7,16. The average annual incidence of IMD was 2.7 cases per 100 000 inhabitants. During the same period, the annual national incidence was 1.6 per 100 000 inhabitants (P=0.000). Since the 1997 rise associated with *N. meningitidis* B:14:P1.7,16 the number of IMD reported has remained high [FIGURE 1].

Of the 86 IMD cases, 32 were notified in 2003, 28 in 2004 and 26 between 1 January and 30 June 2005 [FIGURE 2]. In February 2005 a large peak of eight reported cases was observed. During the two first years the cases occurred mainly in the Dieppe area with 10 cases (incidence 11.8/100 000) in 2003 and 13 (incidence 15.4/100 000) in 2004. The incidences in the rest of the department were 1.9/100 000 (2003) and 1.3/100 000 (2004). In the first six months of 2005, 3 of the 26 cases were from the Dieppe area, with a six month incidence of 3.6/100 000 in the Dieppe area and 2.0/100 000 in the rest of the department. The situation was localized to the department of Seine-Maritime and none of the 6 surrounding departments presented an increase of IMD incidence rate during the study period.

FIGURE 1

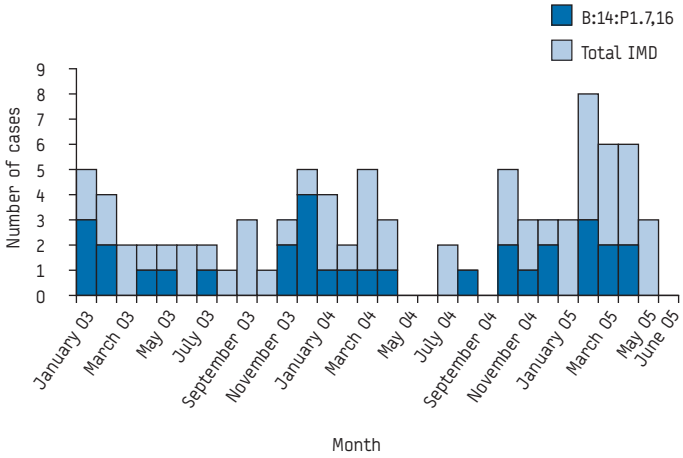
Number of invasive meningococcal disease cases notified, Seine Maritime department, January 1985 to June 2005



Note: Notification criteria were expanded in 2003 to include cases without microbiological confirmation. In 1997, a total of 31 cases were identified in the department but only 20 corresponded to the mandatory case definition at that time

FIGURE 2

Distribution of IMD cases reported by month, Seine Maritime department, France, January 2003 to June 2005



Of the 86 cases, 70 were laboratory confirmed: 61/70 (87%) were serogroup B, 8/70 (11%) were serogroup C and one (1%) was serogroup W135 or Y. Among the 61 serogroup B strains, 31 (50%) were B:14:P1.7,16, 15 (25%) could not be typed nor subtyped and 15 (25%) belonged to a variety of different types and subtypes.

The male:female ratio was 1.3 (48/38) compared with 1.0 in the whole of France (P=0.260). All age groups were affected with the highest age specific incidences observed among children less than 5 years and teenagers 15-19 years old [TABLE 1]. Teenagers accounted for 26% of the cases, compared with 18% in France (P=0.068).

TABLE 1

Number, percentage and averaged specific incidence of IMD, January 2003 - June 2005, Seine Maritime and France

Age in years	IMD cases		Annual specific incidence, Seine Maritime per 100 000	Annual incidence, France* per 100 000
	No.	%		
<1	6	7.0	18.3	17.3
1-4	18	20.9	13.7	5.5
5-9	10	11.6	5.0	1.1
10-14	9	10.5	4.1	1.3
15-19	22	25.6	9.6	4.5
20-25	7	8.1	3.4	2
≥25	14	16.3	0.7	0.5
Total	**86**	**100.0**	**2.8**	**1.45**

* Corrected for under-reporting

Of the 86 cases, 55 (64%) had septicaemia only or septicaemia associated with meningitis and 31 (36%) had meningitis only. *Purpura fulminans* was observed in 39 cases (45%), in a highest proportion than in France, 29% (P=0.000). During the study period 14 patients

died, giving a case fatality rate (CFR) of 16%. The CFR decreased over time from 25% (8/32) in 2003 to 14% in 2004 (4/28) and 8% (2/26) in the 6 first months of 2005. Two clusters occurred in the Dieppe area: one made up of two friends in the same village (co-primary cases, 1 identified B:14:P1.7,16), the other made up of two brothers (first case identified B:14:P1.7,16, the secondary case occurred within 48 hours although chemoprophylaxis had been given). A girl and her grandfather living in the city of Rouen also developed the disease within 48 hours of one another (the cases were B serosubtype P1.7,16).

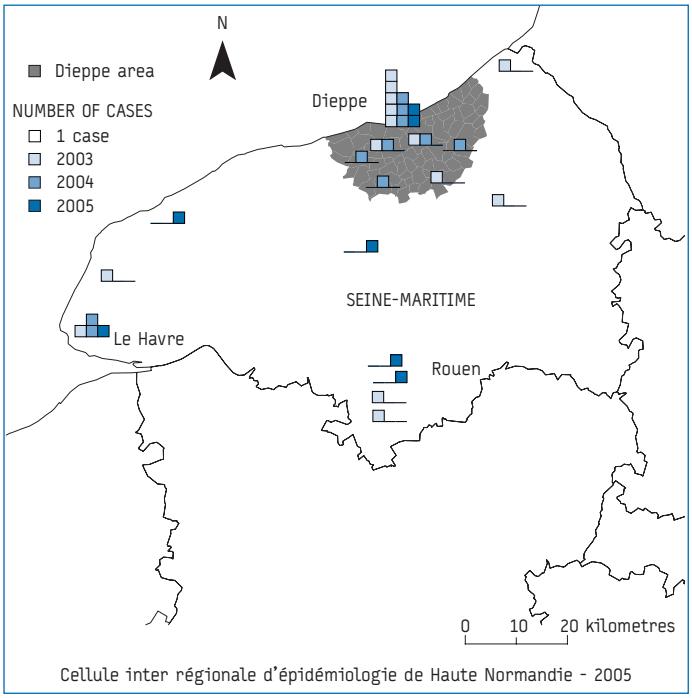
B:14:P1.7,16 confirmed cases

A total of 31 B:14:P1.7,16 cases were confirmed by phenotyping methods at the CNR, 14 in 2003, 10 in 2004 and 7 in the first six months of 2005. In 2003-2004, 16/24 cases (67%) occurred in residents of Dieppe area. Residents of this area make up 6.8% of the population of the Seine-Maritime department. From January to June 2005, among the 7 B:14:P1.7,16 cases, 2 occurred in Dieppe area [FIGURE 3].

The proportion of B:14:P1.7,16 cases varied by age group: 59% of all cases in teenagers (aged 15-19 years) were B:14:P1.7,16, but no B:14:P1.7,16 cases occurred in children aged under 1 year [TABLE 2]. The male:female ratio of B:14:P1.7,16 cases was 1.8 (20/11). In 2004-2005, the sex ratio tended towards 1.

FIGURE 3

Geographic distribution of B:14:P1.7,16 cases identified in Seine Maritime, by year, 1 January 2003 – 30 June 2005



Sources: InVS, NRC

Among the 31 B:14:P1.7,16 cases, the CFR was 19% (6 deaths) (serogroup B IMD CFR in France: 8%, P=0.031) and 42% (13) had purpura fulminans (B IMD national proportion: 24%, P=0.026).

During the study period, the CNR identified a total of 1493 invasive *N. meningitidis* samples in residents of France, of which 62 were invasive isolates of *N. meningitidis* of the phenotype B:14:P1.7,16 from a sterile site. Invasive isolates with phenotype B:14:P1.7,16 accounted for 4.2% of all strains and 7% of serogroup B strains. Twenty eight isolates (45%) of the phenotype B:14:P1.7,16 were from Seine-Maritime (differences with presented data are due to one patient residing outside the department and two cases classified B:14:P1.7,16 in our study because of the presence of clinical and biological signs of meningococcal infection and a B:14:P1.7,16 strain isolated from the pharynx but not taken into account by the CNR). Most of the other 34 invasive isolates were from neighbouring departments, where their presence was not associated with increase in incidence. Isolates from Seine-Maritime were further shown to belong to the clonal complex ST-32/ET-5. Strains with phenotype B:14:P1.7,16 were first isolated in France in 1989 in the Seine-Maritime department. They then appeared sporadically in other departments and were identified from a cluster in the eastern city of Metz in 2003 [6].

Control of the outbreak

Information meetings were organised by the local health authorities from 2004 for hospital physicians and other health professionals working out of hospitals (general practitioners, paediatricians…). Awareness of symptoms was promoted in the general public, with a document entitled *'Les infections invasives à méningocoque en Seine-Maritime : "repérer pour agir"'* that was widely distributed in December 2004, by items in print media articles and radio spots from 2003, and a television programme on the topic in January 2005. From January 2005, reports were produced on the InVS website, four times a year to begin with, changing to monthly. Three meetings with the local and national health authorities and the national experts were organised by the national board of health (DGS, Direction Générale de la Santé) and three telephone conferences were hold during the period. Several meetings of the national vaccination advisory board (CTV, Comité technique des vaccinations) were held in 2004 and 2005 to evaluate the risks and benefits of using an unlicensed outer membrane vesicle (OMV) vaccine developed against *N. meningitidis* phenotype B:15: P1.7,16 in Norway.

Discussion

In 2003, the incidence of IMD began to rise in Seine-Maritime because of the incidence in Dieppe area. Teenagers were more affected by the B:14:P1.7,16 strain than other age groups but 60% of the cases aged 5 to 9 years couldn't be grouped, typed or subtyped and may be therefore considered as possible B:14:P1.7,16. This might reflect different diagnosis practices or feasibility of isolating the strain in samples from this age group. In winter 2004-2005 and spring 2005, the outbreak seemed to spread in the rest of the department.

TABLE 2

Number and percentage of cases of IMD by age, Seine Maritime, France, January 2003 to June 2005

Age in years	B:14:P1.7,16	%	B without antigenic characterisation	%	Clinically diagnosed cases	%	Other confirmed cases	%
<1	0	0	1	7	1	6	3	13
1-4	6	33	4	27	4	25	5	21
5-9	3	30	1	7	4	25	2	8
10-14	4	44	3	20	0	0	2	8
15-19	13	59	3	20	3	19	3	13
20-25	1	14	1	7	2	13	3	13
≥25	4	29	2	13	2	13	6	26
Total	**31**		**15**		**16**		**24**	

The data presented suggest a local and persistent outbreak due to a particular strain. This situation was observed in another French department from 1995 to 1999 [7]. In Seine-Maritime the outbreak was due to *N. meningitidis* phenotype B:14:P1.7,16 belonging to the clonal complex ST-32/ET-5 and was associated with severe infections. This phenotype is not common in France. In 2003 an outbreak of six cases of this phenotype emerged in Metz, which led to a mass prophylaxis campaign for the 8000 people living in the affected area [6]. B outbreaks have been described in the 30 past years in Europe and America with common epidemiological characteristics: high attack rate among teenagers [8], presence of the strain for several years before the emergence of the epidemic [8] and high severity of the disease.

The high CFR and high incidence in teenagers gave the health authorities cause for concern, and justified targeted responses. Evidence suggests that awareness among healthcare professionals and the general population have contributed to minimise the waiting period before treatment and therefore to make the CFR decrease over the outbreak period [10,11].

Mass chemoprophylaxis for the population living in Dieppe and the surrounding areas was considered to be an ineffective response because the strain had already been shown to be present throughout the department, and any untreated members of the population could easily re-introduce the strain into the treated population, and contribute to the emergence of rifampicin resistance [12] and the elimination of non-pathogenic *Neisseria* which can help to boost immunity to meningococcal disease. The absence of a universal vaccine against serogroup B had prompted the development of protein-based, OMV vaccines that have proven to be efficacious against specific strains in Norway and Cuba [13,14]. OMV vaccine especially developed for New Zealand is currently being used in a mass vaccination campaign targeting young people below 20 years of age [15]. These vaccines may be effective against related strains. Vaccination with an OMV vaccine prepared on the basis of a closely related strain was discussed by the Ministry of Health in order to control the persistent outbreak in Seine-Maritime. In 2005, the number of IMD cases in the department continued to rise and the annual incidence was 3.4 per 100 000, with 42 cases. The B:14:P1.7,16 N. meningitis strain was isolated in Dieppe area as well as in the rest of the department and remained associated with high proportion of purpura fulminans and deaths.

On the advice of national vaccination advisory board, the Ministry of health decided in 2006 to offer all those aged between 1 and 19 years in Seine-Maritime vaccination with the Norwegian OMV vaccine developed against the B:15:P1.7,16 strain. The vaccination campaign dedicated to 1 to 19 years old population residing in Seine-Maritime started in June 2006 in Dieppe area and will be offered progressively to the rest of the population. Since June 2006, close contacts of identified B:14:P1.7,16 new cases occurring in France are also offered vaccination.

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SHIGA TOXIN-PRODUCING *ESCHERICHIA COLI* (STEC) O157 OUTBREAK, THE NETHERLANDS, SEPTEMBER – OCTOBER 2005

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In September 2005, the first national food-related outbreak of Shiga toxin (Stx)-producing *Escherichia coli* (STEC) O157 was investigated in the Netherlands. A total of 21 laboratory-confirmed cases (including one secondary case), and another 11 probable cases (two primary and nine secondary cases) were reported in patients who became ill between 11 September and 10 October 2005. Preliminary investigation suggested consumption of a raw beef product, steak tartare (in the Netherlands also known as 'filet américain'), and contact with other symptomatic persons as possible risk factors. A subsequent case-control study supported the hypothesis that steak tartare was the source of the outbreak (matched odds ratio (OR) 272, 95% confidence interval (CI) 3 - 23211). Consumption of ready-to-eat vegetables was also associated with STEC O157 infection (matched OR 24, 95% CI 1.1 – 528), but was considered a less likely source, as only 40% of the cases were exposed. Samples of steak tartare collected from one chain of supermarkets where it is likely that most patients (67%) bought steak tartare, all tested negative for STEC O157. However, sampling was done three days after the date of symptom onset of the last reported case. Since 88% of the cases became ill within a two week period, point source contamination may explain these negative results. It is concluded that steak tartare was the most likely cause of the first national food-related outbreak of STEC O157 in the Netherlands.

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Key words: *Escherichia coli* O157, outbreak, beef products

Introduction

Shiga toxin-producing *Escherichia coli* (STEC) O157 infection is the leading cause of haemorrhagic colitis and haemolytic uraemic syndrome (HUS) in children [1]. In adults, it mainly causes uncomplicated bloody diarrhoea. Well-known vehicles for transmission of STEC O157 include contaminated food products, especially of bovine origin, such as milk and undercooked beef [2-4], but also fresh produce, such as raw fruit and vegetables [5-7]. Other modes of transmission are person-to-person spread, contact with animals or their manure, and contact with contaminated water [4, 8-9].

Since January 1999, the Netherlands has implemented enhanced surveillance of STEC O157 [10]. Notification of STEC O157 infections became mandatory in December 1999. Since then, between 35 and 57 symptomatic cases were reported annually, corresponding to an incidence of about 0.22 to 0.35 laboratory-confirmed cases per 100 000 inhabitants. Although molecular typing and epidemiological information regularly suggested small clusters of fewer than 5 cases, large clusters or outbreaks had not previously been identified [11]. In the first week of October 2005, 18 cases were reported. This high number of cases was unprecedented and an outbreak was suspected. This paper describes the subsequent outbreak investigation.

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Methods

As part of the enhanced surveillance, all Dutch laboratories are requested to report positive results of STEC O157 to the local public health service. Furthermore, they are requested to send the STEC O157 isolates to the National Institute for Public Health and the Environment (RIVM) for O- and H-serotyping, for testing for genes encoding Shiga toxin 1 (stx_1) and 2 (stx_2), *Escherichia coli* attaching and effacing (*eae*) gene and the enterohaemorrhagic *Escherichia coli* haemolysin (*e-hly*) gene by polymerase chain reaction. DNA fingerprints are made by pulsed-field gel electrophoresis (PFGE), using *Xba*I as the restriction enzyme. For the current outbreak, *Bln*I was used as a second restriction enzyme. The fingerprints are processed using Bionumerics software (Applied Maths, Belgium). In addition, for the current outbreak, 15 isolates were sent to the Health Protection Agency's Laboratory of Enteric Pathogens in London for phage typing. The local public health services are requested to contact every reported patient to collect background information using a standardised questionnaire. The questionnaire includes questions about clinical manifestation, exposures in the seven days before symptom onset, such as contact with symptomatic individuals (within or outside the household), travel, food consumption such as beef, pork, poultry, vegetables, fruit, and dairy products), eating in a restaurant, contact with farm animals or manure, water-related activities, and working or playing in the garden. All questionnaires are returned to the RIVM. For further details see [10].

Within the first week of October 2005, an unusual high number of 18 cases was reported. This triggered interviews with 11 of these cases, using a trawling questionnaire to generate hypotheses about possible sources. From these interviews, consumption of steak tartare and contact with other persons with gastroenteritis symptoms emerged as possible risk factors. A case-control study was started on October 10 to test the hypothesis that steak tartare was the source of the outbreak.

We defined a confirmed case as a person with diarrhoea (≥ 3 loose stools within 24 hours) with two or more additional symptoms (nausea, abdominal pain, abdominal cramps, blood in stool, mucus in stool, vomiting or fever) after 1 September 2005, with a stool specimen positive for STEC O157 and a PFGE pattern matching the outbreak type. A probable case was defined as a person with diarrhoea after 1 September 2005, and epidemiologically related to a confirmed case (e.g., household contact, friend, school or work contact). For probable cases, no stool specimens were available for testing for STEC O157. Cases could be primary, if the date of symptom onset was earlier than or equal to the symptom onset of a related case, or secondary, if their illness started at least two days later than a related case. Probable cases were included to measure the magnitude of the outbreak, but were excluded from the case-control study.

The local public health services interviewed all confirmed cases using the surveillance questionnaire and an additional outbreak questionnaire to obtain detailed information about contact with symptomatic persons and consumption of beef products (steak tartare, minced beef, mixed beef and pork mince, minced steak, and

hamburger) within seven days before symptom onset. Questions were asked about the shops where these products were bought to determine whether any foods shared a common source. For each confirmed case, two controls were recruited using a web-based phone book, matching for neighbourhood (streets in the same area) and age group (0-9, 10-17, 18-49, >50 years). Each fifth phone number in a street was called until two eligible controls were found and willing to participate. Controls were interviewed by telephone using a standardised questionnaire composed of the two questionnaires used for the cases. The questionnaire addressed exposures in the week of 17 September, which was for most cases the week before symptom onset. The controls of the last reported case were interviewed about exposures in the week of 26 September. When a control was 17 years or younger, a parent or guardian was interviewed in his or her place.

Univariate and multivariate conditional logistic regression analyses were performed using PROC PHREG in SAS version 9.1. Variables with a P value ≤ 0.15 in the univariate analyses were selected for inclusion in the final multivariate model by (manual) stepwise forward selection. Variables for which the likelihood ratio test gave a P value £ 0.05 and variables with a confounding effect (changing the beta-estimates with at least 15%) were kept in the multivariate model.

The Netherlands participates in Enter-net, an international surveillance network for Salmonella and Verocytotoxin-producing *Escherichia coli* O157 infections, funded by the European Commission [12]. All participating countries were informed about the outbreak and requested to forward information about cases of STEC O157 infection with a similar strain (O-, H-, stx1, stx2 type and PFGE pattern).

On 13 October, the Food and Consumer Product Safety Authority started a national sampling of steak tartare from one chain of supermarkets that was frequently mentioned by the patients. All samples were tested for STEC O157. The agency also interviewed the directors of these supermarkets for details concerning the providers of steak tartare in the week of 17 September.

Results

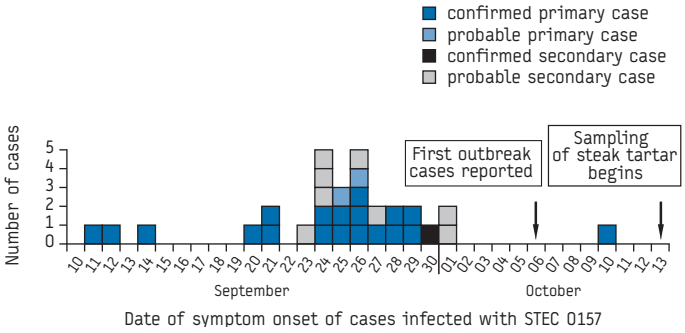
We identified 21 confirmed cases (of which one was a secondary case) and eleven probable cases (two primary and nine secondary cases), who had dates of symptom onset between 11 September and 10 October [FIGURE 1]. All 15 isolates sent for phage typing showed an identical phage type, RDNC. The median age of the confirmed cases was 24 years (range 3-66 years). Compared with the age distribution of cases in the routine surveillance, a lower proportion of outbreak cases was in children aged 0-4 years (10% versus 27% in the surveillance). Fifty two per cent of cases were female. Cases were distributed throughout the Netherlands. After diarrhoea, the most commonly reported symptoms were abdominal pain (95%), abdominal cramps (95%), blood in the stool (81%), looking pale (71%), listlessness/narcolepsy (67%), nausea (57%) and mucus in the stool (52%). None of the cases developed HUS. Seven patients (33%) were admitted to hospital, and the median length of stay was four days (range 3-7 days). Only confirmed primary cases were included in the risk analysis. Based on the univariate analysis, consumption of steak tartare, ready-to-eat raw vegetables, minced beef, contact with horses and swimming were considered in the multivariate model, but only steak tartare and ready-to-eat raw vegetables remained associated with illness (Table). Seventy five per cent of the patients consumed steak tartare, compared with only 20% of the controls. For ready-to-eat vegetables, these proportions were 40% and 25%, respectively. Of the cases who consumed steak tartare, 67% mentioned a specific supermarket chain as the place where they bought the steak tartare, but many of these cases named a second supermarket or butcher as well. Only one of the eight controls who consumed steak tartare mentioned that supermarket chain.

The Food and Consumer Product Safety Authority collected 302 samples of steak tartare from this supermarket chain across the Netherlands. All samples tested negative for STEC O157, but Salmonella was found in three samples. Trace back led to five possible providers, of which one was most likely to have delivered the steak tartare bought by most patients. Inspection at the site of this provider in the week of 24 October did not reveal anything unusual. Further trace back was not feasible, since the provider obtained meat from many different abattoirs, both nationally and internationally.

In the Dutch surveillance database for STEC O157, two historical cases were found with the outbreak PFGE pattern, whose dates of symptom onset were 12 June and 10 July 2005 [FIGURE 2]. The source of infection of these cases remained unknown. Information from Enter-net participants revealed that no other European countries or the United States had ever identified patients with this PFGE pattern. Since the last reported outbreak case, no new cases with the outbreak strain have been reported.

FIGURE 1

Epidemic curve of 20 confirmed cases and 10 probable cases in an outbreak of Shiga toxin-producing *Escherichia coli* (STEC) O157 in the Netherlands, September-October 2005



Note: Symptom onset date for one confirmed primary case and one probable secondary case were unknown: these cases are not included in the figure

TABLE

Matched univariate and multivariate odds ratios of factors associated with the STEC O157 outbreak, the Netherlands, September-October 2005

Exposure	Exposed controls (%)	Exposed cases (%)	Unexposed controls (no.) matched with exposed cases (no.)	Exposed controls (no.) matched with unexposed cases (no.)	Univariate matched OR (95% CI)†	Multivariate matched OR (95% CI)
Steak tartare	8 (20)	15 (75)	22 / 15	0‡ / 5	19.2 (2.5-149.0)	272.2 (3.2-23211.5)
Ready-to-eat raw vegetables	10 (25)	8 (40)	8 / 8	2 / 12	3.4 (0.6-17.9)	24.2 (1.1-528.3)
Minced beef	26 (65)	7 (35)	6 / 7	18 / 13	0.3 (0.1-1.0)	0.1 (0.0-0.8)
Swimming	9 (23)	8 (40)	12 / 8	5 / 12	2.7 (0.7-9.7)	
Contact with horses	2 (5)	5 (25)	9 / 5	1 / 15	8.6# (1.0-74.9)	

Note: 20 cases matched with 40 controls (1:2) according to age group and neighbourhood

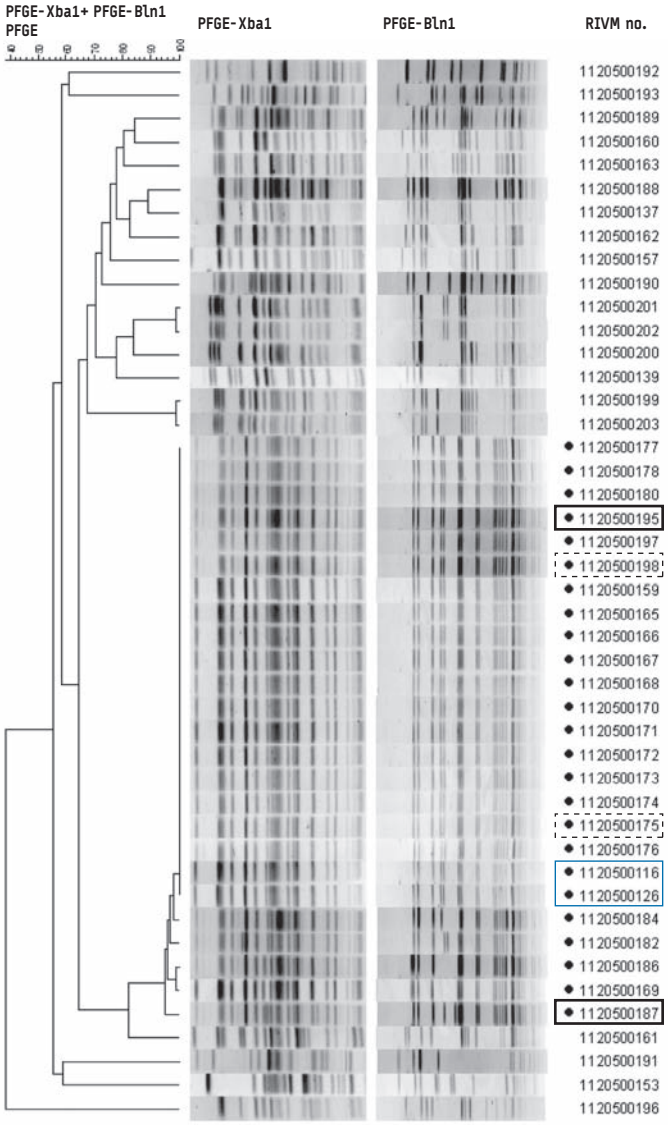
† OR, odds ratio; CI, confidence interval

‡ To be able to calculate odds ratios, one unexposed control matched with an unexposed case was artificially considered as an exposed control in the analysis

Contact took place at different sites, eg. different riding schools and children's farms

FIGURE 2

PFGE patterns of 39 isolates received during enhanced STEC O157 surveillance in 2005 in the Netherlands



• Isolate with the outbreak PFGE pattern (25 isolates of 23 cases shared the outbreak PFGE pattern)

—— Two historical cases with date of symptom onset 12 June and 15 July 2005 For these cases PFGE was not done with the second restriction enzyme Bln I

——, ------ Two isolates of one confirmed case

Discussion and conclusion

This was the first nationwide outbreak of STEC O157 in the Netherlands since the start of the enhanced surveillance. Twenty one confirmed cases were identified, which corresponds with at least several thousand cases in the Dutch community [13,14]. The outbreak was most likely caused by consumption of steak tartare, a beef product that is consumed raw. Because this food is generally known to be a risk product, few young children consume it, explaining the relatively low number of young outbreak cases and the absence of HUS. The second risk factor in the outbreak, ready-to-eat raw vegetables, was considered a less likely source as it could explain fewer cases, and the sales outlets were diverse. Strikingly, subtyping with PFGE showed a unique pattern that was first found in the Netherlands in June 2005 and has not been observed internationally. Phage typing of part of the isolates also showed an unusual type.

Cattle form the major reservoir of STEC O157 and foods of bovine origin caused many outbreaks of STEC O157 internationally [2-4]. In the Dutch surveillance, consumption of raw or undercooked beef was more frequently reported in 2004 (42%) than in previous years (14% to 23%), when contact with animals or their manure dominated. This may be caused by a change in consumption pattern of the Dutch population or a higher prevalence of STEC at retail due to less hygienic slaughter practices [11]. There is no indication for a higher prevalence of STEC O157 in cattle at the Dutch farms [15], butr most of the beef consumed in the Netherlands is imported. It is of interest that several other European countries also experienced national STEC O157 outbreaks at around the same time, [16-18], one of which was also related to a beef product [18].

In the case-control study, controls were interviewed about exposures in the week before symptom onset of most cases, and thus had a similar recall period. A few cases had an earlier date of symptom onset, and therefore they had a longer recall period than their controls.

Although the case-control study clearly indicated steak tartare as the source of infection, samples taken from this product tested negative for STEC O157. However, sampling started on 13 October , one week after the first outbreak cases were reported, while the last outbreak case became ill on 10 October. This suggests that the outbreak may have been caused by a point source contamination of steak tartare. As trace back was incomplete, it could not provide an indication of the level of the food production and processing chain where the STEC O157 contamination was introduced.

Because trace back of meat is difficult and time-consuming, and sampling in the relevant period is often not possible, current national monitoring programmes for beef products should be continued. In addition, since other European countries also recently experienced outbreaks of STEC O157 and *Salmonella* related to beef [18-20], the place of origin of beef should be recorded in these monitoring programmes. To prevent future outbreaks, more attention should be given to hygienic slaughter practices. However, even with improved hygiene in slaughterhouses, pathogens may still be present in raw meat. Therefore, public education is needed to discourage consumption of raw meat products, especially by high risk groups.

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ORIGINAL ARTICLES

Outbreak report

EPIDEMIC CONJUNCTIVITIS IN GERMANY, 2004

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Epidemic conjunctivitis can be associated with viral or bacterial pathogens, whereas epidemic keratoconjunctivitis is caused mainly by adenoviruses type 8,19 and 37. In Germany, the incidence of adenovirus conjunctivitis cases increased from 0.2 per 100 000 inhabitants (in 2001 and 2002) eventually to 0.5 in 2003 and 0.8 in 2004. The detection of adenovirus in conjunctival swabs is notifiable to the local health departments. Data about cases with positive conjunctival swabs are then transmitted to the Robert Koch-Institut. Quality control of data takes place and national surveillance data of confirmed cases with adenovirus conjunctivitis are published. From January to April 2004 the national surveillance system captured an outbreak with 1024 cases (131 laboratory confirmed). Analysis of the national surveillance data showed that in March 2004 the group primarily affected by epidemic keratoconjunctivitis was young men between 18 -29 years old followed by an increased number of notifications from women in the same age group. Meanwhile the German Armed Forces experienced an outbreak of conjunctivitis, almost exclusively without laboratory confirmation, affecting 6378 soldiers.

Despite the small number of laboratory confirmed cases it became clear from the analysis of the national surveillance data that person-to-person transmission between young men and similar age groups of the population did occur. Whether the outbreak started within the garrisons of the German Armed Forces or whether it was triggered within these accommodations, there is clearly a need for the national and the military public health institutions to work together on guidelines to handle future challenges.

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Introduction

Acute conjunctivitis is characterised by a red eye, discomfort, discharge and conjunctival injection [1]. A variety of bacterial and viral pathogens can cause acute conjunctivitis, including chlamydia, staphylococci, enterovirus, and herpes virus [2].

Epidemic viral keratoconjunctivitis is generally associated with adenovirus mainly type 8, 19 and 37.

Incubation period ranges from 5-12 days. Adenovirus infections of the eyes can present as epidemic keratoconjunctivitis (EKC), pharyngoconjunctival fever or follicular conjunctivitis. Keratoconjunctivitis disappears after 2-4 weeks, whereas keratitis (opacity of the lenses) may persist for longer. Patients with EKC are infectious during the first 2-3 weeks of infection and transmission occurs via smear infection. Infection routes can include contaminated towels or other contaminated articles of daily use in kindergartens, schools, clinics and swimming pools. To prevent transmission and outbreaks appropriate disinfection of hands and ophthalmological instruments should take place. Strict personal hygiene and revision of hygiene guidelines is recommended where outbreaks have occurred. No specific treatment is available [3].

Adenoviruses are endemic worldwide and are not only responsible for EKC but also for mild respiratory tract infections, atypical pneumonia, and gastroenteritis [4, 5]. Clearly identified risk factors for infection include contaminated ophthalmological solutions, ocular instruments, and insufficient hand hygiene [6-8]. Outbreaks with epidemic viral keratoconjunctivitis have been observed in military settings [9, 10].

In Germany, the number of confirmed adenovirus conjunctivitis cases was 132 in 2001 (0.2 per 100 000 inhabitants), 82 in 2002 (0.2), 397 in 2003 (0.5) and 652 in 2004 (0.8) [11]. The increase in 2003 was caused by an outbreak associated with two private ophthalmology practices in Saxony-Anhalt [12]. In 2004 an outbreak within the German Armed Forces (GAF) was responsible for an increased number of cases with adenovirus conjunctivitis cases picked up by the national surveillance system.

A description and analysis of the national surveillance data of adenovirus conjunctivitis cases for the years 2001-2004 are presented in this article.

Methods

All German laboratories that identify adenoviruses from conjunctival swabs are required to notify these results to the local health departments (LHD). Cases are then relayed via the state health departments to the national public health agency, the Robert Koch-Institut (RKI). At the RKI, quality control of data is performed. Cases are confirmed and accepted for analysis and publications if the following requirements are fulfilled:

A laboratory confirmed case with EKC is defined as a case with reddening of the conjunctiva and laboratory confirmation (detection of adenovirus from either cell culture, nucleic acid reaction or from immune fluorescence testing or enzyme immunoassay).

An epidemiologically confirmed case with EKC is defined as a case with reddening of the conjunctiva and a proven epidemiological link to another laboratory confirmed case [13].

A cluster is defined as a group of two or more cases that are epidemiologically linked. In this presentation of the data we count clusters and meta-clusters. A meta-cluster is defined as two or more clusters that are epidemiologically linked.

Results

A total of 94 clusters was reported in 2004, 18 of which were meta-clusters consisting of up to 197 cases. Ninety one of these clusters (97%) occurred from January to April 2004 (week 3-18). The majority of clusters consisted of 2-5 cases (70%). However, while restricting analysis to cases which met the definition described above, only 33 clusters could be confirmed for the year 2004. In Table 1, clusters from 2001-2004 with at least two confirmed cases are shown.

In January 2004 the GAF noticed the first cases with keratoconjunctivitis in some of its garrisons. Within four weeks, the number of cases - exclusively defined by the clinical symptom 'reddening of the conjunctiva' - increased from several hundred to several thousand. By the end of March 2004, 6378 cases had been registered, according to the GAF. Overall, 197 barracks had reported at least one case of conjunctivitis. Thirteen barracks were completely closed down and 28 barracks partially so between February and April 2006. Several control measures were implemented, such as disinfection of rooms and instruments and a quarantine period of 21 days for soldiers with conjunctivitis. The sensitive case definition used by the GAF was not changed to a more specific definition until mid-March (at least two of the following diagnostic findings: reddening of the conjunctiva, swelling of the plica semilunaris conjunctivae, swollen prae-auriculaer lymphnodes, petechial bleeding of the conjunctivae or opacity of the lenses and at least three of the following symptoms: sudden onset, one sided symptoms, itching, foreign body sensation or photophobia), and thus a rapid decline of cases was observed. The GAF reported taking 1300 eye and nose swabs for virology and antibody assays. Of these, 47 (3.6%) were positive for adenovirus, but only two were positive for the serotypes 8 and 17 [14-16].

From January to April 2004 (week 3-18) 1024 cases were reported to the RKI. Of these, 436 could not be confirmed according to data quality control and were excluded from further analysis. Of the 588 cases accepted for analysis, 115 were laboratory confirmed and 473 were epidemiologically confirmed; 551 cases (95%) were epidemiologically linked to a case diagnosed with EKC. Two hundred cases within three clusters (one meta-cluster included) could be linked to kindergartens and schools (26 cases with clinical and laboratory confirmation included), and 343 cases within 22 clusters (11 meta-clusters included) could be linked to the GAF (51 cases with clinical and laboratory confirmation included). Of 13 clusters, the LHDs reported a link between kindergartens or schools and the GAF. Table 2 shows all clusters with their links for the whole year 2004.

From week 10 to 14 (March 2004), young men between 18 -29 years old were the group primarily affected by EKC. An increased number of notifications from women of the same age group were registered between one and two weeks later. During week 14 the reported number of children (0-17 years old) of both sexes increased [FIGURE].

Of the 1024 cases with civilian and military background that were reported to the RKI 131 cases were confirmed by civilian laboratories. Seven cases (5%) were specified as serotype 8, and were all linked to two clusters from the GAF. The remaining samples were positive for adenoviruses but their types were unknown.

Conclusions

The clinical picture of EKC is not very specific and identical or similar syndromes may result from different causes such as infectious, allergic, toxic or physical irritation. The procedure of taking a conjunctival swab containing sufficient material for testing requires experience and can be very unpleasant for the patient [16]. Therefore laboratory confirmation of the diagnosis EKC may not always be carried out.

There may be further reasons for the low number of positive results, for example, that the samples were taken at a late stage of disease development or that samples were inadequately stored.

Table 1

Number of clusters with confirmed cases with epidemic keratoconjunctivitis, Germany, 2001-2004

Year of notification	2-5 cases		6-10 cases		11-50 cases		>50 cases	
	Number of:		Number of:		Number of:		Number of:	
	Clusters	Cases	Clusters	Cases	Clusters	Cases	Clusters	Cases
2001	0	0	0	0	3	61	0	0
2002	3	7	0	0	0	0	0	0
2003	1	2	2	17	1	31	1	262
2004	17	51	5	38	9	235	2	269

Table 2

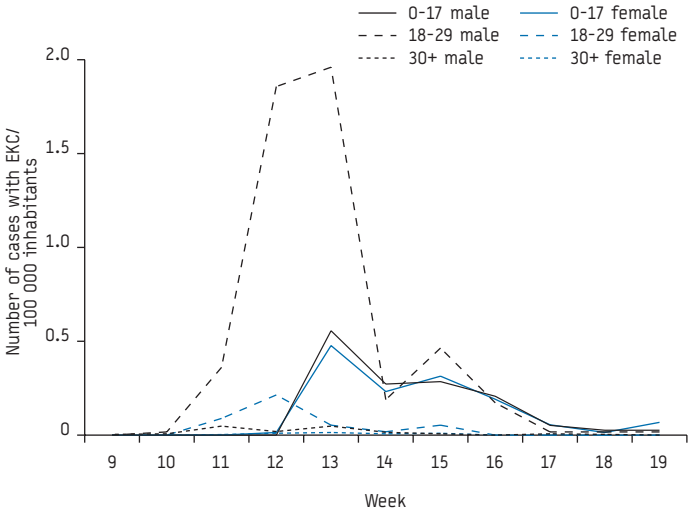
All clusters with confirmed cases with epidemic keratoconjunctivitis according to their link, Germany, 2004

Link	Number of clusters	Number of cases	Number of laboratory confirmed cases		Number of epidemiologically confirmed cases	
	N	N	N	%	N	%
Kindergartens/schools	4	212	27	13	174	87
German Armed Forces	27	372	53	14	319	86
Other*	2	9	3	33	6	67

*Including one residential home and one household

FIGURE

Incidence of confirmed epidemic keratoconjunctivitis (EKC) cases by age group (years) and sex in Germany, 2004



Nevertheless, this outbreak highlights the importance of receiving early laboratory confirmation for suspected cases. For the interpretation of diagnostic tests, basic knowledge of the meaning of sensitivity and specificity is essential, as well as the correlation of prevalence and the positive predictive value of a test. If it is assumed that a performed test has a sensitivity of 99% and a specificity of 95%, then a higher prevalence of a disease can affect the positive predictive value of a test profoundly. Thus a rise of the prevalence from 1% to 5% only can result in a change of the positive predictive value from 17% to 51%.

During this outbreak it became clear that a large but unidentifiable number of soldiers did not have EKC. Because of the small number of specified adenoviruses it can be assumed that a 'population' was tested with a low prevalence of adenovirus infections. Hence the positive predictive value was low and a number of tests delivered false positive results.

Our data clearly show that the population outside of the GAF was also affected [FIGURE]. The hypothesis that the outbreak began within the GAF and then spread to the civil population is supported by the chronological order of EKC affecting young male adults first, then young women, and finally children. Person-to-person transmission apparently took place when the young men were sent back to their own homes outside the garrisons. It is also possible that GAF was affected by the occurrence of conjunctivitis in the civilian population Germany, and that transmission was simply facilitated within the environment of the garrisons.

This is relevant with regards to the strategy for dealing with outbreaks of infectious disease within the military service. On the one hand, keeping infected soldiers confined to barracks may increase the risk of infection for other soldiers. On the other hand, sending affected military personnel home may result in the spread of the disease to the civil population. While the burden of disease seems to have been limited in this particular situation, the consequences in outbreaks caused by other pathogens could be more severe. In the outbreak reported here, the GAF and RKI cooperated closely from the outset, and successfully limited the impact on the civilian population. However, to prepare for future challenges, public health institutions within the GAF and at national level should formulate guidelines and common control strategies to enhance cooperation.

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OUTBREAK OF *SALMONELLA* KEDOUGOU IN NORWAY ASSOCIATED WITH SALAMI, APRIL-JUNE 2006

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Nasjonalt folkehelseinstituttet (the Norwegian Institute of Public Health, NIPH) has recently completed the investigation of a nationwide outbreak of *Salmonella* Kedougou infections. The outbreak was detected by the reference laboratory at NIPH on 18 May 2006 after verifying six cases without travel history during the previous month [1]. On 22 May, an urgent enquiry was sent out through Enter-net, the international surveillance network for the enteric infections Salmonella and VTEC O157 (http://www.hpa.org.uk/hpa/inter/enter-net_menu.htm). Other participating countries indicated that they had no cases, suggesting a source in a food product sold mainly in Norway.

A total of 54 cases were verified by the national reference laboratory by 28 June (Figure 1). The case definition was patients with *S.* Kedougou verified in faeces, blood or urine by the national reference laboratory, onset of symptoms between April and June 2006 and with no history of travel. The patients' ages ranged from 9 months to 90 years, with a predominance of cases in the age groups 0-9, 50-59 and 80-89 years. Twenty six cases were female and 28 male (Figure 2). The onset of symptoms was 11 April for the first case and 6 June for the last case. The cases were spread over 37 out of 436 municipalities in Norway. No cases were reported from the northern part of the country. One of the patients, a man aged between 50 and 59 years with serious underlying illness, died due to *Salmonella* sepsis. All the patients had diarrhoea.

Based on answers from pilot interviews with the first 12 patients, a more detailed questionnaire focusing on spices and salami types was prepared and distributed to the patients. Food samples were collected from the patient's homes by the NFSA.

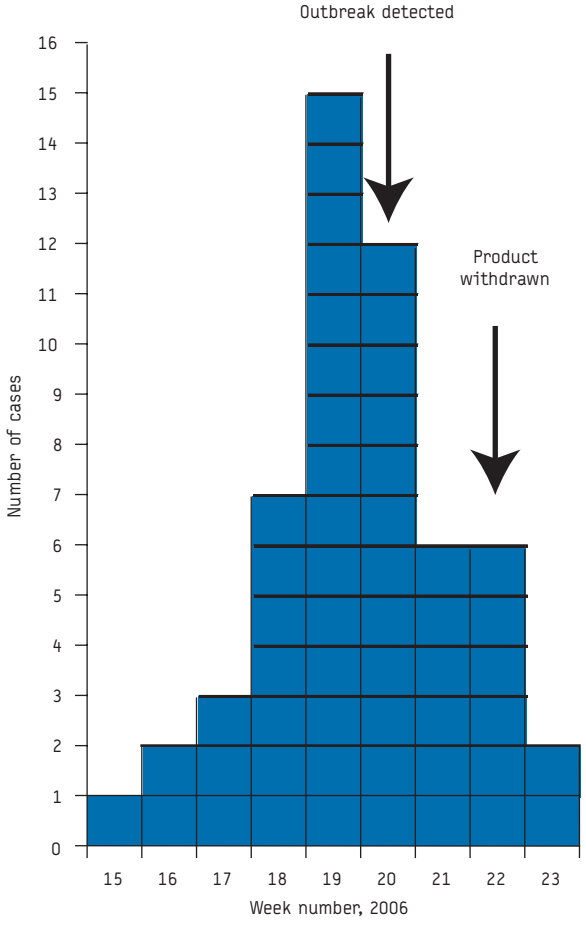
S. Kedougou was isolated from an opened package of a particular barnd of Danish-style salami on 1 June, and on 3 June the preliminary results from a case-control study (at that time 6 cases and 12 matched controls) supported the suspicion that this specific salami product was the probable source of the outbreak. On 4 June *S.* Kedougou was isolated from an unopened package of the same product from a shop, and NFSA recalled the product from the market the same day.

The product was produced in Norway for the Norwegian market only, and was not distributed in northern Norway, which explains the geographical distribution of the cases. Further investigation did not reveal how the contamination of the production batch could have occurred.

Kedougou is a very rare serotype in Norway. The isolates in this outbreak are fully sensitive to antibiotics. Only 7 cases were reported in Norway between 1979 and 2005, of which 6 had a history of travel abroad during the incubation period. In 2005, only 48 cases of this serotype were reported to Enter-net, accounting for 0.05 % of the total number of *Salmonella* isolates reported.

FIGURE 1

Cases of *Salmonella* Kedougou in Norway associated with salami, by week of symptom onset, April-June 2006, Norway. n=54



Acknowledgements:

The outbreak investigation was a collaboration between NIPH (Department of Infectious Disease Epidemiology and Department of Foodborne Infections), Norwegian Food Safety Authority (NFSA), the National Veterinary Institute and municipal medical officers.

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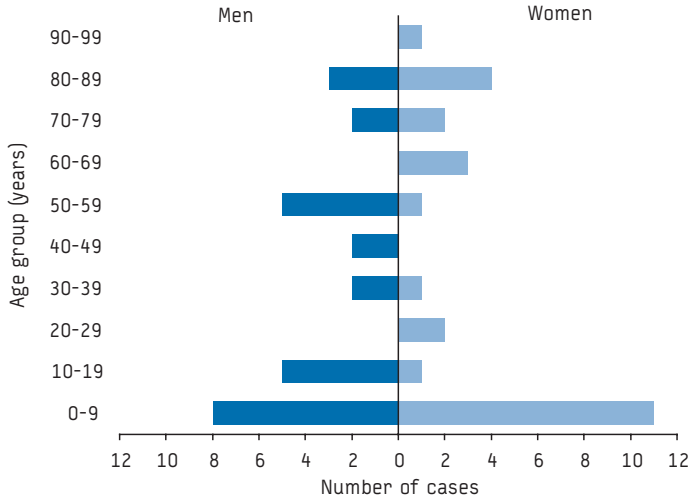
FIGURE 2

Cases of *Salmonella* Kedougou in Norway associated with salami, by age and sex, April-June 2006, Norway. n=54



Botulism associated with vacuum-packed smoked whitefish in Finland, June-July 2006

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On 29 June 2006, a 65 year old woman fell ill with vomiting and diarrhoea in southern Finland. The next day she developed muscular weakness of her upper and lower limbs, and was admitted to hospital. She developed difficulty in breathing and required mechanical ventilation in an intensive care unit for one week. The patient is now recovering, but still has some difficulties in swallowing, and is not yet able to walk. The patient did not receive botulinum antitoxin, since the symptoms had already begun to resolve upon diagnosis. The patient's husband also had diarrhoea on 29 June and later had some difficulties in swallowing, but no other neurological symptoms were observed. He was admitted to hospital for one night (1-2 July) because of diarrhoea.

Serum samples from the female patient taken on 30 June and 1 July were positive for botulinum neurotoxin by mouse bioassay, and the neutralisation test suggested that the patient's illness was caused by botulinum toxin type E. Gastric fluid and serum samples taken on 4 July did not yield neurotoxin or *Clostridium botulinum*. No specimens were available from the husband, as botulism was not diagnosed during his hospital stay, and he was not called back to hospital for specimens.

An interview with the husband revealed that the couple had eaten smoked vacuum-packed whitefish on 28 June. The wife had eaten most of the fish, and the husband ate only a small portion. The whitefish had been imported from Canada, but smoked and packed in Finland. There was no leftover fish for microbiological examination. Flush samples were taken from the fish's plastic packaging, but they were negative for *C. botulinum* by PCR [1] and culture.

The suspected fish product was recalled by the manufacturer, and production of the product was suspended. The national and local food control authorities inspected the production plant and the distribution centre. The entire manufacturing process and storage temperatures throughout the cold chain, including the retail outlet, were investigated. The inspections did not reveal any factors that could have created an increased risk of botulinum neurotoxin production. Microbiological analysis of ten vacuum-packed fish made from the same raw fish batch that was used to make the product eaten by the patient, and from fish from earlier and later batches, were all negative for *C. botulinum*.The investigators have therefore hypothesised that there may have been storage temperature abuse at a later stage, such as in the retail outlet or the home. After inspection of the facility and microbiological examination of fish samples, production of the product has started again.

C. botulinum type E is naturally highly prevalent in aquatic environments and fish [2,3], leading to a high risk of contamination. The hot-smoking processes are usually too low to eliminate botulinum spores [4]. Growth and toxin production from spores in vacuum-packed smoked fish products with anaerobic atmosphere and limited preservative factors is likely during extended storage at temperatures above 3°C. Therefore the most important factors controlling *C. botulinum* growth and toxin production are efficient heat treatments, restricted shelf life and continuous storage below 3°C.

Human botulism is a very rare disease; the most recent case to be reported in Finland before the case mentioned here occurred in 1999 [5], A similar outbreak that affected two people in Germany in 1997 is described in the literature [6]. However, it is of utmost importance that physicians remain aware of the disease as a possible diagnosis. Botulism should be considered whenever a patient develops neurological symptoms that include blurred vision, difficulties in swallowing or speech and symptoms of descending flaccid paralysis. This should be followed by appropriate epidemiological and laboratory analyses to confirm the diagnosis and to improve the epidemiological understanding of the disease [7].

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OUTBREAK OF INVASIVE MENINGOCOCCAL DISEASE AMONG SOLDIERS IN SKWIERZYNA, POLAND, MARCH 2006

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The outbreak

Four cases of invasive meningococcal disease were reported between 22 and 24 March 2006 in newly recruited soldiers in Skwierzyna in Lubuskie, a western province of Poland. Two soldiers had been referred to a physician on 21 March with influenza-like symptoms, and one of them had consulted a physician in a local hospital, but was not admitted to hospital for treatment. On 22 March both soldiers had sudden onset of petechial rash, general discomfort and fever. They were immediately admitted to the intensive care unit of the regional hospital in Gorzow Wielkopolski. A third soldier had similar symptoms of malaise and signs of meningeal irritation on 23 March. He was admitted to the local hospital for observation, where he developed a petechial rash. A fourth soldier developed pharyngitis on 23 March, and was also admitted to the local hospital for observation, where he developed severe headache and vomiting on 24 March. Both soldiers were admitted to the intensive care unit in Gorzow Wielkopolski immediately after symptom onset. Preliminary investigation of blood and cerebrospinal fluid samples at the National Reference Centre for Bacterial Meningitis revealed that all cases were caused by *Neisseria meningitidis* serotype C.

Further investigations

An investigation was begun, led by epidemiologists at the Wojewodzki Osrodek Medycyny Prewencyjnej (Military Preventive Medicine Centre) in Wroclaw. The laboratory facilities of three military centres (Wroclaw, Bydgoszcz and Krakow) and the provincial Sanitary-Epidemiological Station in Gorzow Wielkopolski were used for this investigation. All four soldiers had recently been recruited to this army unit and had lived in the army barracks for 14 days. If the sub-unit living in the barrack is considered as the exposed group, the overall attack rate was 4/250 (1.6%). The affected soldiers lived in four different rooms on the same corridor (Table 1).

Investigation of throat swabs collected from close contacts (roommates, n=61)) between 23 and 27 March revealed that six were carriers of N. meningitidis serotype C. Molecular typing indicated that strains collected from all four cases and six contacts were identical (serogroup C, clonal type ST11/ET37, serotype PFGE A2) and were identical to a strain isolated in 2005 from a soldier residing in the same army unit. Samples collected from all other residents of the Skwierzyna Army Unit (n=1300) allowed isolation of different *N. meningitidis* strains.

Control measures

The affected army sub-unit was quarantined from 24 March until 4 April and all soldiers of this sub-unit (n=250) received prophylactic treatment of 500 mg of ciprofloxacin. After confirmation of the bacterial strain causing the outbreak, prophylactic treatment was extended to all residents of the unit, including civil personnel (n=1300). Movement of soldiers within and outside the army unit was restricted between 21 March and 4 April. All staff members in the intensive care unit in Gorzow Wielkopolski were given rifampicin as prophylactic treatment.

Discussion

Invasive meningococcal disease is an acute bacterial disease, characterised by early onset of symptoms of meningitis, septicaemia and/or other syndromes, and a moderate to high case-fatality rate [1]. In recent years, the incidence of meningococcal disease has been decreasing in Poland, but the proportion of cases caused by group C strains has been increasing (Table 2), causing small-scale outbreaks each year [2]. The incidence of meningococcal disease is underestimated in Poland. Surveillance of the disease was implemented in the 1970s, and was based on passive reporting of diagnosed cases by physicians to local health departments. Up to 2004, only neuroinfection cases were reported. Since 2004, all cases of meningococcal disease have been mandatorily reportable. Meningococcal vaccine is recommended for children over 2 months of age, and for all people without a spleen, but is not available free of charge. According to recent official data, fewer than 2000 doses of meningococcal vaccine have been administered each year. Meningococcal vaccine uptake is low compared with other vaccines which are also not usually available free of charge, such as *Haemophilus influenzae* b (given to 7% of children under 4 years in 2004) influenza (over 1.3 million doses given to people of all ages in 2004), streptococcal vaccine (given to 6658 people in 2005) and chickenpox vaccine (given to 4452 people in 2005). Poland's routine childhood immunisation schedule can be seen at the World Health Organization's Centralized Information System for Infectious Diseases (CISID) website (http://data.euro.who.int/cisid/)

The outbreak described here was extensively reported in the Polish media, making the investigation and implementation of control measures very difficult. All four patients were severely ill with fulminant septicaemia (three cases) or meningitis (one case), but there were no deaths. The index patient is still in intensive care and a rehabilitation of several months is foreseen.

TABLE 1

Number of soldiers at risk and attack rates by barrack room, Skwierzyna Army Unit, Poland, 21-23 March 2006

Room number	Area (m²)	No. of soldiers sleeping in room	No. of cases	Attack rate
1	38	18	1	5.60%
2	36	16	1	6.30%
3	36	16	1	6.30%
4	38	15	1	6.70%

TABLE 2

Officially reported cases of meningitis caused by *N. meningitidis*, Poland, 1996-2004 [3]

	1996	1997	1998	1999	2000	2001	2002	2003	2004
Number of cases	144	140	129	121	110	100	90	76	119
Incidence per 100 000 inhabitants	0.4	0.4	0.34	0.33	0.28	0.27	0.24	0.2	0.31
Proportion of cases with serogroup confirmed	29.9	36.4	41.9	38.8	35.5	25	24.44	51.3	58
Proportion of serogroup C	23%	18%	9%	11%	18%	28%	32%	36%	27%

Since this is not the first outbreak of invasive meningococcal disease among newly recruited soldiers in Poland, a discussion of how to protect this population group has begun at national level, expressing a need to better monitor their health status and adopt procedures for immediate prophylaxis and treatment. Other countries, such as the United Kingdom, have introduced vaccination against meningococcal disease after establishing that armed forces recruits had a significantly increased risk of disease when compared with age-matched civilian counterparts [4].

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Twenty years of active paediatric surveillance in the UK and Republic of Ireland

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In July 2006 the British Paediatric Surveillance Unit (BPSU, http://bpsu.inopsu.com/) celebrated its twentieth year of surveillance. The unit was founded in 1986 by the Public Health Laboratory Service (now the Health Protection Agency), the Royal College of Paediatrics and Child Health, the Institute of Child Health (London), the Royal College of Physicians (Ireland) and the Scottish Centre for Infection and Environmental Health (now Health Protection Scotland). The unit's aim was, and is, to undertake surveillance of rare conditions in childhood (0 to 15 years), including infections, and to provide a mechanism to rapidly investigate acute public health events affecting children.[1] The unit was created to address concerns from paediatricians and communicable disease consultants that conditions such as Reye's syndrome, haemolytic uraemic syndrome (HUS), Kawasaki disease and the then newly emerging condition of paediatric-AIDS were not being reported to existing 'passive' surveillance systems in sufficient numbers to enable meaningful analyses of data. The BPSU therefore set about establishing an 'active' surveillance system, seeking monthly reports from all consultant paediatricians in the United Kingdom and Ireland. Clinicians are asked to report any cases from a menu of conditions listed on the monthly report card and are asked to choose 'nothing to report' if no cases had been seen.

This active surveillance system has encompassed over 70 conditions during its first 20 years of operation, many of which have been related to infection. Compliance with reporting to the system has been high, with an average of over 90% of monthly reports completed per year [1].

The effectiveness of the BPSU's surveillance methodology has had a major impact on national policy on infectious diseases and related conditions. The BPSU has made important contributions to the monitoring of childhood diseases targeted by vaccination programmes as well as the safety of vaccines. Findings from reports of meningoencephalitis after MMR contributed to the withdrawal of the Urabe strain of the vaccine's mumps component [2]. Reports of congenital rubella contribute to monitoring the effectiveness of the national immunisation programme and the impact of the recent decline in coverage of MMR vaccination in the UK [3]. Surveillance of subacute sclerosing panencephalitis undertaken through the BPSU over 15 years, has provided good evidence that this known complication of measles infection is not associated with receipt of the measles component of the MMR vaccine [4]. BPSU data have contributed to evaluation of the effectiveness of the newly introduced *Haemophilus influenzae* b vaccine. Finally, a study of the incidence and severity of varicella infection in children admitted to hospital provided a baseline of the disease burden due to this infection in the pre-vaccination era and contributed to informing the development of national vaccination policy [5].

Throughout its history the BPSU has also provided a mechanism for responding to and investigating emerging public health concerns. Emerging diseases are usually rare and may remain unrecognised, potentially allowing the condition to spread. The HUS survey, undertaken in the 1980s through the BPSU, was one of the first studies to confirm the link between *Escherichia coli* 0157 and paediatric HUS in the UK. The study was replicated in the late 1990s in response to the Pennington Report [6], which highlighted the effectiveness of the BPSU methodology in identifying *E. coli* 0157 outbreaks. In 1997, a BPSU study clarified that diagnosed hepatitis C in children was largely the result of horizontal transmission through blood products rather than vertical transmission from mother to child [7]. More recently, childhood tuberculosis and malaria infection have been included in BPSU surveillance. In response to public health concern about the potential impact of variant Creutzfeld-Jakob disease (vCJD) on children in the UK, the BPSU is currently undertaking surveillance for cases of progressive intellectual and neurological deterioration in order to identify cases of vCJD and has reported six cases in children since 1997 [8].

Findings from the BPSU have influenced national screening policies. The BPSU's surveillance of HIV in children contributed to the policy introduced in England in 2000 to offer antenatal screening to all pregnant women [9]. Information about disease prevalence and the burden of disease for other neonatal and congenital infections, such as toxoplasmosis, herpes simplex and Group b streptococcal infections, has contributed to decisions not to initiate screening programmes for these conditions.

In summary, on review after 20 years of operation, there is evidence that the system is acceptable, sustainable and is producing high quality data about a range of relatively rare but important childhood conditions that are informing and influencing a variety of activities concerned with child health in the UK. The success of the BPSU surveillance system has encouraged similar surveillance schemes in the UK and abroad. In 1998, the International Network of Paediatric Surveillance Units (INoPSU, http://www.inopsu.com/) was established. This network now covers 14 countries (including eight within the European Union), and involves 10 000 paediatricians covering a population of 50 million children [10].

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Case of Lassa fever imported into Germany from Sierra Leone

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A 68 year old man who recently travelled from Sierra Leone to Germany via Belgium has been diagnosed with Lassa fever [1].

The patient had a history of progressive neurological deterioration over several months in Sierra Leone. On 5 July 2006, he developed high fever and his neurological symptoms worsened. On 10 July the patient travelled by air from Freetown (Sierra Leone) via Abijian (Ivory Coast) to Brussels, Belgium. All of this journey was in the same aeroplane. In Brussels, the patient changed plane for the connecting flight to Frankfurt, where he arrived on 11 July.

Immediately after arriving, he was taken to the university hospital in Münster. On 16 July, the patient's condition worsened, and he was intubated and treated in isolation. Although the patient's clinical presentation was in accordance with his known underlying disease, additional tests for tropical infectious diseases were carried out. On 20 July, IgG for Lassa virus was detected in a cerebrospinal fluid sample and RT-PCR was positive. On 21 July, an RNA-PCR for Lassa virus was detected in blood, urine and sputum.

A message was posted on the confidential European Early warning and Response System on Friday 21 July. While the risk to co-passengers is judged to be low, passengers on the following flights are being traced and contacted to inform them about the risk.

- SN Brussels Airlines flight SN 207 on 10 July from Brussels (Belgium) via Freetown (Sierra Leone) to Abidjan (Cote d'Ivoire) in seat rows 23 to 29
- SN Brussels Airlines flight SN 207 on 10 July from Freetown (Sierra Leone) via Abidjan (Cote d'Ivoire) to Brussels (Belgium) in seat rows 23 to 29
- SN Brussels Airlines flight SN 2607 on 11 July, which departed Brussels (Belgium) to Frankfurt (Germany) at 0630, all seats

The patient has been transferred to a special treatment centre in Frankfurt. Flight crew members as well as aeroplane cleaning personnel are being contacted by public health authorities.

Since 1970, at least 16 cases of Lassa fever have been imported into Europe or North America; in none of these has onward transmission to another person been reported. The last reported imported case into Europe was in 2003 in a soldier from the United Kingdom who had been serving in Sierra Leone [2]. In 2000, a European meeting to discuss the management of Lassa fever cases was held, after several importations in 1999/2000 [3,4,5,6].

The World Health Organization has produced a Lassa fever fact sheet which can be found here: http://www.who.int/mediacentre/factsheets/fs179/en/

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Unexpected increase in case fatality of invasive group B streptococcal infections in infants in Norway, January-July 2006

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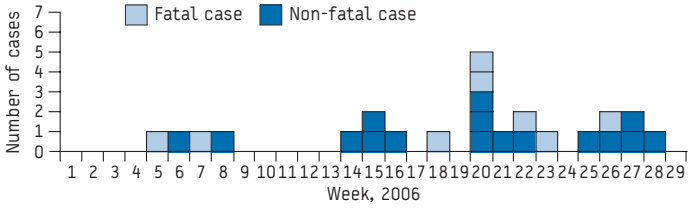
A marked increase in case fatality has been observed among reported cases of invasive group B streptococcal infections (GBS) in infants younger than 90 days old (thereafter referred to as 'infant') in Norway since the beginning of 2006. Twenty four cases of GBS in infants were reported to the Norwegian communicable disease notification system (MSIS) between 1 January and 21 July, and eight cases (33%) have been fatal [1].

The 24 cases were reported from nine hospitals: thirteen of the cases were in boys (54%). Four of the eight deaths were in girls and four in boys, and occurred in six major hospitals in southern Norway. The distribution of all reported cases of infant GBS infection does not show any difference from previous years in relation to geographical distribution. Clinical data were available for all cases: three cases developed meningitis (13%), fourteen had signs of sepsis (58%), and two cases had both (8%). One case had pneumonia (4%), and other clinical symptom has been reported in four cases (17%). Nineteen cases occurred in the second quarter of 2006, between the 15th and 29th week in 2006 (Figure 1).

Figure 1

Fatal and non-fatal cases of invasive GBS infection in infants under 90 days, by week, Norway, weeks 1-29, 2006 (n=24)

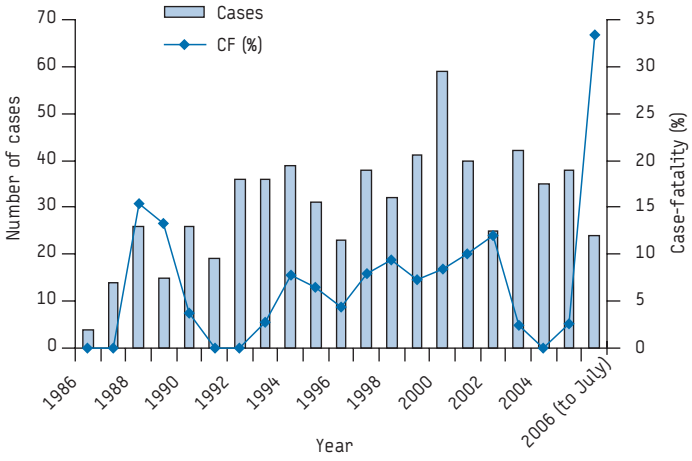


The average incidence rate of invasive GBS infections was 0.7/ 1000 live births (range 0.45-1.0) in 2000-2005, comparable with recent findings in other European countries [2]. The estimated incidence rate in the first six months of 2006 based of the number of cases reported as of 21 July is 0.85/ 1000 live births. The case-fatality (CF), however,

is nearly six times higher than the average case fatality (5.8%) reported in the years 2000-2005 (Figure 2). Further investigation is pending to establish what factors may have led to this increase in case fatality. Six of the eight deaths reported in this recent period were associated with early onset disease (0-6 days; CF=46%), and two with late onset disease (7-90 days; CF=18%). Recently, an overall case fatality of 4% has been reported in Germany [3] and 10% in the United Kingdom and Ireland [4].

Figure 2

Cases of invasive GBS infection and case fatality (%) in infants under 90 days, by year, Norway, 1986-2006



The Norwegian Institute of Public Health has contacted all maternity, neonatal, paediatric and hospital microbiology departments in Norway to raise awareness of the disease and to enhance the surveillance of invasive GBS infection which has been a notifiable disease in Norway since 1986. Detailed characterisation of isolates from all cases reported in 2006 referred to the national reference laboratory is ongoing. An epidemiological study will be launched to identify factors that may have contributed to the increase in case fatality. An enquiry was sent via the European Union's Early Warning and Response System (EWRS) on 21 July to find out whether other countries have recently observed a similar increase in case fatality among infants with diagnosed systemic GBS infection. So far we have not received such information.

Guidelines issued in 1998 by the Norwegian Society of Gynaecologists and Obstetrics specify the use of penicillin prophylaxis during delivery for one or more of the following: previous newborn with GBS infection, recurrent GBS urinary tract infection, preterm rupture of the membranes, signs of infection or fever during delivery [5]. Norwegian guidelines for antenatal care from the Directorate for Health and Social Affairs in 2005 do not recommend universal antenatal microbiological screening for GBS carriage [6]. Although the reason for the increased case fatality has not yet been identified, the Norwegian health authorities are considering a revision of current policies.

Any relevant information about recent increase in case fatality in infants with systemic and severe invasive GBS infection in other countries would be appreciated, and should be sent to the corresponding author (details above).

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Wound infections due to *Vibrio cholerae* in Sweden after swimming in the Baltic Sea, summer 2006

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In recent weeks, three people in Blekinge County in southeast Sweden were reported to have developed mild to severe wound infections caused by non-agglutinating (not O1 or O139) and non-toxin-producing *Vibrio cholerae* bacteria after outdoor water contact (Baltic Sea and possibly an irrigating pond). All 3 people had skin breakages, and two had other underlying diseases.

Environmental water samples from various sources have been analysed, and several samples from Baltic Sea coastal waters, and from four lakes have tested positive for non-agglutinating and non-toxin-producing *V. cholerae*. These strains have not yet been compared to those found in humans. The weather has been hot and sunny in Sweden during July, and unusually high surface water temperatures of over 20°C recorded.

There are 200 serotypes of the bacterium *V. cholerae*, of which O1 and O139 are toxin-producing and cause classical cholera with profuse, watery diarrhoea (sometimes exceeding 20 litres per day). Variants of the bacteria that are non-agglutinating and non-toxin-producing may rarely cause wound infections, mild diarrhoea and external otitis in people with skin breakages who bathe outdoors in warm, brackish water. The optimal growth conditions for these bacteria include a salinity of 0.4-1.7% and a water temperature exceeding +20°C. In such conditions the bacteria have been found in the Baltic Sea.

Classical cholera has been a notifiable disease in Sweden since 1919, and all forms of *V. cholerae* infection became notifiable on 1 July 2004. The last case of imported classical cholera to Sweden was notified in 2004. The same year, a severe, septic wound infection with non-agglutinating and non-toxin-producing *V. cholerae* was contracted after a patient bathed in an outdoor hot tub containing water from the Baltic Sea that had been heated to about 38°C [2].

The Swedish Institute for Infectious Disease Control is now advising people with any skin breakages not to bath and swim outdoors. A message has been posted on the European Union's Early Warning and Response System to inquire about *V. cholerae* wound infections recently seen in other European countries. Information may be sent by email to the author.

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Diversity of needle exchange provision in the UK: findings from a national survey

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Needle exchanges are key to reducing transmission of bloodborne viruses (BBVs) in injecting drug users (IDUs) through the provision of sterile injecting equipment and related interventions [1]. In the United Kingdom (UK), the extent and type of service provision by needle exchanges has received little attention [2]. Information on the availability, use and coverage of harm reduction measures for IDUs is needed to help assess the effectiveness of existing, and inform the development of future, services [3]. A national survey of needle exchange facilities was undertaken in 2005, and reports of the findings from Scotland have recently been released Scottish Executive [4]. The National Treatment Agency for Substance Misuse (NTA) has released summary finding from England and will shortly be publishing a report on the full findings [5]; results for Wales and Northern Ireland are not yet available.

The survey was initiated in response to the Department of Health's 2004 *Hepatitis C Action Plan for England* [6], and examined the extent, nature, and commissioning of needle exchange provision in the UK. Three postal questionnaires and three focus groups were used to collect quantitative and qualitative data from pharmacy exchange coordinators, non-pharmacy needle exchange providers and drug action team (DAT) coordinators, commissioning managers or their equivalents. Each country is split into DAT regions (149 in England and 22 in Scotland), which are partnerships responsible for overseeing and commissioning drug services at a local level. There was a good overall response rate, but incomplete questionnaires meant that some questions had a much lower response rate.

The survey identified 188 needle exchange facilities in Scotland, and at least 1326 in England; the total number of facilities in England could not be ascertained due to the lack of response from around a quarter of the DATs. Pharmacies made up 80% of services for which responses were received in England and 72% in Scotland. The remainder were specialist services, some of which were mobile or outreach in nature. There were only a small number of exchanges based in police custody facilities and hospital accident and emergency departments. Although there are benefits to having different types of services, both reports noted that pharmacy services should be developed to complement specialist services rather than as an alternative.

A low number of responses to questions on the distribution of injecting equipment made it difficult to estimate the national levels of needle and syringe provision. Overall, data suggested that 'on average, clients of specialist needle exchange services and pharmacy schemes were given the equivalent of approximately one syringe for every two days' [4]. Although pharmacies made up the majority of needle exchange facilities in both England and Scotland, approximately half of all syringe distribution was through pharmacy exchanges and half through non-pharmacy exchanges, with a notable variation in the amount distributed in different regions within both countries.

There was geographical variation in the types of injecting related equipment provided by services. The majority of services provided swabs, sharps bins and citric acid. English services were more likely to distribute filters, sterile water and vitamin C, while Scottish services were more likely to distribute wipes or swabs. There was also geographical variation in the provision of BBV interventions. For example, almost 80% of specialist services in northwest England reported offering hepatitis C testing, compared with under 20% in the southwest. Half of the specialist services in England offered on-site hepatitis B vaccination, compared with only 29% in Scotland. English centres were more likely to offer other BBV interventions such as testing for HIV, hepatitis C or hepatitis B (Table). However, data were not collected on the uptake of BBV interventions and therefore it was not possible to assess the extent of BBV testing or vaccination at these services.

A recurring theme in both reports was the inconsistency in services provided by needle exchanges. The English report concluded that 'what interventions injectors received was often not determined by their needs but by where they lived'.[5]

Transmission of BBVs among IDUs continues to be a problem in the UK [7]. It is important that needle exchanges are developed to deliver a range of services to clients, including the provision of sufficient sterile injecting equipment and other BBV interventions (such as vaccination, testing, counselling and awareness raising), and that the effectiveness of these services at preventing the spread of BBVs among IDUs are also evaluated. The reports from Scotland and England make a number of recommendations to develop standards for needle exchange services, including guidelines for paraphernalia (drug taking equipment) distribution.

Table

Proportion of specialist needle exchanges offering bloodborne virus interventions in England and Scotland.

Bloodborne virus intervention	Proportion of exchanges providing service	
	England	Scotland
Hepatitis A vaccination	25%	16%
Hepatitis B vaccination	50%	29%
HIV testing	31%	29%
Tetanus vaccine	11%	2%
Hepatitis C testing	43%	40%
Hepatitis B testing	42%	33%

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Vibrio vulnificus wound infections after contact with the Baltic Sea, Germany

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Health authorities in the state of Mecklenburg-Vorpommern, Germany have reported three cases of wound infections with the bacterium *Vibrio vulnificus* so far this summer. The patients had typical symptoms of vibrio wound infections, and these developed after bathing in the Baltic Sea. All of them had underlying chronic illnesses. One patient was a 57 year old diabetic, one was a 72 year old man with coronary heart disease and chronic leg oedema, and

one was a 76 year old man with a chronic skin ulcer. All were treated with antibiotics and are recovering. Two patients' wound samples tested positive for *V. vulnificus*. Since the end of July 2006, water samples taken from 9 out of 10 bathing places along the Mecklenburg-Vorpommern Baltic Sea coast have consistently tested positive for *V. vulnificus* (testing is done every 14 days at these locations). *V. alginolyticus* and *V. parahaemolyticus* have also been detected, but so far, there have been no reports of human infections with these species [1].

In summer 2003, two cases of wound infections with *V. vulnificus* were also reported in Mecklenburg-Vorpommern [2]. In both cases, the patients also had underlying illnesses. One of the patients, a 50 year old man, suffered from diabetes mellitus. The other patient, a 62 year old woman, suffered from liver cirrhosis and died after developing the wound infection. Both had had open wounds on the legs when they bathed or waded in the sea before illness onset.

Other vibrio infections in Europe linked to Baltic Sea

In recent weeks, three people in southeast Sweden were reported to have developed mild to severe wound infections caused by non-agglutinating (not O1 or O139) and non-toxin-producing *V. cholerae* bacteria after bathing in the Baltic Sea, and possibly an irrigating pond. All three had skin breakages, and two had other underlying diseases [3]. In Denmark this year, there have so far been reports of two children (both immunosuppressed) with wounds infected with *V. alginolyticus* and *V. parahaemolyticus*, and one fatal case of *V. vulnificus* wound infection in an adult. All of these cases were linked to bathing in the Baltic Sea [4].

Discussion

Vibrio are facultatively anaerobe Gram negative bacilli from the Vibrionaceae family, which are medium to highly halophile (requiring salt). Several different species belong to the genus *Vibrio*: *V. vulnificus* and *V. cholerae* among others. Vibrio bacteria can multiply in salty water, especially at temperatures over 20°C, which is currently the case in many areas of the Baltic Sea. No German coastal sea water samples have yet tested positive for *V. cholerae*.

Seafood containing vibrio bacteria can cause diarrhoea if eaten raw. If open wounds come into contact with sea water, vibrio bacteria can infect the wounds. Elderly and immunosuppressed people (e.g., with diabetes mellitus or liver disease) are at particular risk of infection. Without medical attention, superficial wounds can spread, necrotise and cause septicaemia. For this reason, prompt diagnosis, wound care, and appropriate antibiotic therapy are important, even if a vibrio infection is only suspected.

It should be stressed that people with open wounds and underlying chronic illnesses or who are immunologically compromised should not have contact with sea water. Vibrio infections should be considered in the differential diagnosis if there are supporting clinical symptoms. Patients presenting with wound infections should be asked whether they have had contact with sea water and if so, appropriate therapy needs to be prescribed.

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Outbreak of *Salmonella* Enteritidis infections in people attending a village event in Latvia

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An outbreak of gastroenteritis due to *Salmonella* Enteritidis associated with an outdoor public holiday event occurred in a small village in southern Latvia on 21 July 2006. The outbreak lasted from 22–25 July. Descriptive and analytical epidemiological investigations were conducted to determine the extent of the outbreak, and to identify outbreak-related risk factors. Of approximately 260 people who attended the event, 107 participants were interviewed and 49 people fulfilled the criteria of an outbreak case (attack rate 46%). Stool specimens from 26 people including 17 kitchen workers, were microbiologically tested, and eight specimens were found to be positive for *S.* Enteritidis. The retrospective cohort study revealed that a fried pork dish made with raw egg was the likely cause of the outbreak (RR: 7.8, 95% CI 5.2-11.78; P=<0.001).

Outbreak background

A cluster of three cases of gastroenteritis with onset on 22 July in patients from the same area was reported to the local branch of the State Agency "Public Health Agency" in Jelgava (PHA, Valsts agenturas "Sabiedribas veselibas agentura" Jelgavas filale) on 24 July 2006. The investigation revealed a relationship between the cases and attending an event in small village X on 21 July. On 24 July it was decided by public health authorities that a full investigation should be carried out to determine the extent of the outbreak and to identify the outbreak cause by using a retrospective cohort study.

Outbreak case definitions

Probable case

A probable case was defined as a person who attended the event in village X on 21 July, ate dishes served there, and then became ill with symptoms of diarrhoea.

Confirmed case

A confirmed case was defined as a person who attended the event in village X on 21 July, ate dishes served there, and then became ill with symptoms of diarrhoea and had a microbiologically confirmed *S.* Enteritidis infection.

An exposure was defined as consumption of a food item prepared and served by the staff of restaurant Y, which prepared all the food available at the event. The food items available included two different soups, smoked sausages, a rissole dish made from salad with cut potatoes and other boiled vegetables, pickled cucumbers, boiled eggs and meat products mixed with mayonnaise, braised cabbage, bread, pâté with bacon, fried pork (fried with raw egg), cake, vegetables (tomatoes and cucumbers), beer, coffee and soft drinks (made up on site from syrup and water).

Patients who developed diarrhoea (with or without vomiting), abdominal pain or fever in the four days after attending the event were considered to have been ill with acute gastroenteritis.

The municipality provided a list of all the people who participated in the public holiday event in village X (n=260). Information about the outbreak was released to the media in order to invite participants to come forward for interview. A total of 107 people were considered for the cohort analysis: eight were contacted in hospital and 99 were contacted at home. A questionnaire was developed at the local branch of PHA using Epi Info 3.2.2. Interviews were carried out face to face

or by telephone, and included questions on basic demographic data, symptoms and clinical signs, date and time of clinical onset, duration of illness, admission to hospital and food history, which included using the list of food items available at the public holiday event.

We compared the food-specific attack rates (AR) for each food item on the list among the exposed and the non-exposed cohort members in the univariate analysis (all statistical tests, including chi-square, 95% confidence interval and P value). The measure of association was the relative risk (RR).

Results

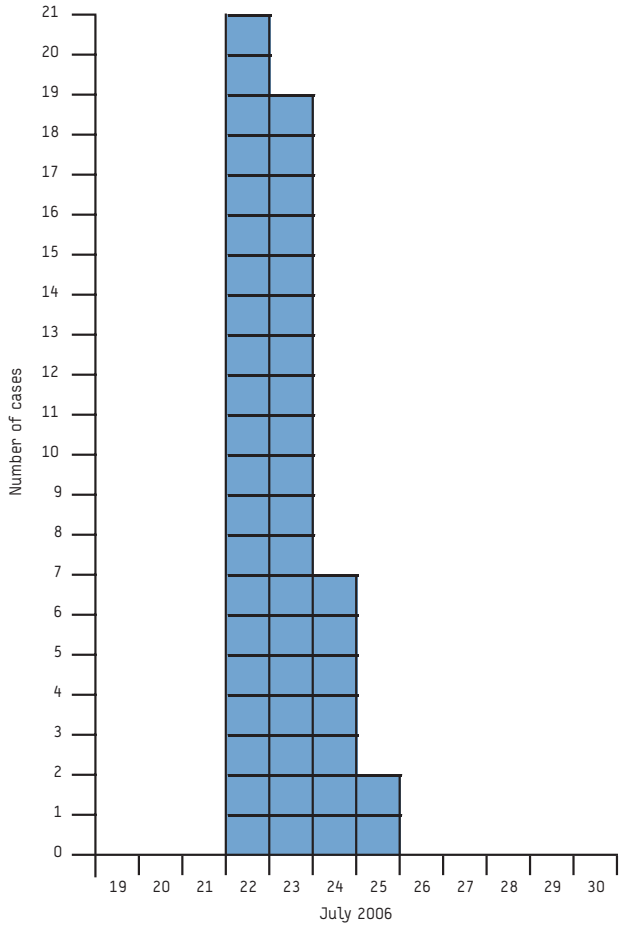
Of approximately 260 people who attended the village event, 107 participants were interviewed and 49 people fulfilled the criteria of an outbreak case (attack rate = 46%). Stool specimens from 28 people, including all 17 kitchen workers from restaurant Y, were microbiologically tested, and eight specimens were found to be positive for *S.* Enteritidis.

On 27 July, a clinical microbiology laboratory reported a cluster of stool samples positive for *S.* Enteritidis.

The local food safety authority was regularly updated about the situation, so that it could perform control measures in the implicated restaurant Y, which had prepared and served food for the participants of the event.

FIGURE

Cases of *S.* Enteritidis infection by date of symptom onset, after attending a village public holiday event in Latvia on 21 July 2006 (n=49)



Analysis

The questionnaires were completed for all cohort members. Women made up 65 (61%) of the 107 cohort members. The median age was 42 years (range 2–70). The outbreak lasted from 22–25 July, peaked on July 22 and indicated a common point source outbreak.

Forty nine patients in the cohort met the case definition of an outbreak case (attack rate (AR) = 46%). Among these 49 cases were 29 women (59%) and 20 (41%) men, and the median age was 39 years (range 2–70). The case distribution by age group and sex is illustrated in Table 1.

Stool specimens from 26 people, including eight symptomatic participants, two symptomatic kitchen workers of restaurant Y, 15 asymptomatic kitchen workers and one asymptomatic participant, were tested for salmonella, and eight specimens, including two from kitchen workers, were found to be positive for S. Enteritidis and fulfilled the definition criteria of a confirmed outbreak case.

In addition to diarrhoea, 20 patients (41%) reported nausea, 16 patients (33%) reported vomiting and 34 patients (69%) reported fever. The mean duration of illness was 5 days. Nine patients were admitted to hospital. All 49 patients recovered.

Epidemiologists from the local branch of PHA collected six table eggs from restaurant Y's kitchen, where all meals for the public holiday event had been prepared. The eggs were from the same supplier as those used for the event, but were from a later batch. No other food item served at the event was available for microbiological examination at this time. Salmonella test results for the eggs were negative.

During the epidemiological investigation, it was established that the food prepared in restaurant Y was stored unrefrigerated, from around three hours after preparation until consumption.

The univariate analyses of food exposures revealed that only the consumption of pork was positively associated with illness. An association with disease risk at a 5% significance level was found for fried pork (RR: 7.8; 95% CI 5.2-11.78; P=0.001) (Table).

TABLE

Food-specific attack rates for S. Enteritidis infections associated with attending a public holiday event, July 2006

Dishes available	Exposure: Yes			Exposure: No			RR	95% CI	P value
	Ill	Total	AR%	Ill	Total	AR%			
Fried pork	48	92	52.2	1	15	6.7	7.8	5.2-11.78	0.001
Rissole	26	65	40	23	42	54.8	0.7	0.44-1.20	0.13
Smoked sausages	28	67	41.8	21	40	52.5	0.8	0.49-1.29	0.28
Mixed salad	33	76	43.4	16	31	51.6	0.8	0.53-1.32	0.44
Cake	23	51	45.1	26	56	46.4	1	0.56-1.69	0.89
Soup I	21	53	39.6	28	54	51.9	0.8	0.44-1.32	0.2
Soup II	0	0	-	0	0	-	-	-	0
Braised cabbage	17	42	40.5	32	65	49.2	0.8	0.44-1.52	0.375
Drink	4	13	30.8	45	94	47.9	0.6	0.20-2.09	0.246
Bread	5	11	45.5	44	96	45.8	1	0.30-3.25	0.981
Beer	13	31	41.9	36	76	47.4	0.9	0.43-1.81	0.609
Pâté	17	51	33.3	32	56	57.1	0.6	0.33-1.04	0.014
Vegetables	13	31	41.9	36	76	47.4	0.9	0.43-1.81	0.608
Coffee	16	38	42.1	33	69	47.8	0.9	0.46-1.68	0.569

Conclusions

The epidemiological investigation revealed that a fried pork dish made with raw egg was the likely cause of the outbreak, and that inadequate preparation and storage of the food contributed to the outbreak's development.

REMOVAL OF TICKS: A REVIEW OF THE LITERATURE

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Eurosurveillance recently reported that travellers who discover ticks attached to them should remove the tick by grasping the mouthpiece with tweezers (forceps) and rotating the tick whilst withdrawing it

[1]. Subsequently, readers and a posting to *ProMED-mail* [2] have pointed out that other guidelines, including those of the World Health Organization [3] and the United States' Centers for Disease Control and Prevention [4] do not advise rotating the tick during removal. Yet these guidelines also differ from one another with respect to whether it is advisable to suffocate ticks with paraffin or equivalent. Reasons behind the differing advice and some basic common points shared by all guidance are discussed below.

Anatomy and physiology of feeding ticks

Ticks are arthropod vectors of a number of pathogens that cause potentially serious human diseases such as Lyme borreliosis, Rocky Mountain spotted fever, tickborne encephalitis, tularaemia and Q fever. A single tick can carry a number of different pathogens [5], leading to atypical presentation of tickborne illness.

Two classes of tick are responsible for disease in humans, hard ticks (family *Ixodidae*) and soft ticks (family *Argasidae*), the principle difference being the hard plate or scutum that hard ticks possess. There is a third class of tick, family *Nutalliellidae*, of which only one species is known, which is not of medical importance [6], Because soft ticks take smaller, quicker blood meals at shorter intervals, they can transmit pathogens much more quickly (within a minute of biting) than hard ticks (hours or days) [6]. However, hard ticks are more common, harder to remove and more likely to transmit disease.

Ticks have a barbed, harpoon-like mouthpiece called a hypostome which they insert into their host to suck blood. Many hard ticks also secrete a cement which further strengthens their attachment. When removing ticks, it is important not to squash the body (which could inject toxins or microbes into the host), break off the mouthpiece or leave cement behind (which could lead to allergic irritation from tick proteins or secondary bacterial infection).

Experimental evidence for tick removal techniques

There is very limited experimental evidence to support most suggested tick removal strategies, and only a few reviews [7,8]. While both mechanical removal and chemical incapacitation have their advocates, experimental evidence suggests that chemical irritants are ineffective at persuading ticks to detach, and risk triggering injection of salivary fluids and possible transmission of disease-causing microbes. In addition, suffocating ticks by smothering them with petroleum jelly is an ineffective method of killing them because they have such a low respiratory rate (only requiring 3-15 breaths per hour) that by the time they die, there may have been sufficient time for pathogens to be transmitted.

One study compared several different techniques for removing ticks [9]. Application of petroleum jelly, fingernail polish, 70% isopropyl alcohol, or a hot kitchen match failed to induce detachment of adult American dog ticks (*Dermacentor variabilis*). Using forceps or grasping with fingers as close to the skin as possible did remove the ticks. Rotating the tick during removal did not appear more likely to damage the mouthparts than pulling straight out, though twisting the tick was ultimately not recommended, because of the risk of breaking of the mouthparts.

Three commercially available devices were compared to conventional forceps for their effectiveness in removing lone star (*Amblyomma americanum* (L.)) or American dog ticks (*D. variabilis*) from laboratory rabbits [10]. It was found that for adult ticks, forceps and a commercial product that grasped the tick were superior to products with a central V-shaped groove that were designed to scoop the tick off. Conversely, removal of nymphs (immature ticks) with forceps tended to leave the mouthparts behind more often than removal with the grooved devices. A variety of other techniques were tested, including fingernail polish, petroleum jelly, a glowing hot match, 70% isopropanol and injection of local anaesthetics (lidocaine, lidocaine with epinephrine, and chloroprocaine). None of these methods initiated self-detachment.

A Spanish study that compared the outcomes of people who removed ticks using forceps and those who used other methods found that people who used forceps were significantly less likely to experience complications, including the skin disease erythema migrans and secondary bacterial infections [11].

A Dutch study compared the ease of removal and retention of mouthparts using several techniques: applying gasoline, 70% isopropyl alcohol or a hot match, pulling clockwise or pulling straight out with quick or steady even pressure using conventional forceps or 'Tick Solution' forceps [12]. Chemical methods failed to cause ticks to detach within half an hour, and pulling the ticks straight out was significantly less likely to lead to retained mouthparts than rotational pulling. An American study compared conventional forceps against 'Tick Solution' forceps and found the conventional forceps to be superior [13].

Nevertheless, at least one company specifically markets a veterinary product that catches the tick in a groove in a plastic device that is then rotated several times. It claims that the rostrum spikes fold into the axis of rotation, facilitating tick removal without the risk of snapping off the hypostome, and provides video evidence of this technique working on the company's website [14].

Other mechanical techniques have been described, with anecdotal levels of evidence. Lassoing the tick as close to the skin as possible, using a loose knot of cotton thread, such as from clothing, then applying gentle traction, can remove ticks when forceps are not available [15]. Disposable razors have also been suggested [16].

Summary

Relatively few studies have been conducted in this area, and those that have been vary with respect to different tick species, different host species and different time periods of tick attachment before removal. When the species of tick is known to be of the soft family, and disease in humans is not endemic in an area, the World Health Organization recommendation of chemical methods of removing ticks may be appropriate [3]. However, since many people, particularly travellers who are not familiar with an area, will not be able to distinguish between different types of tick or know the local prevalence of disease, it seems sensible to recommend always removing ticks by grasping with forceps as close to the skin as possible and pulling straight out to avoid leaving mouthparts behind. There is a clear and simple image that illustrates this at reference 4.

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Outbreak of extended spectrum beta-lactamase producing *E. coli* in a nursing home in Ireland, May 2006

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In May 2006, a consultant microbiologist noted two isolates of extended spectrum beta-lactamase (ESBL)-producing *Escherichia coli* associated with urinary tract infections in a single week in two residents in a nursing home in Ireland. On review, five additional patients with ESBL-producing *E. coli* positive urine cultures were identified from that the same nursing home in the period January to May 2006. The general practitioners (GP) caring for these patients and the regional department of public health were informed, and a multidisciplinary outbreak team meeting was convened. A case was defined as any resident with significant ESBL-producing *E. coli* bacteriuria (> 100 000 CFU/ml) identified in 2006. In 2005, 56 ESBL producing isolates were detected in the region, but only one of these was from this nursing home, and this case had occurred seven months before January 2006, when the primary case in this outbreak had been reported. The nursing home was visited by members of the outbreak team and data on all residents were collected. Information was provided to residents and consent obtained for collection of rectal swabs to determine the prevalence of colonisation.

In Europe, invasive *E. coli* isolates are reported as part of the European Antimicrobial Resistance Surveillance System (EARSS, http://www.rivm.nl/earss/). In Ireland, the proportion of *E. coli* isolates that were tested for presence of ESBL, and tested positive, increased from 1.3% in 2004 (11/861) to 2.7% in 2005 (30/1132 tested) [1,2]. The 2004 EARSS report comments that the proportion of *E. coli* resistant to third generation cephalosporins increased from 1.5% 2001 to 2.9% (P<0.0001) in 2004, probably due to increased dissemination of ESBL producers [3]. The increase was consistent across the countries surveyed by EARSS.

Site visit

The nursing home is purpose-built, with 50 beds in a mix of one and two bed units, communal dining and recreational areas, and shared toilet and bathing facilities. At the time of detection of the outbreak there were 44 residents: 18 men and 26 women, ranging in age between 33 and 105 years, with a median age of 87 years. High dependency levels were noted, and 32 residents had urinary incontinence (14 men and 18 women) and 14 had faecal incontinence. Only one resident had a urinary catheter. Ten residents were confined to bed or chair (3 men and 7 women) and 14 residents were described as confused or had a diagnosis of dementia. Hygiene standards, the ratio of carer to residents and the care practices were considered satisfactory according to the local Nursing Home Inspectorate, which had inspected the home during the month before the start of the outbreak.

To date, no resident has been diagnosed with major systemic infection related to this ESBL-producing *E. coli* outbreak and there have been no associated hospital admissions or mortality.

During the first five months of 2006, 41 of the 44 residents had received antimicrobial therapy, predominantly for respiratory and urinary tract infections, and 14 patients had received five or more courses of antimicrobial agents. Ten patients had been treated with one or more courses of third generation cephalosporins and six had received fluoroquinolones. Ceftriaxone was the third generation cephalosporin most commonly prescribed and was generally prescribed below the recommended dose. Two patients were receiving continuous antimicrobial therapy directed at prevention of urinary tract infection. Five GPs were involved in the care of these residents and no specific antibiotic prescribing protocol was in place.

Laboratory investigation and results

Rectal swabs from 44 patients were obtained and more than 22 environmental swabs collected from toilet seats and rims, door handles, call bells, and laundry within the nursing home. All were screened for ESBL-producing *E. coli* on MacConkey agar with cefotaxime at 2mg/L. Suspect ESBL-producing isolates were confirmed by the combination disk method of the Clinical Laboratory Standards Institute [4].

In total, 24 residents were positive for ESBL-producing *E. coli* (see Table). All environmental swabs were negative. Pulsed field gel electrophoresis (PFGE) was performed (in accordance with the PulseNet protocol [5]) on 26 of the 28 isolates. Banding patterns generated were analysed using bionumerics software (Applied Maths, Kortrijk, Belgium). Twenty isolates from 18 patients had indistinguishable PFGE banding patterns, and five of the remaining isolates were similar to (79% similar) but distinguishable from the predominant isolate. The outbreak strain was also resistant to fluoroquinolones, gentamicin and trimethoprim, but susceptible to nitrofurantoin. Plasmid analysis was performed on representatives of the predominant strain, on each variant of the predominant strain and on the single distinct strain suggested a plasmid of similar size shared by isolates with predominant, variant or distinct PFGE patterns. A blaCTX-M group 9 gene was confirmed by PCR in all 14 isolates that have so far been examined. The outbreak strain differs from the 'strain A' associated with a major community outbreak in the United Kingdom in 2003/2004, both in respect of PFGE pattern and CTX-M group enzyme expressed [6].

Table

Residents of the nursing home with positive culture for extended spectrum beta-lactamase-producing *E. coli*

Sex	Urine culture	Rectal	Both
Male (n= 18)	3	11	2
Female (n= 26)	5	11	4
Total (n = 44)	8*	22	6

* An additional isolate of ESBL-producing *E. coli*-associated with urinary tract infection was identified during the outbreak.

Control measures

Control measures were planned to balance the risk to patients (no mortality and limited morbidity have been reported to date), and their need for continuity in their room assignments and the pattern of their communal life. These measures included education for residents, their families and staff, and improving hygiene and infection control efforts. The outbreak team recommended limiting the use of antimicrobial agents, and in particular the use of third generation cephalosporins and fluoroquinolones. Draft guidance for antimicrobial prescribing has been circulated for discussion. GPs caring for patients have been advised that in the event of life threatening invasive infection, only carbapenem agents are reliably effective against ESBL-producing *E. coli*.

Discussion

Standards of facilities and practice in this nursing home were found to be satisfactory by the Nursing Home Inspectorate and management, and staff were very cooperative with all control

measures recommended. There is no reason to believe this nursing home is uniquely at risk for an outbreak of ESBL-producing *E. coli*. Recognition of this outbreak is a consequence of

- a policy in this nursing home of routine submission of urine for culture before starting antimicrobial therapy;
- routine screening of *E. coli* from urine for ESBL production; and
- under the Infectious Diseases (Amendment) Regulation 2003, unusual clusters of illness are now notifiable in Ireland and this allows for their notification and thus facilitates full investigation [7].

A review of ESBL-producing *E. coli* isolates from the regional laboratory has identified 19 other nursing homes (out of the approximately 90 nursing homes in the region) where one or more patients was found to have ESBL-producing *E. coli* in the first half of 2006. It is quite possible that ESBL-producing *E. coli* has also disseminated in similar facilities

Conclusions

This report highlights the potential for transmission of ESBL-producing *E. coli* and other antimicrobial resistant bacteria in nursing homes. A dependent and vulnerable group of residents live in close proximity in a setting where strict source isolation is frequently not practical with respect to the overall needs of the residents. Residents of nursing homes are prone to both respiratory and urinary tract infections, and so antimicrobial use may be high. Residents frequently come to these facilities directly from hospitals, and this poses a continuing risk for introduction of antimicrobial resistant bacteria into the facilities. The increasing population of dependent and vulnerable residents of long stay facilities across Europe presents an increasing potential for dissemination, maintenance and amplification of antimicrobial resistant pathogens and other infectious diseases, and deserves a high priority in strategies to control spread of infection.

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24 August 2006

Typing of Legionella isolates during an epidemiological investigation can be helpful but also misleading: an example from Greece
24 August 2006

Reducing the risks of transmitting gastrointestinal infections in home paddling pools
31 August 2006

Four outbreaks of norovirus gastroenteritis after consuming raspberries, Sweden, June-August 2006
7 September 2006

Evidence that mild or asymptomatic human H5N1 infections have not occurred in a Cambodian village with poultry infections
7 September 2006

Ostreopsis ovata algal blooms affecting human health in Genova, Italy, 2005 and 2006
7 September 2006

Universal childhood immunisation with pneumococcal vaccine and meningococcal serogroup C vaccine introduced in Germany
7 September 2006

Tuberculosis outbreak linked to pubs in South Wales
7 September 2006

Epidemiological surveillance implemented in southeast France during the 2006 Olympic Winter Games
7 September 2006

Emergence of Clostridium difficile toxinotype III, PCR-ribotype 027-associated disease, France, 2006
14 September 2006

Epidemiology of Clostridium difficile toxinotype III, PCR-ribotype 027 associated disease in Belgium, 2006
14 September 2006

First isolation of Clostridium difficile PCR ribotype 027 in Austria
14 September 2006

Enteroviral meningitis outbreak, Kosovo, July-September 2006
14 September 2006

Human trichinellosis acquired from wild boar meat: a continuing parasitic risk in France
14 September 2006

Large tularaemia outbreak in Värmland, central Sweden, 2006
21 September 2006

Outbreak of legionellosis associated with a spa pool, United Kingdom
21 September 2006

Human H5N1 vaccines – WHO produces guidance on virus composition
21 September 2006

Outbreak of community-acquired legionnaire's disease, July-September 2006, Paris, France
28 September 2006

Extensive drug-resistant TB: a threat for Europe?
28 September 2006

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National Bulletins

Austria

Mitteilungen der Sanitätsverwaltung
Bundesministerium für Gesundheit und Frauen
Stabsstelle I/A/4
Radetzkystrasse 2
A-1031 Wien
Monthly, print only. In German.
Ministry Website: http://www.bmgf.gv.at

Belgium

Vlaams Infectieziektebulletin
Gezondheidsinspectie Antwerpen
Copernicuslaan 1, bus 5
2018 Antwerpen
Quarterly, print and online versions available. In Dutch.
http://www.vlaanderen.be/epibul/

Infectious Diseases in the Spotlights
Institut Scientifique de la santé Publique Louis Pasteur
14, rue Juliette Wytsman
B-1050 Bruxelles
Weekly, online only. In English.
http://www.iph.fgov.be/epidemio/epien/plaben/idnews/index_en.htm

Bulgaria

Epidemiological Surveillance
National Centre of Infectious and Parasitic Diseases
26 Yanko Sakazov blvd.
Sofia 1504
Print version available, online version available soon. In Bulgarian, titles translated into English.
http://www.ncipd.org/bulletin.php

Cyprus

Newsletter of the Network for Surveillance and Control of Communicable Diseases in Cyprus
Medical and Public Health Services
Ministry of Health
Markou Drakou 10
1449 Nicosia
Biannual, print and online versions available. In Greek.

Czech Republic

Zpravy CEM
(Monthly Bulletin of Centre Epidemiology and Microbiology)
Centrum epidemiologie a mikrobiologie Státního zdravotního ústavu (Centre of Epidemiology and Microbiology, National Institute of Public Health)
Srobarova 48
100 42 Praha 10
Monthly, print and online versions available, in Czech with some important notifications in English.
http://www.szu.cz/cema/adefaultt.htm

EPIDAT
Notifications of infectious diseases in the Czech Republic
http://www.szu.cz/cema/epidat/epidat.htm

Denmark

EPI-NEWS
Department of Epidemiology
Statens Serum Institut
Artillerivej 5
DK-2300 København S
Weekly, print and online versions available. In Danish and English.
http://www.ssi.dk

England and Wales

Communicable Disease Report Weekly (CDR)
Health Protection Agency
61 Colindale Avenue
London NW9 5EQ
Weekly, online only. In English.
http://www.hpa.org.uk/cdr

Finland

Kansanterveys
Department of Infectious Disease Epidemiology
National Public Health Institute
Mannerheimintie 166
00300 Helsinki
Monthly, print and online versions available. In Finnish.
http://www.ktl.fi/portal/suomi/julkaisut/kansanterveyslehti/

France

Bulletin epidémiologique hebdomadaire
Institut de veille sanitaire
12, rue du Val d'Osne
94415 Saint-Maurice Cedex
Weekly, print and online versions available. In French.
http://www.invs.sante.fr/beh/default.htm

Germany

Epidemiologisches Bulletin
Robert Koch-Institut
Presse, Oeffentlichkeitsarbeit, Bibliotheken
Nordufer 20
D-13353 Berlin
Weekly, print and online versions available. In German.
http://www.rki.de/DE/Content/Infekt/EpidBull/epid__bull__node.html

Hungary

Epinfo (Epidemiológiai Információs Hetilap)
National Center For Epidemiology
Gyali ut 2-6
1097 Budapest
Weekly, online version available. In Hungarian.
http://www.antsz.hu/oek/epinfo/szoveg/Heti2004/hetiindit04.htm

Ireland

EPI-INSIGHT
Health Protection Surveillance Centre (HPSC)
25-27 Middle Gardiner Street
Dublin 1
Monthly, print and online versions available. In English.
http://www.ndsc.ie/EPI-Insight/

Italy

Notiziario dell'Istituto Superiore di Sanità
Istituto Superiore di Sanità
Reparto di Malattie Infettive
Viale Regina Elena 299
I-00161 Roma
Monthly, online only. In Italian and English.
http://www.iss.it/publ/serie.php?id=4

Bolletino Epidemiologico Nazionale (BEN)
Istituto Superiore di Sanità
Reparto di Malattie Infettive
Viale Regina Elena 299
I-00161 Roma
Monthly, online only. In Italian and English.
http://www.epicentro.iss.it/ben/

Latvia

Epidemiologijas Bileteni
State Public Health Agency
7 Klijanu Street
1012 Riga
Online. In Latvian.
http://www.sva.lv/epidemiologija/bileteni/

Netherlands

Infectieziekten Bulletin
Rijksinstituut voor Volksgezondheid en Milieu
PO Box 1
NL-3720 Bilthoven
Monthly, print and online versions available. In Dutch, some summaries in English.
http://www.rivm.nl/infectieziektenbulletin/

Northern Ireland

Communicable Disease Monthly Report
Communicable Disease Surveillance Centre (Northern Ireland)
McBrien Building, Belfast City Hospital,
Lisburn Road
Belfast BT9 7AB
Monthly, print and online versions available. In English.
http://www.cdscni.org.uk/publications/

Norway

MSIS-rapport
Folkehelseinstituttet
Postboks 4404 Nydalen
N-0403 Oslo
Weekly, print and online versions available. In Norwegian.
http://www.folkehelsa.no/nyhetsbrev/msis/

Poland

Reports on cases of infectious disease and poisonings in Poland
Instytut Naukowo-Badawczy (National Institute of Hygiene)
ul. Chocimska 24
00-791 Warsawa
Fortnightly. In Polish and English.

Portugal

Saúde em Números
Direcção-Geral da Saúde
Alameda D. Afonso Henriques 45
1049-005 Lisboa
Sporadic, print only. In Portuguese.
Ministry website: http://www.dgsaude.pt/

Romania

Info Epidemiologia
Bulletin of the National Center for Surveillance and Control of Communicable Diseases, Institute of Public Health of Bucharest
1-3 Dr Leonte Street (Strada Dr.Leonte 1-3)
Sector 5 Bucharest Romania
Sporadic, print only.

Scotland

Health Protection Scotland Weekly Report
Health Protection Scotland
Clifton House, Clifton Place
Glasgow, G3 7LN
Scotland
Weekly, print and online versions available. In English.
http://www.show.scot.nhs.uk/scieh/wrhome.html

Slovenia

CNB Novice
Institut za varovanje zdravja Republike Slovenije
Center za nalezljive bolezni
Trubarjeva 2
Ljubljana
Monthly, online only. In Slovene.
http://www.ivz.si/ivz/aktualno/

Spain

Boletín Epidemiológico Semanal
Centro Nacional de Epidemiología - Instituto de Salud Carlos III
C/ Sinesio Delgado 6 - 28029 Madrid
Bi-weekly, print and online versions available. In Spanish.
http://193.146.50.130/htdocs/bes/bes.htm

Sweden

EPI-aktuellt
Smittskyddsinstitutet
171 82 Solna
Weekly, online only. In Swedish.
http://www.smittskyddsinstitutet.se/SMItemplates/Article____2414.aspx

Smittskydd
Smittskyddsinstitutet
171 82 Solna
Monthly, print only. In Swedish.

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